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The Safety of Therapeutic Doses of Vitamin E in Man

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Summary

Vitamin E is a natural antioxidant that is used in miscellaneous diseases in doses far exceeding the daily requirement. The use of a fat-soluble vitamin in such large doses raises a question about its potential hazards. In fact, various clinical and laboratory disorders have been ascribed to "megadoses" of vitamin E. Although in more recent studies vitamin E has been regarded to be generally innocuous, caution has been recommended for the use of large doses. In this study vitamin E administered in a daily dose of 1000 mg for 28 days did not exert any adverse clinical effects, and routine laboratory tests were within normal ranges after treatment. However, a slight but significant decrease was observed in serum albumin concentration ($p < 0.05$). Serum uric acid was also significantly reduced ($p < 0.005$). The clinical importance of these findings requires further investigation.

Key Words: Vitamin E, Blood chemistry, Hematologic parameters, Blood pressure, Body weight.

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Introduction

Vitamin E, a natural antioxidant, is used in miscellaneous diseases and in many countries can be obtained without prescription. It is so widely used that Americans spent \$ 212 million on vitamin E preparations in 1983.¹ The daily doses ranging from 200 to 2000 mg (IU)² far exceed the daily requirement of 10 to 30 mg.³ While the beneficial effects of vitamin E and the rationale for its use are open to discussion, the potential hazards of using a fat-soluble vitamin in large doses need to be considered. In fact, a daily intake of vitamin E in excess of 100 to 300 mg has been regarded as a "megadose" and has been suggested to result in various clinical and laboratory disorders.^{4, 5, 6} In a more recent review daily doses of 200 to 600 mg were considered to be safe in most people; however, it was noted that experience with larger doses was limited.²

In this study the possible adverse effects of vitamin E administered in a daily dose of 1000 mg for 28 days were sought. Vitamin E was given to evaluate its effects in relevance to atherosclerosis. The results pertaining to this subject are going to be reported in another article. Here, the effects of vitamin E on clinical and routine laboratory findings are presented.

Materials and Methods

Thirty-five patients (17 men, 18 women) with atherosclerotic heart disease and/or hyperlipidemia from the outpatient clinic were studied. Their ages ranged from 34 to 71 years, with an average of 56 years. Eleven patients had type II diabetes mellitus. None was taking supplemental vitamin E. All the patients were informed about the nature of the study, and they consented to participate.

On the first day of the study after an 12-hour overnight fasting, blood samples were obtained for measuring plasma α -tocopherol and serum concentrations of glucose, blood urea nitrogen, creatinine, uric acid, sodium, potassium, chloride, GOT, GPT, LDH, albumin, globulin, and total bilirubin. Hematocrit and hemoglobin values, leucocyte and platelet counts, and plasma prothrombin activity were also determined. Systolic and diastolic blood pressure and body weight were measured. On the same day vitamin E supplied as 500 mg dl- α -tocopheryl acetate (Rhone-Poulenc, France) in soft gelatin capsules was started. The patients were instructed to take one capsule twice daily after meals. Patient compliance was checked by capsule counts and plasma α -tocopherol concentrations measured on the fourth, fifteenth, and twenty-ninth days. The patients' diets and the drugs they had been taking were not changed

throughout the study period. On the twenty-ninth day the laboratory analyses performed on the first day were repeated; blood pressure and body weight were checked.

Plasma α -tocopherol was assayed by reversed-phase high-performance liquid chromatography.⁷ Blood chemistries were done with an autoanalyzer (Techicon RA 1000); only serum bilirubin was measured manually. Platelets were counted by phase-contrast microscopy. Plasma prothrombin activity was determined with calcim thromboplastin from Stago.

Data are expressed as mean \pm S.D. Differences were analyzed for statistical significance by paired t-test. P values less than 0.05 were considered to be significant.

Results

Vitamin E treatment was well tolerated by all the patients. No side-effects were observed. The body weight and systolic and diastolic blood pressure were not affected (Table I).

TABLE I
VALUES OF BODY WEIGHT AND SYSTOLIC AND DIASTOLIC BLOOD PRESSURE BEFORE AND AFTER VITAMIN E TREATMENT

| | Before vit. E | After vit. E |
|----------------------------------|--------------------|--------------------|
| Body weight (kg) | 72.96 \pm 11.24 | 72.94 \pm 11.85 |
| Systolic blood pressure (mm Hg) | 148.13 \pm 21.13 | 148.28 \pm 25.89 |
| Diastolic blood pressure (mm Hg) | 93.44 \pm 12.34 | 93.75 \pm 13.74 |

Mean plasma α -tocopherol concentration doubled up on the fourth day and reached a plateau on the fifteenth day. The difference between the values measured on the first and twenty-ninth days was highly significant ($p < 0.0005$) (Table II).

TABLE II
CONCENTRATIONS OF PLASMA α -TOCOPHEROL ($\mu\text{g/ml}$)

| 1st day | 4th day | 15th day | 29th day |
|------------------|------------------|-------------------|--------------------|
| 21.29 \pm 5.75 | 42.88 \pm 13.1 | 48.25 \pm 18.47 | 48.44 \pm 12.89* |

* $p < 0.0005$ for difference from the value on the 1st day

Serum uric acid concentration which was within normal ranges initially decreased significantly after vitamin E treatment ($p < 0.005$). A significant decrease also occurred in serum albumin concentration ($p < 0.05$); however, the posttreatment values were within normal

limits. The slight increase in serum sodium concentration was not statistically significant ($p > 0.05$) (Table III). Other biochemical and hematologic parameters were not affected from vitamin E treatment (Tables III and IV).

TABLE III
BIOCHEMICAL FINDINGS BEFORE AND AFTER VITAMIN E

| | Before vit. E | After vit. E |
|-----------------------------------|-----------------|-----------------|
| Glucose (mg/dl) (in diabetics) | 177.55 ± 69.25 | 152.27 ± 30.18* |
| Glucose (mg/dl) (in nondiabetics) | 99.04 ± 11.56 | 94.52 ± 9.72* |
| BUN (mg/dl) | 15.61 ± 5.06 | 14.88 ± 5.67 |
| Creatinine (mg/dl) | 0.99 ± 0.24 | 0.97 ± 0.31 |
| Uric acid (mg/dl) | 5.35 ± 1.85 | 4.66 ± 1.51** |
| Sodium (mEq/l) | 143.58 ± 5.23 | 145 ± 5.53* |
| Potassium (mEq/l) | 4.61 ± 0.49 | 4.68 ± 0.47 |
| Chloride (mEq/l) | 110.04 ± 6.58 | 109.71 ± 5.59 |
| SGOT (units) | 18.65 ± 11.63 | 16.62 ± 8.19 |
| SGPT (units) | 20.32 ± 9.33 | 18.71 ± 9.15 |
| LDH (IU) | 236.69 ± 137.11 | 223.48 ± 78.39 |
| Albumin (gm/l) | 4.58 ± 0.58 | 4.47 ± 0.47*** |
| Globulin (gm/l) | 3.19 ± 0.69 | 3.21 ± 0.71 |
| Bilirubin (mg/dl) | 0.48 ± 0.22 | 0.55 ± 0.19 |

* $p > 0.05$, ** $p < 0.005$, *** $p < 0.05$

TABLE IV
HEMATOCRIT AND HEMOGLOBIN VALUES, LEUCOCYTE AND PLATELET COUNTS, AND PLASMA PROTHROMBIN ACTIVITY BEFORE AND AFTER VITAMIN E TREATMENT

| | Before vit. E | After vit. E |
|-------------------------------------|----------------------|----------------------|
| Hematocrit (%) | 41.07 ± 3.86 | 40.68 ± 5.02 |
| Hemoglobin (gm/dl) | 13.21 ± 1.16 | 12.96 ± 1.61 |
| Leucocyte (counts/mm ³) | 6039.29 ± 1077.49 | 6032.14 ± 1082.88 |
| Platelet (counts/mm ³) | 207185.19 ± 38210.99 | 214444.44 ± 40793.41 |
| Prothrombin activity (%) | 95.29 ± 7.58 | 95.09 ± 7.78 |

Discussion

Vitamin E in large doses has been accused of resulting in various clinical disorders including severe fatigue, muscle weakness, and gastrointestinal disturbances.^{4, 5, 6} On the other hand, in a placebo-controlled study vitamin E administered in daily doses of 600 IU to a large group of healthy volunteers was reported not to have a significant undesirable effect on general health conditions.⁸ In a more recent review adverse symptoms ascribed to large doses of vitamin E were suggested to be subjective and based on limited observations, and transient gastro-

intestinal disturbances (nausea, flatulence, or diarrhea) were reported to be the most commonly encountered complaint.² Our patients experienced no adverse symptoms. On the contrary, most of them had a sense of well-being and wanted to go on taking the drug when the study was completed. The sense of well-being in patients using vitamin E has also been noted in a previous study.⁹ Although vitamin E has been reported to cause hypertension,⁶ in our study systolic and diastolic blood-pressure was not affected.

Both hypoglycemia and aggravation of diabetes mellitus have been reported to result from vitamin E supplementation.⁶ In our nondiabetic patients serum glucose concentrations showed a tendency to decrease with vitamin E treatment, but the difference was not statistically significant, and none of our patients had hypoglycemia. On the other hand, vitamin E did not elevate serum glucose concentrations of our diabetic patients. Contrarily, in these patients also, serum glucose concentrations had a tendency to decrease; but again the difference did not reach the limit of significance.

Of the other biochemical parameters serum uric acid and albumin concentrations were affected significantly. Although the values were within normal ranges before and after vitamin E treatment, the decreases were statistically significant. In a study carried out in a large ambulatory elderly population in those using vitamin E, serum uric acid and total protein in women and serum chloride in men were lower and SGOT in men was higher in comparison to non-users. The differences were statistically significant; however, when adjustments for sex and age were made, only SGOT in men using vitamin E, although within normal ranges, was found to be significantly higher than in non-users.¹ In our study biochemical parameters other than serum uric acid and albumin were not affected significantly.

As for the hematologic parameters, hematocrit and hemoglobin values and leucocyte and platelet counts were not altered by vitamin E treatment. Also in other studies, erythrocyte count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, and leucocyte count were reported not to be affected from vitamin E supplementation in elderly people and healthy volunteers.^{1, 8}

It has been reported that vitamin E may prolong prothrombin time and cause hemorrhage by interfering with vitamin K-dependent coagulation factors in patients receiving oral anticoagulants, especially when they are administered in large doses and with another potentiator of oral anticoagulants and also in those with vitamin K deficiency.^{10, 11}

However, in healthy volunteers receiving vitamin E 600 IU daily prothrombin time has been found not to be different from those receiving placebo.⁸ Also in our patients, prothrombin activity was not affected from vitamin E treatment.

Conclusively, vitamin E in a daily dose of 1000 mg was found to be free of adverse effects on clinical findings and routine laboratory tests except on serum albumin. The clinical significance of this finding and the probably beneficial effect on serum uric acid concentration in hyperuricemic patients need to be investigated.

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Value of Endometrial Sampling in Evaluation and Treatment of Dysfunctional Uterine Bleeding

Tekin Durukan, M.D.* / Bülent Urman, M.D. /
Emek Özen, M.D.*****

Summary

248 patients with presumed dysfunctional uterine bleeding (DUB) were subjected to routine endometrial sampling using a Karman canula and a sharp curette to assess the endometrial changes and direct the therapy. Proliferative and secretory endometrium was reported in 21,4 % and 16,5 % of the specimens respectively. Endometrial hyperplasia of varying severity was present in 20,9 % of the patients. Mixed endometrium, endometritis, decidual reaction and iatrogenic changes were reported to a lesser extent. 16,1 % of the specimens were inadequate for histologic diagnosis. Pregnancy was reported in 2,6 % of the patients even in the presence of meticulous effort to rule out this entity. Endometrial sampling is a very useful method to evaluate DUB and to select a rational approach for treatment.

Key Words: Dysfunctional uterine bleeding, endometrial sampling.

Introduction

Dysfunctional uterine bleeding (DUB) is defined as bleeding of endometrial origin in the lack of evident organic disease. It is manifested as episodic, excessive bleeding of varying frequency.¹ Diagnosis requires the exclusion of local and systemic disease and endometrial sampling is

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essential for instituting correct treatment schemes. The purpose of this study was to evaluate the histologic patterns of the endometrium in 248 patients with presumed DUB.

Material and Methods

The study was undertaken on 248 women presenting with presumed DUB to the University of Hacettepe Faculty of Medicine Department of Obstetrics and Gynecology between the years 1982-1987. All the data were obtained from the patient files and the pathology reports. The mean age of the patients were $41,4 \pm 5,7$ years with a range of 31-55 years. None of the patients were postmenopausal with cessation of the menses for more than 12 months. A detailed history with special emphasis to menstrual history was taken and a physical examination was performed on all patients. Only patients with a negative pelvic examination were included in the study. Hormone levels and B-hCG were determined when indicated. A complete endometrial sampling was performed using a Karman canula and a sharp currete on all patients.

Results

Endometrial biopsy patterns in 248 presumed cases of DUB are shown in Table I. Proliferative and secretory endometrium was reported on 21,4 % and 16,5 % of the biopsy specimens respectively. 20,9 % of the specimens were reported as endometrial hyperplasia of varying severity (Table II). 3,6 % were reported as mixed endometrium and 3,6 % as decidual reaction. Endometritis was seen in 6,4 % of the specimens accompanied by secretory changes. Iatrogenic influence was reported on 8,8 % of the patients and even with meticulous efforts to eliminate pregnancy, chorion villi with pregnancy complications was seen in 2,6 % of the specimens.

TABLE I
RESULTS OF ENDOMETRIAL SAMPLING IN 248 PATIENTS WITH DUB

| Histopathologic diagnosis | No. of Patients | % |
|-----------------------------------|-----------------|-------|
| Proliferative endometrium | 53 | 21,4 |
| Secretory endometrium | 41 | 16,5 |
| Endometrial hyperplasia | 52 | 20,9 |
| Mixed endometrium | 9 | 3,6 |
| Endometritis | 16 | 6,4 |
| Decidual reaction | 9 | 3,6 |
| Iatrogenic changes | 22 | 8,9 |
| Inadequate material for diagnosis | 40 | 16,1 |
| Pregnancy | 6 | 2,6 |
| Total | 248 | 100,0 |

TABLE II
HISTOLOGIC SUBTYPES OF ENDOMETRIAL HYPERPLASIA IN 52 PATIENTS

| Histologic type | No. of Patients | % |
|--------------------------------|-----------------|-------|
| Simple endometrial hyperplasia | 16 | 31,0 |
| Cystic hyperplasia | 20 | 38,4 |
| Adenomatous hyperplasia | 4 | 7,7 |
| Focal hyperplasia | 11 | 21,0 |
| Stromal hyperplasia | 1 | 1,9 |
| Total | 52 | 100,0 |

Four of the 52 patients demonstrating hyperplasia had the adenomatous form (7,6 %) and hysterectomy was performed on all. Other patients with endometrial hyperplasia recieved either progesterone or cyclic hormonal therapy in the for of birth control pills, with a control curetage 6 months later.

Patients with mixed endometrial findings had their menstruel pattern revert to normal after curetage. Antibiotics in the form of tetracycline together with progestetional agents were prescribed to patients with endometritis. Other patients recieved cyclic progesterone therapy in the form of medroxyprogesterone acetate.

Discussion

DUB in the reproductive and perimenapousal age group can be a distressing symptom for the patient and puzzling for the physician. After appropriate and basic steps are taken, routine endometrial sampling can be a very useful guide in planning therapy. Endometrial hyperplasia with it's more severe forms and even endometrial cancer can only be ruled out efficiently by routine sampling of the endometrium. In the adolescent girl it would be unusual to find an organic disease of the reproductive tract, but organic disease is not unusual in the sexually mature women or the women approaching menapouse. Anovulation and chronic unopposed estrogen stimulation of the endometrium is a common finding in this age group.^{2,3}

Once an organic cause for the bleeding has been eliminated a regimen of medical therapy directed at supressing chronic estrogen stimulation is instituted.⁴ This is usually in the form of progesterone. It should be noted that in our series the rate of anovulatory DUB was 21,4 %. DUB can be ovulatory as in postpartum states, persistant corpus luteum, mixed endometrium and intermenstruel spotting due to a decline of hormone levels in the midcycle.⁵ Endometritis can also present as DUB.

Therapy should be directed to the underlying cause in these patients. In patients with bleeding of long duration, excessive sloughing of the endometrium can result in inadequate tissue for pathologic interpretation. This was the case in 16,1 % of our patients.

In summary endometrial sampling in presumed patients with DUB will direct the physician to rational diagnosis with resultant therapeutic approaches and success.

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Histopathological Findings in Women with Postmenopausal Uterine Bleeding

A Review of 250 Cases

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Kunter Yüce, M.D.*** / Ayşe Ayhan, M.D.**** /
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Summary

250 patients with postmenopausal bleeding (PMB) were histopathologically evaluated. Of these patients, 38 (15 %) had cervical pathology, 91 (36 %) had organic uterine lesions and 121 (48 %) had non-organic uterine pathology. Cervical invasive cancer, endometrial cancer, endometrial hyperplasia and atrophic endometrium were found to be 5 %, 11 %, 20 %, and 32 %, respectively. The diagnostic role of hysteroscopy in patients who had inadequate tissue on dilatation and curettage (D+C) was observed and stressed.

Key Words: Postmenopausal bleeding, Endometrium, Histopathology, Cervix.

Introduction

Postmenopausal bleeding (PMB) is serious and an alarming sign associated with uterine malignancy. The causes of PMB include endometrial cancer, endometrial hyperplasia, polyps, atrophic, proliferative,

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secretory and mixed endometrium.¹⁻⁵ In recent publications, it has been shown that the incidence of endometrial cancer varied from 1.5 % to 17.9 % in patients with PMB.^{4, 6, 7} The most common diagnostic method employed is fractional curettage in these patients.^{8, 9} The hysteroscopic evaluation and biopsy appear to be an ideal diagnostic tool in patients who have recurrent bleeding episodes and fail to show any pathology on fractional curettage.¹⁰

The purpose of this study is to evaluate the histopathological findings in women with PMB.

Materials and Method

During a period of 5 years (1983-1988) 250 patients with documented PMB were subjected to fractional dilatation and curettage (Fr D+C) under general anesthesia. Data were obtained from patient files, follow-up forms and pathology reports. PMB was defined as vaginal bleeding of menses. All of the specimens were evaluated in the Pathology department by a co-author pathologist.

Pathologic findings were divided into three groups these were cervical pathology, organic endometrial lesions (endometrial carcinoma, polyps and endometrial hyperplasia) and non-organic endometrial lesions (atrophic, proliferative, secretory and mixed endometrium). 16 patients were reported to have inadequate tissue for diagnosis and these patients were subjected to hysteroscopic evaluation and biopsy. The statistical analysis of the results were made by using the students t test and Fisher's exact test.

Results

The causes of PMB were cervical pathology in 38 patients (15.2 %), organic uterine pathology in 91 patients (36.4 %) and non-organic uterine pathology in 121 patients (48.4 %) (Table I).

Of the 38 patients with cervical pathology 24 (63 %) had cervical polyps, 13 (34 %) had invasive cervical cancer, 1 (3 %) had cervical myoma.

The histopathological findings in patients with organic uterine lesions revealed 28 patients (30.8 %) with endometrial cancer, 2 patients (2.2 %) with uterine sarcoma, 10 patients (11 %) with endometrial polyps and 51 patients (56 %) with endometrial hyperplasia. Despite normal adnexial findings on pelvic examination 1 patient with endometrial cancer and 2 patients with endometrial hyperplasia showed granulosa cell tumors upon microscopic examination of their hysterectomy specimens.

TABLE I
HISTOPATHOLOGICAL FINDINGS IN 250 PATIENTS WITH PMB

| Histopathological findings | No. of patients | | % | |
|---------------------------------|-----------------|-----|------|------|
| CERVICAL PATHOLOGY | 38 | | 15.2 | |
| Cervical polyp | | 24 | | 9.6 |
| Cervical cancer | | 13 | | 5.2 |
| Cervical myoma | | 1 | | 0.4 |
| ORGANIC UTERINE PATHOLOGY | 91 | | 36.4 | |
| Endometrial cancer | | 28 | | 11.2 |
| Uterine sarcoma | | 2 | | 0.8 |
| Endometrial polyp | | 10 | | 4.0 |
| Endometrial hyperplasia | | 51 | | 20.4 |
| NONORGANIC UTERINE PATHOLOGY | 121 | | 48.4 | |
| Atrophic endometrium | | 80 | | 32.0 |
| Proliferative endometrium | | 15 | | 6.0 |
| Secretory endometrium | | 5 | | 2.0 |
| Iatrogenic endometrium | | 5 | | 2.0 |
| Inadequate tissue for diagnosis | | 16 | | 6.4 |
| Total | 250 | 250 | 100 | 100 |

Of the 121 patients with non-organic lesions, 80 patients (66.1 %) had atrophic endometrium. The other findings were distributed among proliferative, secretory, iatrogenic and inadequate endometrium. 4 patients had also CIN associated with atrophic endometrium. 16 patients were subjected to hysteroscopy and an endometrial cancer was detected in one. The incidence of missing malignant lesions with fractional curettage in these series was 1/250, hence 0.4 %.

Of the 28 patients with endometrial cancer, 20 (71.4 %) were adenocarcinoma. The other patients had either adenoacanthoma, papillary adenocarcinoma, adenosquamous carcinoma or mucinous adenocarcinoma.

51 patients were reported to have endometrial hyperplasia. Focal hyperplasia was seen in 9.8 %, cystic hyperplasia in 68.6 %, polypoid hyperplasia in 13.7 %, adenomatous hyperplasia in 3.9 % and atypical adenomatous hyperplasia in 3.9 % of the patients.

Other variables effecting the incidence of endometrial neoplasia such obesity, diabetes, hypertension and estrogen replacement therapy was also assessed in patients with endometrial cancer, endometrial hyperplasia and the rest of the patients, but statistical difference was not found utilizing the Fisher's exact test (Table II).

TABLE II
SOME VARIABLES IN PATIENTS WITH PMB

| | Endomet. Ca. | Hyperplasia | Others | Total |
|---------------------------------------|--------------|-------------|------------|------------|
| Mean age ¹ | 58.9 ± 1.0 | 52.5 ± 0.7 | 54.4 ± 0.5 | 54.8 ± 0.4 |
| Duration of ² menopause | 11.0 ± 1.1 | 5.4 ± 0.8 | 7.1 ± 0.6 | 7.4 ± 0.5 |
| ERT* | - | 2 | 7 | 9 |
| Obesity | 4 | 7 | 21 | 32 |
| Diabetes | 2 | 2 | 7 | 11 |
| Hypertension | 4 | 5 | 20 | 29 |
| Concomittant gyn. pathology | 4** | 20*** | 19**** | 43 |

* Estrogen replacement therapy

** One patient had a granulosa cell tumor of the ovary

*** Two patients had granulosa cell tumors of the ovary

**** Four patients had CIN

1 The difference in the mean age regarding the three groups were significant ($p < 0.05$)

2 The duration of menopause was significantly different ($p < 0.05$) between the cancer group and the other two groups

Discussion

There is no screening method for asymptomatic endometrial cancer as effective as the one developed for cervical cancer.¹¹ All patients with PMB require further investigation to exclude malignancy of the uterus. In addition to this, the gynecologist should also be aware of non-uterine causes of PMB which include cervical pathologies, atrophic vaginitis, vulvitis and rarely tubal or ovarian malignancies.

Recently it has been shown that the incidence of endometrial cancer in patients with PMB ranged between 15-17.9 %.^{7, 12, 13} In the present study the incidence of uterine malignancy was found to be 11.2 %.

The incidence of hyperplastic endometrium is reported to be 15-45 %.^{3, 7, 14, 15} This figure in our study was 20.4 %. The lower incidence may be ascribed to the lower incidence of women receiving estrogen replacement therapy.

Cervical cancer is reported to cause 1-53 % of all cases of PMB.^{4, 13, 16} In this study the incidence of cervical cancer and cervical intraepithelial neoplasia (CIN) was 5.2 % and 1.6 % respectively.

Atrophic endometrium has been reported to be a frequent cause of PMB.^{1, 2} Its incidence varies from 16 to 82 % in some studies.^{10, 14} The incidence of atrophic endometrium, in our study, was 32 %. It has been reported that there was a relation between PMB in atrophic en-

ometrium and chronic endometritis, sclerotic degeneration of the endometrial vessels, passive congestion due to uterine prolapse, rupture of endometrial cysts or blockage of venules due to overdistended glands.^{17, 18, 19} In the present study chronic endometritis and sclerotic vessels with atrophic endometrium were found to be 7.5 % and 27.5 % respectively.

In one study, endometrial polyps, proliferative endometrium and cervical polyps were found to be responsible for 8 %, 14 %, and 10 % of the cases of PMB respectively.¹⁴ These figures in our study were 4 %, 6 %, and 9.6 % respectively.

In one of the 16 patients who had inadequate tissue for diagnosis on Fr D+C, endometrial adenocarcinoma was found via hysteroscopic evaluation.

All patients with PMB warrant a histologic evaluation. Malignancy should be definitely ruled out. In patients with inadequate tissue on Fr D+C, hysteroscopy should be performed to detect any lesion in the endometrium.

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Cytologic and Colpohistologic Correlation of Cervical Intraepithelial Neoplasia*

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Summary

480 patients with Class I-IV Papanicolaou (PAP) smears were subjected to colpo-histologic evaluation. 142 patients with Class I pap smears had clinical erosion and/or ectropion of the cervix. Incidence of cervical intraepithelial neoplasia (CIN) was 19 %, 56 %, 65 %, and 100 % for Class I, II, III and IV pap smears respectively. It is concluded that if colposcopy was applied to patients with abnormal cervix and Class I pap smear, and to patients with Class II pap smear without atypia, recognition of more CIN would be possible.

Key Words: Histology, Colposcopy, Cervical Intraepithelial Neoplasia.

Introduction

The Pap smear is a standart screening method for invasive and preinvasive cancer of the cervix. Colposcopy established itself for clinical evaluation of patients with abnormal pap smear by recognizing the abnormal region in the cervix and/or vagina for further histologic

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study.^{1, 2, 3} Diagnostic accuracy is at least equivalent to cervical conization when the transformation zone is entirely seen and the procedure is without serious complications.

In this study, cervical cytological and colposhisticological correlations were discussed in all levels of pap smears excluding Class V smears and/or invasive conditions.

Material and Methods

In State University of New York at Buffalo (SUNYAB) affiliated hospitals, pap smear and histologic analysis of 480 patients with cervical intraepithelial neoplasia (CIN) were available between the years 1977 and 1980. For communication purposes, only patients whose smears were read according to the Papanicolaou classification were included into the study. Patients with Class V smears and/or invasive carcinoma were excluded. Patients with cervical erosion and normal pap smear, and all patients with Class II and above pap smears were colposcopically evaluated. In patients with Class II pap smears, co-existing candida, trichomonas and other infections, if present, were treated prior to colposcopic evaluation. Colposcopic examinations were performed by experienced colposcopists. 3 % acetic acid was used to verify the white epithelium. Atypical vessels, mosaicism, punctation and white epithelium were recognized as abnormal transformation zone, as recommended by the Terminology Committee of the International Federation of Cervical Pathology and Colposcopy.

Results

Of the 480 patients, 47,7 % had cervical intraepithelial neoplasia. Of 142 patients with clinical erosion and/or ectropion type cervical lesion and Class I pap smear, 19 % had -CIN. CIN was found in 56 % of patients with Class II pap smears without atypia and the incidence rose to 65 % and 100 % for Class III and IV pap smears respectively (Table I).

TABLE I
CORRELATION OF CYTOLOGIC AND HISTOLOGIC FINDINGS

| Cytology* | CIN** | PATHOLOGIC RESULTS | | | Total |
|-----------|------------|--------------------|-----------|-----------|-------|
| | | Cervicitis | Normal | Other | |
| I | 27 (19 %) | 82 (58 %) | 15 (10 %) | 18 (13 %) | 142 |
| II | 143 (56 %) | 68 (27 %) | 30 (12 %) | 12 (5 %) | 253 |
| III | 48 (65 %) | 15 (20 %) | 8 (11 %) | 3 (4 %) | 74 |
| IV | 11 (100 %) | - | - | - | 11 |
| Total | 229 (48 %) | 165 (34 %) | 53 (11 %) | 33 (7 %) | 480 |

* Papanicolaou classification** Cervical Intraepithelial Neoplasia

In an analytical study of 229 patients with CIN, Class II pap smears mostly correlated with CIN II and Class III and IV pap smears mostly correlated with CIN III (Table II).

TABLE II
CYTOLOGIC DISTRIBUTION OF CIN

| | CYTOLOGICAL FINDINGS | | | | Total | % |
|---------|----------------------|------------|-----------|----------|-------|-----|
| | I | II | III | IV | | |
| CIN I | 17 (14 %) | 94 (78 %) | 9 (8 %) | — | 120 | 52 |
| CIN II | 4 (7 %) | 31 (51 %) | 21 (34 %) | 5 (8 %) | 61 | 27 |
| CIN III | 6 (12 %) | 18 (38 %) | 18 (38 %) | 6 (12 %) | 48 | 21 |
| Total | 27 (12 %) | 143 (62 %) | 48 (21 %) | 11 (5 %) | 229 | 100 |

Discussion

In centers where pap smears are reported according to the Papanicolaou classification, Class II readings are determined by enlarged inflammatory changes unless presence of atypia is specified. Some pap smears are reported in descriptive form indicating the degree of intraepithelial neoplasia rather than referring to a classification code alone. Although a clinicians preference, along with recent laboratory trends, are toward more precise reporting of normal or abnormal pap smear, it is still not uncommon to have suspicious interpretations.

Colpo-histologic evaluation complements pap smear testing for accurate diagnosis and it eliminates unnecessary conizations resulting from false positive pap smears.^{4,5} Difficulty in diagnosis is the presence of high false-negative pap smear rates which range anywhere from 6 % to 50 % CIN.^{6,7} According to this study, if colposcopic examination was omitted, 19 % and 56 % of CIN would have been missed for Class I and II pap smears, respectively.

However pap smear screening deserves credit for the decrease of invasive carcinoma of the cervix, since its introduction by Papanicolaou. In Yajima's study, roughly 90 % of the cases of carcinoma in situ and invasive carcinoma were from a group of women who had not been screened with a pap smear previously.

Recently sampling and/or interpretation errors have been held responsible for false negative results and modalities, such as using plastic swabs, combining endocervical smears with scrapings, or two simultaneous pap smear have been recommended to reduce false-negative pap smear rates.⁹⁻¹¹

To replace pap smears with colposcopic evaluations as screening test would be impractical. If the spectrum of indications for the need of colposcopic evaluation were broadened to include Class I cytology with cervical lesions and Class II cytology without atypia, the number of diagnosed CIN would most likely increase.

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The Accuracy of Colposcopically Directed Biopsy in Patients with Suspected Intraepithelial Neoplasia of the Cervix

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Summary

Fifty-six patients with Class III to V Papanicolaou (Pap) smears were subjected to colposcopic evaluation. Incidence of cervical intraepithelial neoplasia was 84.4 %, 82.4 % and 100 % for Class III, IV and V Pap smears respectively. The accuracy rate between the cytologic results and the final histologic diagnosis was 85.8 %. The accuracy rate of colposcopically directed biopsy was found to be 98 %.

Key Words: Cytology, Histology, Colposcopy, Cervical Intraepithelial neoplasia.

Introduction

Pap smear is a standard screening method for invasive and preinvasive carcinoma of the cervix. Colposcopy was established for clinical evaluation of patients with abnormal Pap smears allowing recognition of the abnormal region in the cervix and/or vagina for further histologic study.^{1,2} Diagnostic accuracy is at least equivalent to cervical conization when the transformation zone is entirely seen, and it is without serious complications.

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In this study, cervical cytological and colposcopic correlations were evaluated in patients with Class III, IV and V Pap smears excluding invasive conditions.

Material and Methods

56 patients with positive Pap smears were subjected to colposcopic and histologic evaluation. Colposcopic examination was undertaken in our department and the materials were analysed by the department of Pathology.

3 % acetic acid was used to verify the abnormal regions on the cervix and/or vagina. Atypical vessels, mosaicism, punctation and white epithelium were recognized as abnormal transformation zone, as defined by the Terminology Committee of the International Federation of Cervical Pathology and Colposcopy. After colposcopically directed biopsy and endocervical curettage (ECC), all material were evaluated by a co-author pathologist. After tissue diagnosis, of these 56 patients with positive cytology, 9 were subjected to conization for negative colposcopic findings, 5 for positive ECC and 42 for testing the accuracy of colposcopically directed biopsy.

All histologic findings such as CIN I, CIN II, CIN III and Carcinoma In situ are described as positive in this study.

Results

The accuracy rate comparing the cytologic results and the final histologic diagnosis was 85.8 %.

Table I shows the cytological findings obtained before colposcopy which are compared with the final histologic diagnosis.

TABLE I
RESULTS OF CYTOLOGY COMPARED TO THE FINAL HISTOLOGIC DIAGNOSIS

| Cytology | FINAL HISTOLOGIC DIAGNOSIS (Colposcopic directed bx.) | | Total |
|-----------|--|----------|-------|
| | Positive* | Negative | |
| Class III | 27 | 5 | 32 |
| Class IV | 14 | 3 | 17 |
| Class V | 7 | - | 7 |
| Total | 48 | 8 | 56 |

* CIN I, CIN II, CIN III and Carcinoma Insitu

Table II presents a comparison between the histological results obtained from colposcopically directed biopsies and the final tissue diagnosis obtained by cone or hysterectomy. The overall accuracy rate of colposcopically directed biopsies were found to be 98 %.

TABLE II
COLPOSCOPIC RESULTS COMPARED TO CONE/HYSTERECTOMY RESULTS

| RESULT OF COLPOSCOPY | RESULT OF CONE/HYSTERECTOMY | | Total |
|----------------------|-----------------------------|----------|-------|
| | Positive | Negative | |
| Positive | 36 | 11 | 47 |
| Negative | 1 | 8 | 9 |
| Total | 37 | 19 | 56 |

Of the 47 patients with positive colposcopically directed biopsies, 11 did not have any tumor in their conization specimens. In other words these 11 patients were treated by colposcopically directed biopsies.

Of nine patients with a negative colposcopic biopsy, 1 had tumor on the conization specimen.

Discussion

Colposcopy is an excellent means of evaluating abnormal cervical cytology and is a clinical method of proven accuracy.^{1, 2, 3} Colposcopic examination is satisfactory in nearly all young patients who most need conservative treatment and in whom good results can be achieved by local destructive therapy such as laser and cryosurgery.^{4, 5}

The accuracy of the method depends on some factors which include, the experience of the colposcopist, ability to entirely visualize the transformation zone and the co-existing benign cervical lesions such as papillomas, granulomatous syphylitic lesions and trichomoniasis.^{3, 6}

In this series, underdiagnosis by directed biopsy occurred in one patient, in whom a satisfactory colposcopic examination couldn't be accomplished which gave a false negativity rate for the procedure of 11.1 %. Compared to the total colposcopic examinations performed this figure is 2 %.

The equivalent underdiagnosis figures given by Staf1 and Mattingly, Kirkup *et al.*, Ortis *et al.* and Veridiano *et al.* were 0, 0.2, 0.3 and 0.5 % respectively.^{2, 3, 7, 8}

On the other hand, 4 patients had final histologic diagnosis by more than one histologic degree of neoplasia. In addition 11 patients did not

have any lesions in their cone specimens. Similar results have been reported by StafI and Mattingly and Luesley, Delke and Tancer in their cone specimens.^{3, 8, 9}

This study confirms that colposcopically directed biopsy can be advocated as a method of reaching an accurate, hence safe diagnosis in patients with abnormal cervical cytology. Only if the entire transformation zone is not visualized and endocervical curettage is positive, cold conization is essential to reach the final diagnosis.

As more women with CIN's are discovered due to expansion of cervical cytology screening programs, there is need for an extension of colposcopy services to all areas so that patients with abnormal smears can have a preliminary colposcopic examination.

In conclusion, the cytopathologist can determine with a great degree of accuracy the specific morphology represented by the Pap smear. However it must be recognized that there are occasional errors in cytodiagnosis. For this reason, colposcopy is an ideal method for patient evaluation and will substantially reduce the number of unnecessary and costly operative procedures.

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Increased Incidence of Sister Chromatid Exchange Among Workers in A Ferrochromium Factory

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Summary

The prevalence of structural chromosome aberrations and sister chromatid exchanges (SCEs) in cultured lymphocytes were examined in a group of 50 workers employed in the ferrochromium factory. The chromosome aberration rates were not different among the workers and controls. SCE rates obtained from these subjects (9.41 ± 0.71) were higher than that of the control group (8.18 ± 0.17), ($P < 0.01$). Depending on the working place, the exposed group was divided into 5 subgroups such as Furnace, Breakage, Workshop, Laboratory and Others. The mean SCE rates of these subgroups were compared with each other and the control group. All of the SCE levels detected in the subgroups were significantly higher than those among the controls. The highest SCE level was observed in the furnace subgroup. The study suggests that workers in the ferrochromium factory are exposed to genetically active chromium compounds.

Key Words: Chromium, SCE.

Introduction

An association between carcinogenicity and mutagenicity of several metals has been previously discussed and carcinogenicity of chromium compounds has also been evaluated.¹⁻⁴ The carcinogenicity of chromium is related to its valence state; hexavalent chromium compounds induce

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point mutations in bacteria and yeast, infidelity of DNA replication in vitro, chromosomal aberrations and SCE in mammalian cell cultures, and cell transformation in vitro. Whereas trivalent chromium compounds are inactive in mutagenicity tests, unless they are allowed to interact in vitro with pure DNA.⁵⁻¹¹ Epidemiologic evidence has been presented which shows an association between prolonged inhalation of hexavalent chromium compounds in exposed workers and the development of cancer of the respiratory system,¹²⁻¹⁵ and the gastrointestinal tract.^{16, 17} Such associations have also been shown in workers employed in ferrochromium factories where trivalent chromium compounds were used.¹⁸⁻²⁰ Therefore, the investigation of possible genotoxic effects produced by chromium compounds in somatic cells of ferrochromium factory workers was relevant.

In the present study, the incidence of chromosome aberrations and the frequency of SCE in cultured lymphocytes of exposed workers were examined. The data was analysed according the location of the workers in the factory.

Material and Method

Subjects Analysed: Fifty males occupationally exposed to chromium in ferrochromium factory and 10 control men from health personel working for the faculty were examined for the analysis of sister chromatid exchange. The mean age of the control and exposed group was 28.6 and 36.0 respectively. Chromosomal aberrations were studied in cultured lymphocytes obtained form 20 males of exposed group. None of the subjects had recently had any notable viral infections or diagnostic irradiation.

Lymphocyte Cultures: Lymphocytes from 2 ml of peripheral blood obtained from each exposed and control subject were cultured in a 5 ml of growth medium supplemented with 20 % fetal calf serum and 3 % phytohemagglutinin (PHA) in the presence of 10 $\mu\text{g}/\text{ml}$ 5-bromodeoxyuridine (BrdU) for the analysis of sister chromatid exchanges. The culture time was 72 hours in + 37 °C. Lymphocytes were cultured for 72 hours in the same medium in the absence of BrdU for the analysis of chromosome aberrations. Colchicine (0.1 $\mu\text{g}/\text{ml}$) was added for 2 hours before fixation.

Chromosome Preparations: Metaphase cells were dislodged by gently pipetting the overlaying medium and collected by centrifuging the suspensions at 1200 rpm for 7 minutes. The cell pellet was suspended in a 5 ml of hypotonic buffer (0.075 M KCl) at 37 °C for 7 minutes and

fixed in methanol/acetic acid (3/1). Fixed cells were dropped onto a clear slide and air dried. The slides were heated at 88 °C for 10 minutes in 1 M NaH₂PO₄ (pH = 8.0 - 8.1) and stained with Giemsa (5 %) for SCE analysis.²¹ Trypsin-Giemsa banding technique was used for the examination of chromosomal aberrations.^{22, 23} All slides were coded and analysed by the same person. 20 harlequin stained metaphases per subject were scored for sister chromatid exchange and 50 metaphases per culture were analysed for chromosome aberrations.

Results

Notable chromosome aberrations were not detected among chromium-exposed subjects whereas the mean frequency of SCE in 50 exposed workers was 9.41 ± 0.71 and corresponding value in nonexposed controls was 8.18 ± 0.17 . SCE rates obtained from this exposed group was higher than that of control group (Table I). Depending on working place, this exposed group was divided into 5 subgroups such as Furnace (20 Workers), Breakage (7 workers), Workshop (8 workers), Laboratory (5 workers) and others who were employed in various part of factory (10 workers). The mean frequencies of SCEs in these subgroups were 9.70 ± 0.12 ; 9.52 ± 0.19 ; 9.37 ± 0.16 ; 9.27 ± 0.22 ; 8.84 ± 0.14 respectively. These values were compared with each other and that of the control group. All of the SCE levels detected in these subgroups were

TABLE I
FREQUENCIES OF SCEs IN WORKERS EXPOSED TO CHROMIUM AND CONTROLS

| | No. of Subjects | Metaphases Counted | SCEs/Metaphase \pm S.E |
|----------|-----------------|--------------------|--------------------------|
| Workers | 50 | 1000 | 9.41 ± 0.71 |
| Controls | 10 | 200 | 8.18 ± 0.17 |

Statistically significantly different $P < 0.01$ Student's t test.

TABLE II
THE FREQUENCIES OF SCEs IN SUBGROUPS OF EXPOSED WORKERS

| Subgroups | No. of Subjects | Metaphases Counted | SCEs/Metaphase \pm S.E |
|------------|-----------------|--------------------|--------------------------|
| Furnace | 20 | 400 | 9.70 ± 0.12^a |
| Breakage | 7 | 140 | 9.52 ± 0.19^a |
| Workshop | 8 | 160 | 9.37 ± 0.16 |
| Laboratory | 5 | 100 | 9.27 ± 0.22 |
| Others | 10 | 200 | 8.84 ± 0.14 |
| Controls | 10 | 200 | 8.18 ± 0.17 |

For each subgroup the difference was significant ($P < 0.01$) compared with controls; between the exposed subgroups the difference was significant ($P < 0.01$) only between workers in furnace^a and breakage^a as compared with others.

significantly higher than that of the control group, but the highest level was observed in the furnace subgroup. Some groups have the higher SCE value than the others (Table II). No correlation was detected between exposure time and SCE levels of the exposed subjects.

Discussion

Carcinogenic effects of chromium compounds have been demonstrated with experimental and epidemiologic studies.^{4, 24-27} On the basis of several studies only the hexavalent chromium compounds seem to be active carcinogens whereas the trivalent chromium compounds are commonly considered inactive.²⁸⁻³¹ However, it has been reported that workers have an increased risk of lung cancer at ferrochromium factories where trivalent chromium compounds are used as the raw material, but hexavalent chromium compounds which are detected in the plant atmosphere, especially in furnaces would be responsible for the increased risk of cancer.¹⁸⁻²⁰

For this reason, chromosomal aberrations and SCEs as indicator of DNA damage have been studied to find out cytogenetic effects in lymphocytes of human subjects working at a ferrochromium factory where concentrated chromite ($\text{Cr}_2^{+3}\text{O}_3$) is being used. Although no increase was observed in the prevalence of chromosomal aberrations in the exposed group, significant increase ($p < 0.01$) was found in the SCE rates between the exposed and the control group. This finding indicates that there is no direct correlation between the increase of structural chromosomal aberration and the SCEs as has been observed with some other agents as well.³² It has been suggested that the carcinogenic effects observed in individuals working at the ferrochromium plants using trivalent chromium compounds result from inhalation of the hexavalent chromium compounds which occur during the processing of raw material at furnace.¹⁸ Therefore the workers were divided into subgroups depending on their working place. When the mean SCEs of all groups were compared with control group and between themselves, the mean SCEs of all groups were found significantly higher than that of control group ($p < 0.01$). The highest level of mean SCE observed in subjects working at the furnace, is supporting the suggestions that hexavalent chromium compounds occur during the processing of trivalent chromium compounds.

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Accessory Deep Peroneal Nerve and its Clinical Importance

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Summary

The lower extremities of 50 healthy individuals were studied electrophysiologically to determine the frequency of the accessory deep peroneal nerve, which is a quite common but generally unknown anomaly. This nerve arises from the superficial peroneal branch of the common peroneal nerve and innervates the extensor digitorum brevis, which is normally supplied only by the deep peroneal nerve. In this study, this anomalous communication was present in 18 % of the cases.

We tried to emphasize the importance of being aware of this anomaly, especially in cases with peroneal neuropathy, in whom routine nerve conduction studies reveal conflicting results in the presence of this condition.

Key Words: Nerve conduction studies; accessory deep peroneal nerve; anatomical variation; peroneal nerve lesions.

Introduction

The most frequent anomalous nerve of the lower extremity is the accessory deep peroneal nerve (ADPN). It arises from the superficial branch of the common peroneal nerve on the lateral aspect of the leg. After passing behind the lateral malleolus, it proceeds anteriorly to innervate the extensor digitorum brevis (EDB). This muscle is normally supplied by the deep peroneal nerve which is commonly used in routine

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nerve conduction studies of the lower extremity. ADPN is seen in 19-28 % of an unselected population.¹⁻³ It usually supplies the lateral portion of the EDB, therefore a compound muscle action potential (CMAP) recorded from this part of the muscle has a larger amplitude than one obtained from the belly of the muscle.²⁻⁴ The inheritance mode of ADPN is reported to be autosomal dominant.¹

The presence of ADPN should be suspected if the CMAP of the EDB is smaller with stimulation of the deep peroneal nerve at the ankle than with stimulation of the common peroneal nerve at the knee. The anomaly can be verified by stimulating behind the lateral malleolus and activating the lateral portion of the EDB which is accompanied by the dorsiflexion of the 4th and/or the 3rd toe.

In patients with peroneal nerve lesions who also have this anomalous communication, nerve conduction studies may lead to erroneous interpretations if the condition is not considered. The aim of this study is to determine the frequency ADPN and emphasize the importance of keeping it in mind particularly, in cases where peroneal nerve lesions yield confusing results.

Material and Methods

This study was carried out in 50 healthy volunteers at the Neurology Clinic of Akdeniz University, School of Medicine. The age range of the cases was between 15 and 65 years (mean: 34.3), 22 females and 28 males. Medelec MS-6 electromyograph was used for the nerve stimulations with bipolar surface electrodes. Recordings were made with surface disk electrodes using the belly-tendon method. Stimulus duration was 0.2 - 0.3 msec with supramaximal intensity. First, the deep peroneal nerve was stimulated on the dorsum of the foot, 8 cm proximal to the recording electrodes on the belly of the EDB. The common peroneal nerve was stimulated next, 2 cm below the fibular head. Finally, to look for the presence of ADPN, a third stimulation was done on the posterolateral aspect of the ankle behind the lateral malleolus (Figure 1).⁴ The movement of the toes were observed carefully during the stimulation. Any potential recorded with plantar flexion or eversion of the foot was discarded because it did not fit with the expected movement. In cases with the anomalous innervation, the potentials were recorded first with the active electrode on the belly of the muscle and repeated after the electrode was placed on its lateral portion where the nerve commonly terminates. If the second stimulation produced a CMAP with a larger amplitude, this was accepted as the valid measurement.

TABLE I
ELECTROPHYSIOLOGICAL FINDINGS IN CASES WITH ADPN

| Case | Age/ Sex | Side | Latency (msec) | | | Amplitude (mV) | | | NCV of ADPN |
|------|-------------|------|-------------------|-----------------|----------------------------|-------------------|-----------------|---------------------------|-------------------|
| | | | Ankle (dorsum) | Fibular head | Ankle (posterolateral)* | Ankle (dorsum) | Fibular head | Ankle (posterolateral) | |
| 1 | 19 M | L | 5.1 | 12.9 | 6.0 | 3.0 | 4.2 | 0.7 | 63.7 |
| 2 | 23 M | L | 4.2 | 10.5 | 5.8 | 0.6 | 1.0 | 0.2 | 56.5 |
| 3 | 15 M | L | 3.8 | 9.2 | 3.6 | 2.6 | 2.8 | 0.5 | 52.0 |
| 4 | 24 F | L | 4.8 | 12.4 | 3.6 | 1.5 | 1.9 | 0.6 | 48.0 |
| 5 | 22 M | R | 4.0 | 9.8 | 3.0 | 3.7 | 4.0 | 0.2 | 57.3 |
| 6 | 30 M | L | 4.5 | 11.2 | 5.5 | 2.0 | 3.0 | 0.4 | 56.7 |
| 7 | 42 F | R | 4.4 | 11.2 | 6.3 | 0.7 | 1.0 | 0.2 | 55.0 |
| 8 | 38 M | L | 4.6 | 10.4 | 3.8 | 1.4 | 2.5 | 0.4 | 48.0 |
| 9 | 32 F | L | 4.8 | 11.9 | 6.5 | 1.2 | 1.4 | 0.5 | 51.6 |
| | | R | 4.1 | 10.8 | 5.1 | 1.4 | 2.0 | 0.4 | 52.0 |

* Behind the lateral malleolus

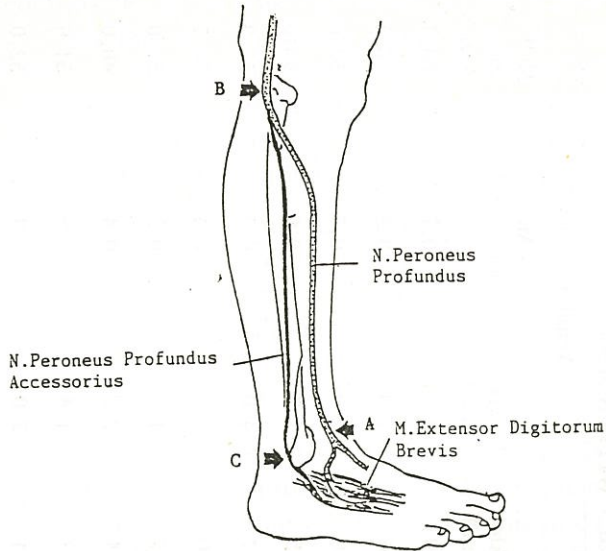


Figure 1

Stimulation points used in the detection of ADPN:

A) Dorsum of the ankle, B) Fibular head, C) Behind the lateral malleolus.

In all the cases the amplitudes and latencies of the CMAPs were measured and the nerve conduction velocities determined in both legs. The conduction velocity of the ADPN was also determined whenever present.

Results

The ADPN was found in 9 cases (18 %) among which only 1 had this nerve bilaterally (Table I). The mean CMAP amplitudes and conduction velocities of routine peroneal nerve studies in the whole series are summarized in Table II.

TABLE II
MEAN CMAP AMPLITUDES AND NCVs OBTAINED BY PERONEAL NERVE STIMULATION

| Right LEG | | | Left LEG | | |
|---------------------|--------------|-------------|---------------------|--------------|-------------|
| CMAP amplitude (mV) | | | CMAP amplitude (mV) | | |
| Ankle (dorsum) | Fibular head | NCV (m/sec) | Ankle (dorsum) | Fibular head | NCV (m/sec) |
| 2.8 | 2.5 | 55.3 | 2.4 | 2.1 | 54.4 |
| (0.3-4.8) | (0.3-4.1) | (40-60) | (0.3-4.7) | (0.3-4.6) | (42-60) |

Figure 2 shows the characteristic CMAP amplitudes in a case with ADPN. In all cases with this nerve, the CMAP amplitude was found larger with stimulation at the fibular head than with stimulation at the dorsum of the foot. The amplitude recorded at the fibular head is approximately equal to the sum of the amplitudes obtained from the dorsum of the foot and the lateral malleolus (Table III).

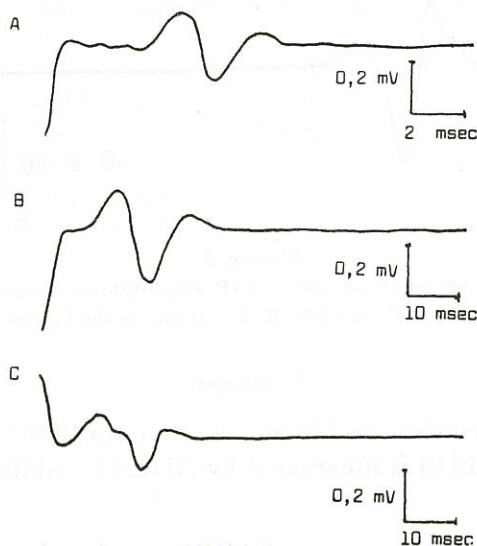


Figure 2

CMAPs obtained from the EDB in a case with ADPN. Points of stimulation: A) Dorsum of the ankle, B) Fibular head, C) Behind the lateral malleolus.

TABLE III
MEAN CMAP AMPLITUDES IN CASES WITH ADPN

| CMAP amplitude (mV) | | |
|---------------------|------------------|-------------------------|
| Ankle (dorsum) | Fibular head | Ankle (posterolateral)* |
| 1.9 (0.6-3.7) | 2.1 (1.0-4.2) | 0.3 (0.2-0.6) |

* behind the lateral malleolus

Figure 3 shows that the CMAP amplitude is larger when the recording electrodes are placed on the lateral part of the EDB as compared to the recordings obtained from the belly of the muscle.

During stimulation of ADPN at the lateral malleolus, dorsiflexion of the 4th toe was observed in 7 out of 9 cases while in the remaining 2 both the 4th and the 3rd toes showed this movement.

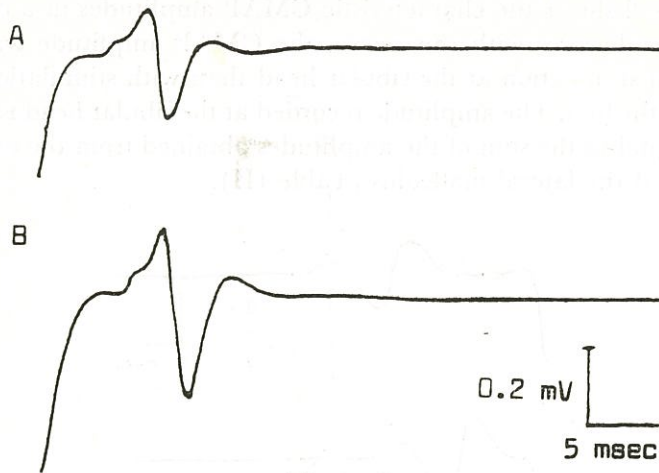


Figure 3

Effect of recording points on the CMAP amplitude in a case with ADPN
 A) Electrode on the belly of EDB, B) Electrode on the lateral part of EDB.

Discussion

ADPN was first described in man by Bryce in 1897.⁵ In persons with this anomaly the EDB is innervated by ADPN in addition to the deep peroneal nerve.

In this study, the frequency of ADPN was found to be 18 % which is consistent with the results of the previous reports.¹⁻³ Bryce had found this anomalous nerve in only 3 out of 110 cadaver legs (2.7 %). The low rate in his study may reflect the difficulties in the dissection of the specimens. Another detailed anatomical study is that of Winckler's who found this nerve in 7 of 19 cadaver legs.⁶ However in only 4 of these cases, muscular branches to the lateral part of the EDB (21 %) were demonstrated. The remaining 3 cases had only articular branches.

The first electrophysiological demonstration of ADPN was reported by Lambert in 1969.³ He found this variation in 28 % of 50 cases. Infante and Kennedy reported a frequency of 18.7 % in their electrophysiological study.²

Crutchfield and Gutmann investigated the genetic aspect of this condition and stated that its mode of transmission was autosomal dominant.¹ They found it in 78 % of the relatives of their 5 cases.

The presence of this condition may lead to atypical electrophysiological findings, particularly during the work-up of a patient with peroneal neuropathy.⁷

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DISCUSSION

The present study is the first to report the effects of a specific... (text is extremely faint and largely illegible)

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Reading Epilepsy

Abdurrahman Ciğer, M.D.* / Münife Müftüoğlu, M.D.**

Summary

Reading epilepsy is a type of reflex epilepsy which was first described by Bickford and associates. In this report we presented three cases of this very rarely occurring type of epilepsy.

Key Words: Reading, epilepsy, reading epilepsy, reflex epilepsy.

Introduction

Reading epilepsy is an infrequently occurring type of epilepsy. Bickford *et al*¹, in 1956, considered the reading epilepsy as a form of Myoclonic epilepsy triggered by a group of sensory stimuli on a hyperexcitable cortical focus. In 1960, several factors in the production of seizures such as, the visual pattern, proprioceptive impulses from the jaw and ocular muscles, attention to the reading, etc., were proposed by Critchley *et al*.² Forster,³ in 1977, postulated that reading epilepsy is a communication disorder and the seizure is induced by superior cognitive functions.

In this report, the results of the clinical and electroencephalographic investigations of three patients are presented.

The medical and developmental histories were unremarkable as were their family histories for all of our patients. Results of their general physical, neurological and laboratory examinations were normal. Their EEGs were normal during the resting state and hyperventilation and photic stimulation provoked no abnormalities on the EEG. During investigations, the patients were requested to: (1) read a newspaper a technical material about EEG, and a comic magazine silently. A pornographic material was added to the materials mentioned above for our third case. (2) read the same materials aloud; (3) speak; (4) make active eye movements as if mimicing the reading state; (5) make articulatory movements as if mimicing the reading state. The fourth and fifth steps weren't applied to the first patient.

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Case Reports

Case 1: A 17-year-old, right-handed male presented with myoclonic jaw jerkings during reading. He gave up his education because of this complaint. He was treated with phenytoin and carbamazepine in combination with little success. His first EEG during reading was performed under the anticonvulsive treatment. During reading silently, the EEG showed high-voltage, 4-6 cyc/sec, bilateral paroxysmal spike-wave and multiple spike-wave discharges which were recorded predominantly on the left hemisphere electrode combinations (Figure 1). Reading aloud increased these epileptic discharges in frequency. During speaking, no abnormalities were observed on the EEG. The patient experienced myoclonic jaw jerkings almost always during the paroxysmal spike-wave discharges. The patient stopped the medication by himself because of its little success. 6 months later, a second record was performed. The second showed 4-6 cyc/sec, paroxysmal spike-wave discharges more frequently than the first EEG. The dominance of the left hemisphere was remarkable in this second EEG, too. The test were repeated after 10 mg diazepam during the second record and no abnormalities were observed on the EEG for 20 minutes.

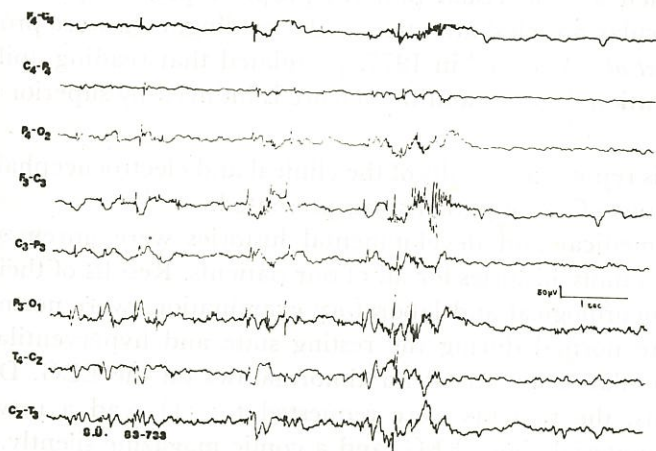


Figure 1

High voltage, 4-6 cyc/sec bilateral paroxysmal spike-wave and multiple spike-wave discharges predominantly on the left hemisphere electrode combinations (Case 1, during reading silently)

Case 2: A 30-year-old, right-handed male complained of generalized tonic-clonic seizures, preceded by tingling sensation in his tongue and myoclonic jerking of his jaw while he was reading. When the reading

was stopped, the preceding symptoms would also cease. Sleep deprivation, fatigue and especially emotional stress made him more susceptible to the seizures. His EEG during reading silently showed paroxysmal, high-voltage, 4-6 cyc/sec sharp wave and sharp slow wave discharges bilaterally and synchronously which was followed by the muscle activity on the frontal and temporal regions. Reading aloud increased the frequency of sharp wave discharges. When the sharp wave discharges occurred on the EEG, the patient experienced jaw jerkings. Speaking, eye movements and articulatory movements provoked no abnormalities on the EEG. Then, the patient again requested to read aloud. After a while of reading, generalized multiple spike-wave discharges occurred on the EEG paroxysmally, bilaterally and synchronously. During these discharges, the patient's reading interrupted by myoclonic jaw jerkings.

The multiple spike-wave discharges prolonged (Figure 2) and following an epileptic cry, a tonic-clonic seizure occurred which was continued for 60 seconds. The test was ended.

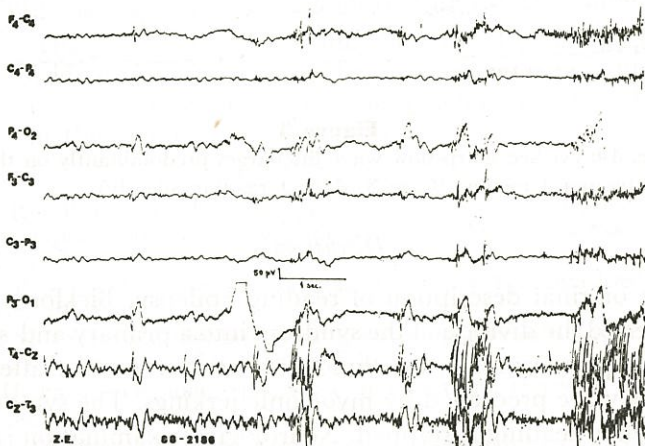


Figure 2

High voltage spike, sharp wave, multiple spike-wave discharges predominantly on the fronto-temporal regions, followed by muscle activity. (Case 2, during reading aloud)

Case 3: A 37-year-old, right-handed male presented with tonic-clonic seizures for 8 years. He, also, complained of nervousness, sensation of tightness of his throat and jaw musculature during talking to his chief or sometimes during reading. He experienced two major tonic-clonic seizures during reading which were preceded by the myoclonic jerks of his jaw. He was treated with phenytoin, but the seizures continued in spite of the medication. He told that he experienced jaw jerkings much

more, when he was reading pornographic materials. His EEG, during reading silently, showed high-voltage, 4-6 cyc/sec sharp slow wave discharges predominantly on the left midtemporal region (Figure 3). Reading aloud and especially reading pornographic material increased the discharges in frequency. Speaking, active eye movements, articulatory movements triggered no discharges on the EEG.

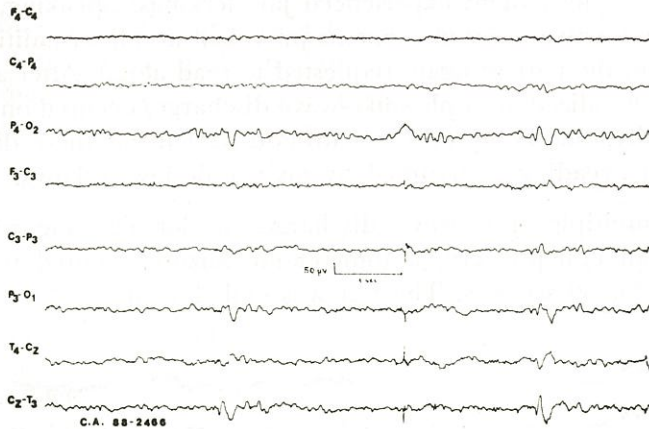


Figure 3

High voltage, 4-6 cyc/sec sharp-slow wave discharges predominantly on the left midtemporal region. (Case 3, during reading silently)

Discussion

In the original description of reading epilepsy, Bickford and associates suggested the division of the syndrom into a primary and secondary form. In the primary form, the tonic-clonic seizures occur after reading only and they are preceded by myoclonic jerkings. The symptoms usually cease when reading is stopped. Neurological examination is negative and the EEG is normal, excluding the reading state. In the secondary form, the tonic-clonic seizures occur spontaneously or are precipitated by various stimuli in addition to reading. The EEG in the resting state is usually abnormal and myoclonic jaw jerking is absent.⁴ Since the original description of Bickford *et al.*, the borders between primary and secondary forms have become less distinct. Case 1 and Case 2 fits to the description of primary form of reading epilepsy. Case 3 can be considered in the secondary form, but his myoclonic jaw jerkings was contrary to the original description of the secondary form. The symptoms of our third patient seem as a combination of primary and secondary forms. Attempting to explain the pathogenesis of the reading epilepsy; visual pattern,

proprioceptive impulses from the jaw and ocular muscles, cortical mechanisms induced in the production of language, combination of cortical and subcortical excitation during reading etc., were proposed in the production of seizures.⁵⁻¹⁰ The pathogenesis of the reading epilepsy still remains controversial. The effect of proprioceptive impulses from jaw and ocular muscles was mentioned for some cases in the literature.^{1, 11} On the other hand the importance of the content of reading material in the production of seizures for some cases is a fact.^{12, 13} Also the seizures being provoked by speaking and writing in addition to reading⁵, support the hypothesis which proposed the role of cortical mechanisms induced in the production of language. We couldn't able to produce neither EEG abnormalities, nor seizure activity with active eye movements and articulatory movements. Pornographic material increased the frequency of paroxysmal discharges on the EEG of our third patient. Although the reading material didn't make a significant difference for two of our patients, we suppose that, when they attempted to understand the meaning of the text, the frequency of the discharges increased on the EEGs. Speaking didn't provoke any EEG abnormalities during these tests.

As a conclusion, we don't dispute the role of proprioceptive and other lower order stimuli in evoking the seizures during reading but we think that our cases support the hypothesis which emphasizes the cortical mechanisms in the production of seizures.

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REPORT

The first part of the report deals with the general conditions of the country, and the second part with the details of the various districts. The first part is divided into three sections: the first section deals with the general conditions of the country, the second section deals with the details of the various districts, and the third section deals with the details of the various districts.

Richter's Syndrome

Diffuse Immunoblastic Lymphoma in Patients with Chronic Lymphocytic Leukemia

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Cansen Çakalır, M.D.*** / Nükhet Tüzüner, M.D.*** /
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Nuran Akman, M.D.*******

Summary

Richter's syndrome has been defined as "histiocytic lymphoma" or Hodgkin's disease supervening in the course of chronic lymphocytic leukemia and related disorders. Clinical findings at the onset of Richter's transformation were uniform and consisted of the abrupt onset of fever, marked asymmetric lymphadenopathy with the formation of masses, splenomegaly and hepatomegaly. We report a patient with CLL whose autopsy examinations revealed extensive infiltrates of large lymphoreticular cells, predominantly in lymph nodes, liver, spleen and the gastrointestinal tract.

Key Words: Richter's syndrome, Chronic lymphocytic leukemia.

Introduction

Histiocytic lymphoma supervening in a patient with preexisting chronic lymphocytic leukemia (CLL) was first reported by Richter in 1928.¹ In 1964, Lotholary *et al.* reported four new cases and applied the term "Richter's syndrome" for both associations.² Later reports have

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also included transformation of Hodgkin's disease and various types of non-Hodgkin's lymphomas under this designation.^{3,9} Some investigators suggest that Richter's syndrome represents a transformation or dedifferentiation of CLL³⁻⁶ while others feel that it represents two separate and unrelated neoplasms.^{7,8} We describe a new case of Richter's syndrome and review reported cases.

Case Report

A 60-year-old man with a 2-year history of CLL was admitted to our hospital in August, 1986, for sweating, malaise, weakness and generalized lymph node enlargement. The patient had been treated at a different center with oral steroids and chlorambucil, and he was referred to our hematology department for further investigation. Physical examination showed he was pale and thin, had moderate generalized lymphadenopathy, hepatomegaly of 1 cm and splenomegaly of 9 cm. The laboratory findings were as follows: ESR 25 mm/h, hematocrit 28 %, WBC count $388 \times 10^9/l$ of which 100 % were well-differentiated lymphocytes typical of CLL. Urea was 65 mg/dl, creatinine 1.3 mg/dl, total protein: 6.92 mg, albumin 4.61 mg, IgA: 459 mg, IgM: 138 mg, IgG: 700 mg. Other biochemical parameters were within normal limits. Chest film was normal. Following these investigations the patient was evaluated as a CLL (RAI stage IV) and was given Chlorambucil 0.1 mg/kg (total dose of 6 mg). No response was obtained with chlorambucil at the end of three weeks, and he was given cyclophosphamide, vincristine, prednisone (CVP). After 6 courses of CVP treatment a moderate response was achieved with cervical micro lymphadenomegalies, a splenomegaly of 6 cm and no palpable hepatomegaly. Blood counts were; hematocrit 30 %, WBC: $316 \times 10^9/l$, platelets; $160 \times 10^9/l$. He remained partially well for two months and he didn't come for follow-up evaluation for subsequent months. The patient returned to the hospital in October, 1987, complaining of severe weight loss, increased lymphadenomegaly and severe abdominal pain referring to the back. On his current admission physical examination revealed cachexia, massive generalized lymphadenomegaly and a splenomegaly of 7 cm. The epigastrium was painful. Routine examination revealed a hematocrit of 30 %, a WBC count of $317 \times 10^9/l$ with 95 % mature lymphocytes, a platelet count of $180 \times 10^9/l$. Urea was 76 mg/dl, creatinine: 1.8 mg/dl, uric acid: 7.5 mg/dl. The other parameters were within normal limits. Plain X-ray of the abdomen was normal. Gastroscopic examinations showed tumoral infiltration of the stomach but a biopsy specimen was not obtained and the patient died in October. Autopsy was performed.

Pathological Findings

On the autopsy, significant lesions related to the disease were found in the organs of the gastrointestinal tract and lymphoreticular system. There was a white coloured, firm infiltration which involved and thickened all layers of the gastric wall for a 3 X 2 cm area in the gastric fundus; a similar infiltration in the omentum, mesentery and bowels; an area of perforation with a diameter of 3 cm. with irregular borders in the ileum; tumoral infiltration which involved the whole of the bowel wall and formed a 10 X 5 X 5 cm mass in the distal part of the descending colon; small areas of infiltration in an enlarged liver; tumoral infiltration which comprised a large part of the pancreas as well as peripancreatic lymph nodes (Figure 1) and a similar tumoral infiltration in the highly enlarged spleen (Figure 2). In microscopic studies, infiltration had been formed by two separate groups of cells. One of them was the clinically known leukemic infiltration of the patient and the other was immunoblastic lymphoma. Lymph nodes showed diffuse effacement of architecture by pleomorphic infiltration with transformed immunoblast like cells with large vesicular nuclei, prominent nucleoli and moderate cytoplasm and few residual well-differentiated lymphocytes (Figure 3). Atypical mitotic figures and bizarre nuclear forms were observed in the large immuno-

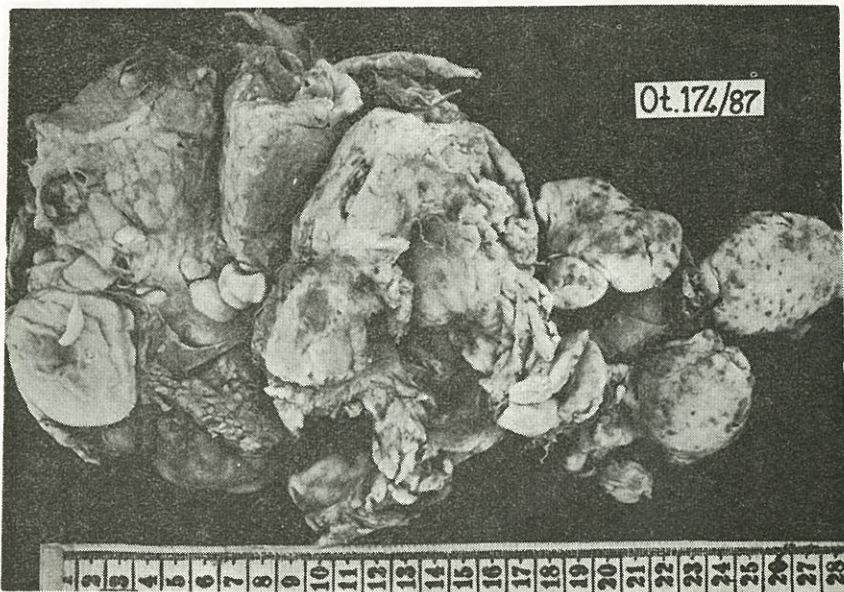


Figure 1
 The development of tumors involving perinodal areas and pancreas in peripancreatic lymph nodes.

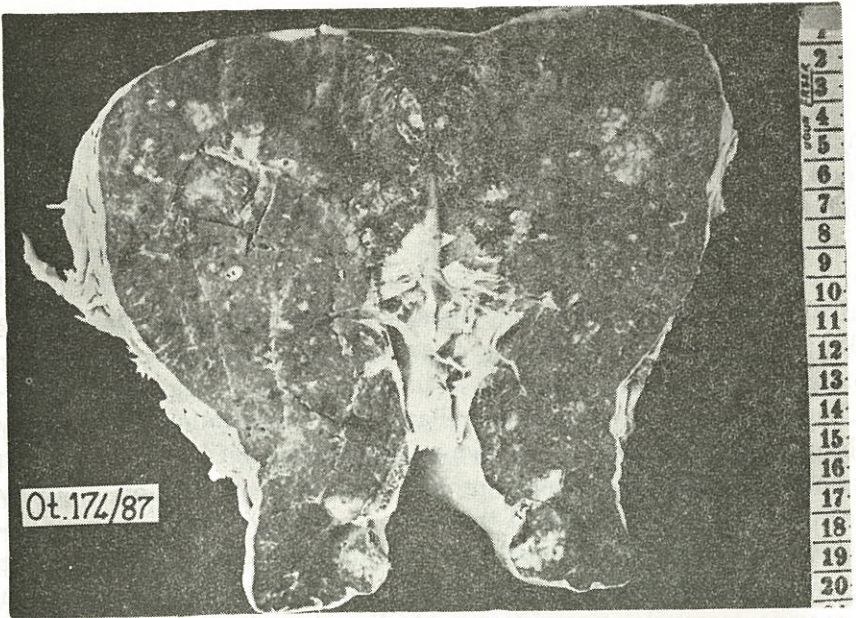


Figure 2

Nodular tumor infiltration in the spleen section showing significant growth.

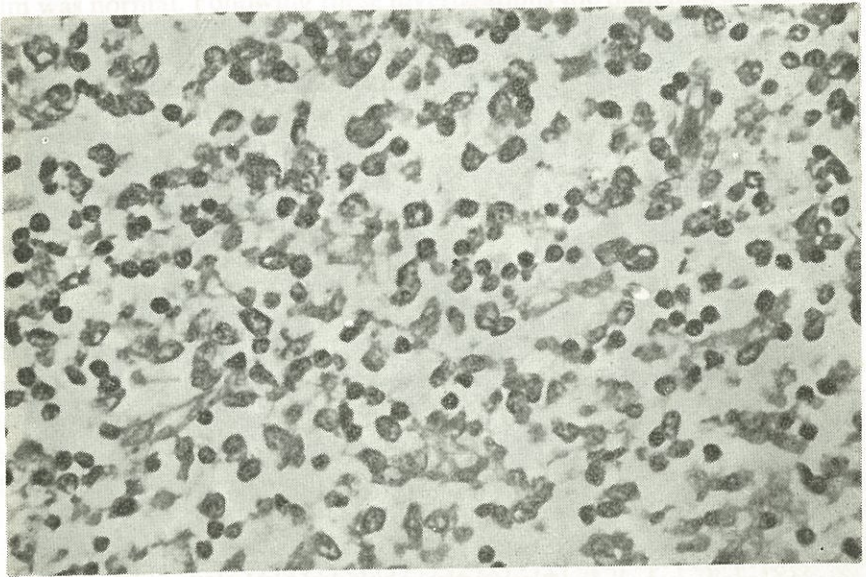


Figure 3

Diffuse proliferation of round, large mononuclear cells with vesicular nuclei and prominent nucleoli in the lymph node and well-differentiated lymphocytes in between (Hem. Eosinx 500).

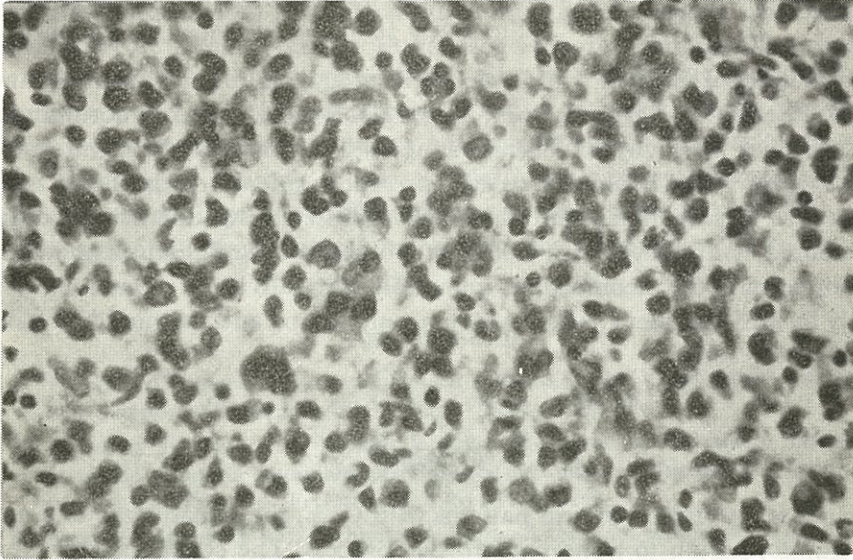


Figure 4

Large, irregular, pleomorphic cells together with well-differentiated lymphocytes in the lymph node. (Hem. Eosinx 500).

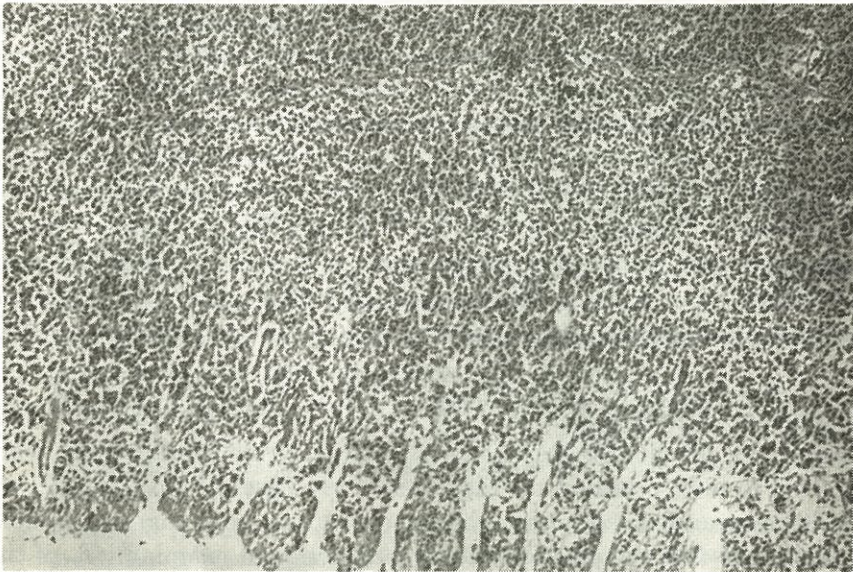


Figure 5

Diffuse tumor infiltration involving the whole gastric wall starting from musoca in the gastric wall sections (Hem. Eosinx 80).

blastic cells (Figure 4). Mature lymphocytes and pleomorphic immunoblastic cells had infiltrated the gastrointestinal tract (Figure 5). In addition portal areas of the liver which were infiltrated by immunoblastic cells and well differentiated lymphocytes, these cells formed actual tumor nodules in the liver parenchyma. There was splenic infiltration with transformed cells within follicles which were also present in splenic cords. Bone marrow was hypercellular and there was diffuse infiltration by well-differentiated lymphocytes but not immunoblastic cells. In lymph nodes the cytoplasm of the pleomorphic immunoblastic cells were stained exclusively by anti λ antisera; other antisera (anti kappa and muramidase gave negative results.

Discussion

It is recognized that in patients with CLL, the disease may undergo a transformation to a more aggressive process. The coexistence of CLL and diffuse histiocytic lymphoma is referred to as Richter's syndrome. Two studies estimate the frequency of development of immunoblastic sarcoma in patients with CLL; 3.3 percent and 10.6 percent respectively.^{10, 11}

Armitage and Aisenberg^{3, 10} reported 2 cases and suggested that the diagnosis depended on three features: 1) initial presentation as CLL, 2) final presentation with weight loss, localized lymphadenopathy and 3) demonstration at autopsy of both pleomorphic malignant lymphoma containing multinucleated giant cells and evidence of infiltration in sites other than those involved by the lymphoma. Fever, increasing lymphadenopathy, weight loss and abdominal pain were believed to herald the development of histiocytic lymphoma.¹² In this case we observed severe abdominal pain, progressive adenomegaly and marked weight loss (9 kg in 6 months) except fever. We documented both pleomorphic malignant lymphomas containing multinucleated giant cells and evidence of CLL.

It is reported that the interval between the initial diagnosis and transformation ranged from 0 to 120 months (median 49 months).³ This interval was 40 months for this case. Bone marrow examinations were reported to have revealed the diagnosis in few cases.^{3, 6} In this case, we didn't find transformed immunoblastic cells in the bone marrow. Faucar et al showed that lymph-node biopsy is superior to examination of the bone marrow.⁶ It was also true for our case. In our case the morphologic appearance of certain lymph nodes extensively infiltrated by immunoblastic cells associated with well differentiated lymphocytes was consistent

with histiocytic lymphoma as defined by Rappaport¹⁴ and immunoblastic sarcoma according to Lukes and Collins.¹³

Some investigators suggested that Richter's syndrome represented a transformation or dedifferentiation of CLL^{3, 4, 5} while others reported that it represented two separate and unrelated neoplasms.^{7, 8} In our case monoclonal staining of immunoblastic cells by anti λ antisera does not support the idea of dedifferentiation or transformation by CLL cells since previous immunological marker studies were not performed.

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Pulmonary Blastoma

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Summary

Pulmonary blastoma is a rare primary malignant tumor of the lung which arise from pulmonary blastema. A case report of this rare entity is presented with its clinical behaviour and early clinical course.

Key Words: Pulmonary blastoma, Pulmonary neoplasm.

Introduction

Pulmonary blastoma is a rare, primary, malignant tumor of the lung, which was first described in 1952 by Barnard as "embryoma of the lung" because of its embryologic similarity to fetal lung.¹ In 1961, Spencer reported three new cases and suggested the name of "pulmonary blastoma" with regard to the histologic resemblance to nephroblastoma of the kidney; suggesting that these tumors arose from the primitive pluripotent pulmonary blastema.² Up to date, about 80 similar cases have been reported in the literature.³ Unlike nephroblastomas which are primarily seen in infancy and early childhood, most of the reported cases of pulmonary blastomas have been established in adults.

In this report, a new case of pulmonary blastoma, and a review of the literature with pathogenetic, diagnostic and surgical considerations is presented. To date, there has been only one reported case of this type of neoplasm in the Turkish literature.⁴

Case Report

A sixty-one year old man was admitted to our institution on June 23, 1987 with main complaints of coughing, haemoptysis, and chest pain on

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the right side of six months duration. He was seen four months previously by his family doctor, and was given a non-specific antibiotic therapy for pulmonary infection. The patient was known to have smoked three packs of cigarettes per day for 40 years.

His physical examination was absolutely normal. In the postero-anterior chest roentgenogram, a density with irregular borders in the posterobasal segment of the right lower lobe was observed. On bronchoscopic examination, a tumoral lesion was seen completely obstructing the orifice of the posterobasal segment bronchus of the right lower lobe. Biopsy specimen was reported as an anaplastic tumor with necrotic and calcified areas. Scalene node biopsy, upper gastrointestinal series, intravenous pyelogram, abdominal ultrasonography, and bone scanning were all negative for primary focus of malignancy and/or metastases.

He underwent a diagnostic operation which was carried out through a posterolateral thoracotomy on June 29, 1987 in which right lower lobectomy was performed. The posterobasal segment was found to be replaced with a grayish-white, solid mass. There were no gross involvement of the hilar or mediastinal lymph nodes. The postoperative period of the patient was uneventful and was discharged on the seventeenth postoperative day. The patients postoperative course was good and he has been completely symptom free, without recurrence and/or distant metastases.

Pathology: Macroscopic examination of the surgical specimen consisted of right lower lobe 15x12x10 cm. in size. The lobe was totally destroyed by a solid, homogenous, bulging mass which was grayish-white in color with focal necrosis and hemorrhagic fields. The tumor extended to the subpleural space, but not infiltrated the pleura. But the bronchial walls and the bronchial lumen were invaded by the tumor.

Microscopic examination of the tumor revealed irregular tubular and glandular structures surrounded by a neoplastic stroma which was in embryonic sarcomatous nature (Figure 1). Tubular structures were lined by a nonciliated stratified columnar epithelium (Figure 2). The stroma was quite variable. In many areas, it was composed of fusiform atypical cells. Some areas were rich in cells, whereas some areas were loose myxoid in nature. Marked pleomorphism, hyperchromasia, giant nuclei, bizzare cells and giant cells were observed in the stromal cells. In the epithelial component, besides the stratified character, marked mitotic activation was observed. No tumor was present both in the hilar, and mediastinal lymph nodes and in the pulmonary venous resection margin.

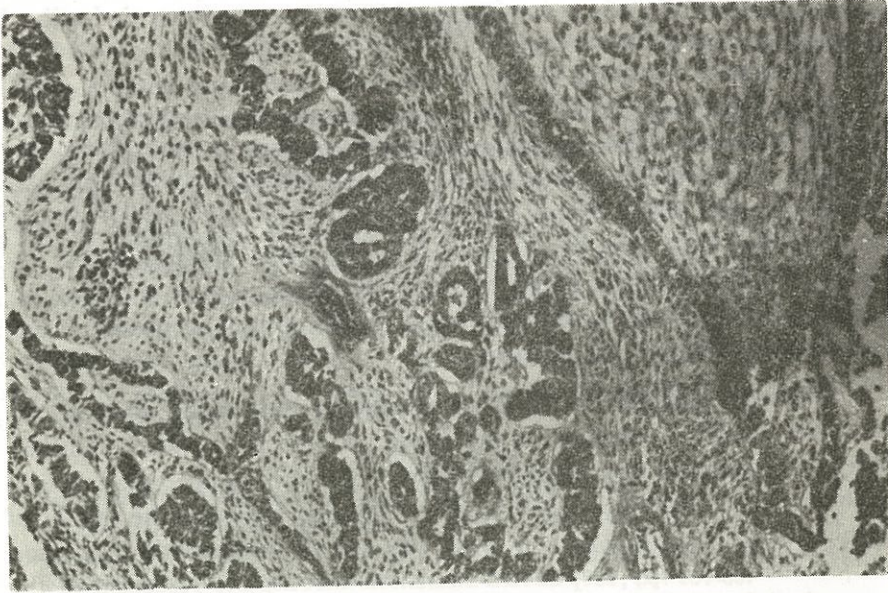


Figure 1
Epithelial tubular structures surrounded by neoplastic stroma. (Hematoxylin and Eosin stain x100)

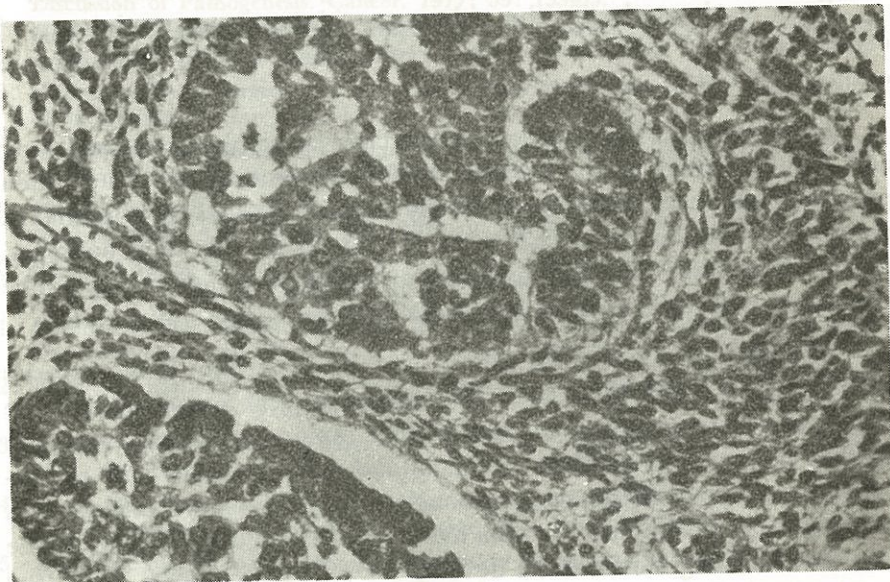


Figure 2
Tubules and glandular structures are lined by nonciliated stratified columnar epithelium. In the stroma, composed of spindle shaped atypical cells, pleomorphism, hyperchromasia, giant nuclei and mitotic figures are shown. (Hematoxylin and Eosin stain. Original magnification x250)

Discussion

Pulmonary blastoma is one of the rarest malignant tumors of the lung which generally arise on the periphery and demonstrate variable clinical behaviour. The age range is from 2 months⁵ to 77 years⁶ in the reported series with a male predominance.^{3,5,7} Review of the reported cases shows that there are no special clinical features to distinguish pulmonary blastomas from other primary neoplasms.⁷ Bronchoscopy, cytology, and scalene node biopsy were of limited value in establishing the diagnosis.^{8,9} Most often, identification of the tumor is possible only during a thoracotomy or autopsy.

Although different methods of treatment have been used in the literature, surgical resection is the choice of treatment, when feasible. External irradiation and chemotherapeutic agents have been used, as well as the surgical excision. There is no correlation between the extent of histologic differentiation and survival. The role of postoperative radiation and/or chemotherapy in patients in whom incomplete resection of the tumor is debatable.⁷⁻¹¹

Although a few long-term survivals ending either with death or a tumor-free life have been reported, the prognosis is generally poor.^{3,8}

Some authors classify the pulmonary blastoma as a subgroup of carcinosarcoma,¹² while some others regard these tumors as a separate entity.^{7, 10, 11, 13, 14}

Histologically, the blastoma shows close resemblance to fetal lung and Wilms' tumor of the kidney. Although pseudocapsules are often present, pulmonary blastoma is locally invasive besides its potential of regional and distant metastases such as liver, brain, adrenals, pancreas, retroperitoneum.¹⁵ The histologic appearance of these tumors can not be correlated with their clinical behaviour with any degree of accuracy.

The histogenesis of these tumors are still uncertain. Some theories concerning its origin have been proposed. Spencer² suggested that the origins of pulmonary blastoma and Wilms' tumor (nephroblastoma) are similar. Both tumors produce epithelial and stromal tissues from a common mesenchymal blastema. Appearance of a pulmonary blastoma at a later age than the nephroblastoma has been attributed by Spencer to the fact that the lung continues to develop for at least ten years, while the renal parenchyma is mature at the time of birth. According to Waddell,¹⁶ pulmonary parenchyma develops in the embryo, similar to the renal parenchyma, through a common mesenchymal blastema, and the peripheral respiratory portion of the lung is derived from mesenchyme while

the distal air passages are formed by canalization of cords of mesenchymal cells which grows in apposition to the termination of the laryngotracheal bud.

Because of the mixed cellular pattern of both tumors, there has been some confusions in distinguishing these tumors from carcinosarcomas. Carcinosarcomas generally consists of squamous carcinoma in a sarcomatous stroma and show no resemblance to the fetal lung.^{11, 14, 17} In contrary, pulmonary blastoma has a distinctive, immature mixture of malignant elements. In these tumors, glandular epithelial component is surrounded by abundant immature sarcomatous stroma which is quite similar to that found in the fetal lung. In addition, carcinosarcomas often originate from major bronchus, whereas pulmonary blastomas from the peripheral portion of the lung. For that reason pulmonary blastoma should be accepted as a separate entity.

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Ganglioglioma Causing Hemorrhagic Stroke

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Cem Akkurt, M.D.*** / Behsan Önel, M.D.****

Summary

A case of ganglioglioma of the occipital lobe is described. The clinical, computed tomographic and surgical intervention findings were unusual. This rare lesion must be considered among brain tumours which cause intracerebral hematoma.

Key Words: Ganglioglioma, Intracerebral Hemorrhage.

Introduction

Gangliogliomas are rare tumours of the central nervous system.^{1,2} They are slowly growing lesions.^{2,3} In angiographies they appear as avascular masses.⁴ CT studies in gangliogliomas reveal either cystic appearance, as an isodense lesion with calcification or a well-demarcated lesion with contrast enhancement.^{4,7}

In this report, we describe a case of ganglioglioma occurring in the right occipital lobe. The patient presented like a hemorrhagic stroke. A computed tomographic scan showed a large intracerebral hematoma located in the occipital lobe. Because of progressive epilepsy we performed surgical intervention. The hematoma and its capsule was evacuated. In this case the clinical findings, the CT appearance was very unusual, and the correct diagnosis was possible only after the histopathological examination. To our knowledge only one case of ganglioglioma causing subarachnoid hemorrhage has been reported previously.²

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Case Report

A 35-year-old male was admitted to Hacettepe University Hospital complaining of headache and blurring of vision. He was referred to our hospital from another institution because of subarachnoid hemorrhage. A lumbar puncture was performed at that hospital, yielded blood-stained CSF. Results of physical examination were normal. Neurological examination revealed a moderate neck stiffness. CT revealed hyperdens lesion in the right occipital lobe. Angiography was normal. The patient was discharged with anticonvulsive medication. Two months later he was admitted again because of seizures. Neurological examination revealed homonymous hemianopia. Slow waves in the right hemisphere was found in EEG. CT revealed a large intracerebral hematoma located in the occipital lobe (Figure 1). Angiography was performed again and it revealed an avascular mass effect.

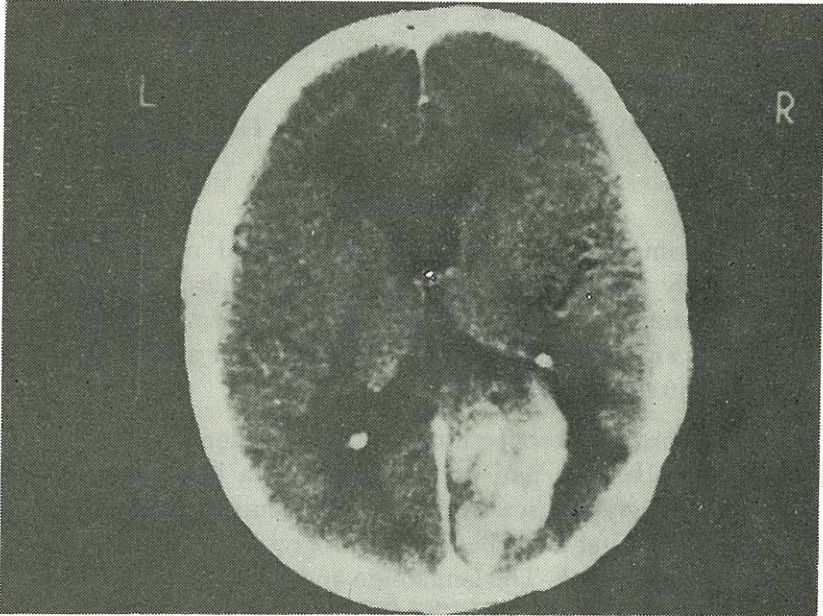


Figure 1

CT examination. Hyperdens lesion at right occipital lobe.

A right parietooccipital craniotomy was performed. In the occipital cortex a hematoma yellow brown in colour was found and evacuated. In the hematoma wall there were some pathologic vessels and they were coagulated. The hematoma capsule which seemed rather gliotic was also removed. The frozen section revealed a hematoma filled with macrophages. The postoperative course was uneventful. The patient was discharged.

ged. In the control examination he was found in good condition with a persistent homonymous hemianopia. Histopathological examination of the specimen revealed a moderately cellular tumour. There were many well differentiated cells as well as bizarre and abnormally formed cells of apparent neuronal origin. By using special stains the well formed Nissl substance was shown. On the other hand, the second most significant microscopic feature of the tumour tissue was the presence of the glial component. There were bi or unipolar cells resembling astrocytes. Another significant feature was the pathologic vessels embedded in tumour tissue which were prominent at capillary level. Some of them were also large in caliber (Figure 2).

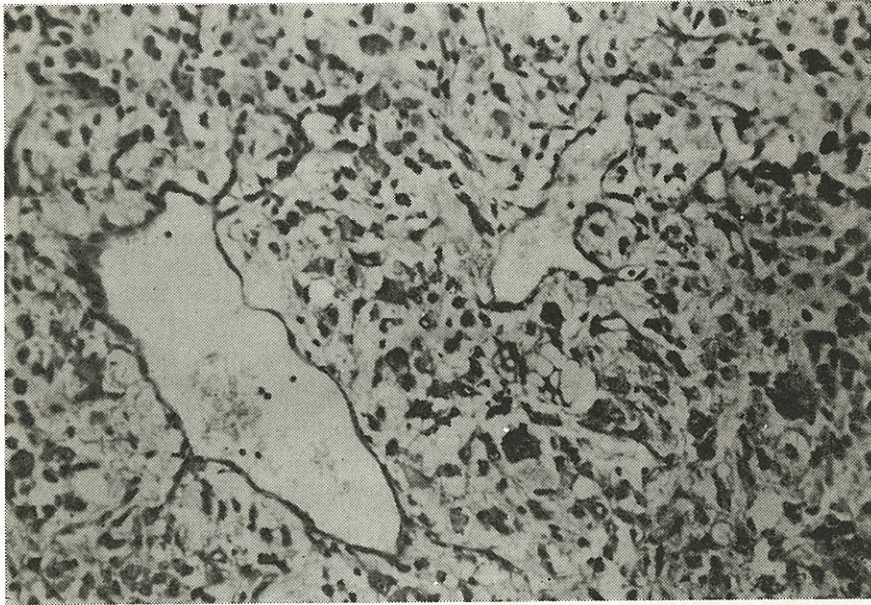


Figure 2

Neuronal and astrocytic components of the tumour tissue as well as large caliber vessels can be seen (Nissl, x150).

Discussion

Gangliogliomas occur most commonly under the age of 30.⁷ According to Henry⁷ the localization in order of frequency was the temporal lobe, cerebellum, parietooccipital lobe, frontal lobe and the spinal cord.

Two percent of subarachnoid hemorrhages occur due to brain tumours.⁸ Subarachnoid hemorrhage due to intracranially located ganglioglioma was reported only once previously.² Our review of the literature failed to find any other report dealing with this uncommon cause.

It is our policy to search for micro arteriovenous malformations and melanomas in intracerebral hematomas especially located at the sites away from the course of major cerebral arteries.⁹ The main reason for the decision of surgery in the present case is the progression of epilepsy plus neurological deficit. The localization of the hematoma was an uncommon site. The histopathologic diagnosis of tumour tissue as ganglioglioma was a surprising finding to us for several reasons. The patient was carefully examined twice in the preoperative period but there was no evidence of tumour in these investigations. In CT studies only large intracerebral hematoma was found. According to Johansson² in gangliogliomas evidence of spontaneous bleeding could be seen. It was probable that the pathologic vessels embedded in the tumour tissue was the source of intracerebral as well as subarachnoid hemorrhage. Gangliogliomas might have vascular stromas.³ The vessels with large calibres could be misdiagnosed as AVM. This was reported by Chovanes and Truex.¹⁰ They found the tumour tissue in the second operation because of micro arteriovenous malformation.

During surgery yellow-brown cystic fluid was supposed as a resorbing hematoma and frozen section from this fluid revealed hematoma filled with macrophages. This type of cyst fluid was also a finding of Rubinstein and Herman.³ As seen from this data gangliogliomas may sometimes have vascular stromas,³ may show evidence of spontaneous bleeding,² and cause intracerebral and subarachnoid hemorrhages.² They must be considered among brain tumours causing intracerebral hematomas.

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A Large Pituitary Adenoma in A Child

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Summary

We have reported a case of non-secreting adenoma in a 12 yearold-boy. This report describes the presentation, preoperative findings, surgical management, and follow-up result of this case.

Key Words: Pituitary adenoma.

Introduction

Pituitary adenoma is a rare tumor in the older pediatric age group.^{1,2} In recent years, numerous publications have been reported on pituitary adenomas in patients of the younger pediatric age group.³⁻¹⁴

In large series of intracranial tumors of the pediatric age period, pituitary adenomas account for only 1 % to 10 % of the total.¹⁵⁻¹⁷ Hoffman mentioned 4 cases of pediatric pituitary adenoma from a series of 344 supratentorial tumors (1.27 %).¹ Guidetti and Fraioli reported that 24 of 319 patients with pituitary adenoma were under 20 years of age (7.52 %).⁶ There is no agreement on the biological behavior of adenomas in this age group.^{11, 12, 14} Pediatric age may be divided into 3 groups based on age at onset of symptoms; 1- prepubertal or childhood, 2- puberty and 3- postpubertal or adolescence. Childhood group is from 5 to 10 years, puberty from 11 to 15 years, and adolescence from 16 to 20 years.⁶

Although Richment and Wilson reported on higher incidence of intrasellar and enclosed adenomas in childhood and adolescence,¹⁵ Kanter et al and Fraioli reported that the patients with onset during the

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pubertal years inclined to be invasive.^{6, 8} Ortiz-Suarez and Erickson suggested that pituitary adenoma in adolescents have a higher incidence of extracapsular extension and invasion of parasellar structures compared to the ones in adults.¹¹

In this report, our patient was 12 years old. His tumor was found to be very large and invaded to the supra and parasellar structures.

Case Report

A 12 year old male was admitted to the Neurosurgical Department at the University of Hacettepe School of Medicine, on December 11, 1987. He had a 6 month history of decreased vision bilaterally. He also had headache but no hypersecreting symptoms of pituitary adenoma.

Physical and Neurological Examination: His height was in the 30th percentile and his weight was in the 25th percentile. The remainder of the general examination was normal. Visual acuity on the right eye was absolute, optic atrophy was evident. On the left, visual acuity was 2/20 and optic atrophy was evident. He had a Macus gunn pupilla on the left eye. The right eye revealed some depression of vision in the superior temporal field. The remainder of the neurological examination was normal.

X-ray examinations revealed sellar enlargement with loss of the sellar floor and erosion of the posterior clinoid and dorsum sella. Endocrine workup results were normal. CT showed that there was a large suprasellar mass which extended to the middle cranial fossa and the base of frontal lobe (Figure 1).

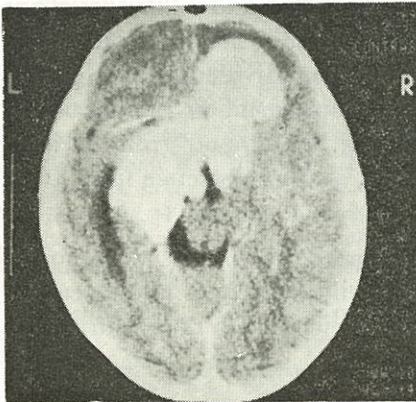


Figure 1a
Preoperative CT appearance.

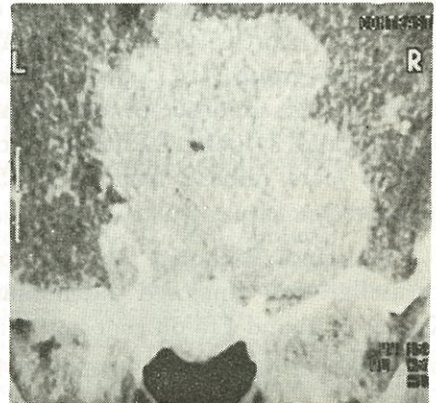


Figure 1b
Coronal section.

Operation: A bifrontal craniotomy was performed revealing a large tumor in close relation to both optic nerves, and extending into the middle cranial fossa and the base of the frontal lobe. The tumor mass was removed subtotally. Histopathological examination showed pituitary adenoma. The postoperative period was complication-free. The patient received postoperative radiation, a total of 5000 rads. At follow-up 3 months later, he had a significant improvement on visual acuity and fields. The control CT is shown in figure 2.

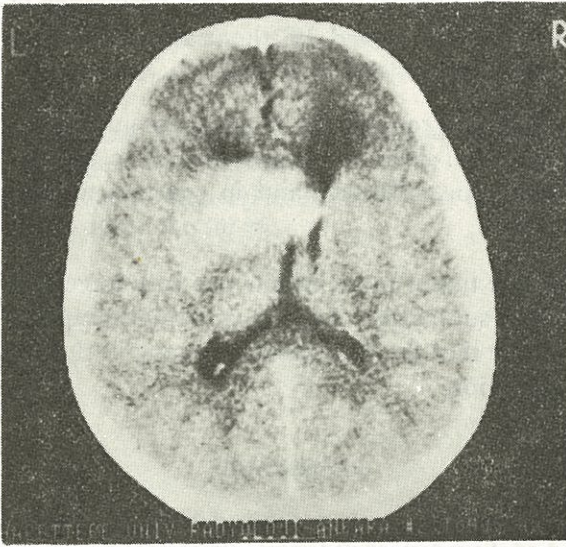


Figure 2
Postoperative CT scanning of the case.

Discussion

Pituitary adenomas are uncommon in the childhood period.^{1, 2, 9} The majority of these are benign hormonally active tumors arising from the 5 hormonal secreting cell types of the adenohypophysis.¹⁸ Only 25 % of these cases are non-functioning.^{13, 18} It is known that the important hormonally active adenomas are GH (gigantism), prolactin and ACTH (Cushing's disease) adenomas. Prolactin secreting adenomas are the most common type of the hormone secreting tumors in adults as in pediatric age group.^{13, 18} The frequency and type of hypersecretion parallels the distribution found in adult series.^{9, 13, 14}

The tumor was enclosed in the majority of adult patients (around 70 %) and invasive in the majority of pubertal patients.^{6, 9} There is an increased incidence of invasiveness in patients with onset of symptoms in

both prepubertal and pubertal years. This condition is inversely proportional to age.⁸

An invasive adenoma may have a very rapid or very long history. Our patient had a six months history. The tumor was located suprasellarly and invaded into the base of frontal and temporal lobe. In addition, it was a non-secreting type adenoma. In this type of patient, surgical intervention should be the first step in treatment. This tumor mass can be removed transcranially, whereas a small enclosed adenoma may be treated by transnasal surgery.^{6, 9, 12, 14} In the preference of the surgical approach, the size and extend of the tumor should be taken into account.^{6, 14}

If it is impossible to remove the tumor mass surgically, postoperative radiotherapy has to be given to the patients. The results with external pituitary irradiation in children stand in contrast to these obtained in adults.¹³

In our case, the tumor mass, which was very huge in size, was transcranially removed subtotally. And than radiotherapy was given externally. We believe that the best chosen therapy in these cases is surgery with external radiation.

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Lumbosacral Intradural Periradicular Ossification

Aydın Paşaoğlu, M.D.*

Summary

The common occurrence of benign arachnoidal plaques has no clinical significance and should be distinguished from the clinicopathological entity of symptomatic arachnoiditis ossificans. Cases involving the cauda equina are very rare. This report presents the occurrence of disabling neurological symptoms from periradicular ossification in the lumbosacral region in a previously healthy man.

Key Words: Arachnoiditis ossificans, Periradicular ossification.

Introduction

Isolated spinal leptomenigeal calcification or ossification is an age-related phenomenon and an incidental finding during an operation or autopsy.^{1, 2} Symptomatic arachnoiditis ossificans is, however, a separate entity and should be distinguished from the former condition.

In the case presented here, ossification developed in the intradural lumbosacral region encasing the roots in the caudal canal with no focal reactive adhesive arachnoiditis. For this, "periradicular ossification" thought to be an appropriate descriptive term.

Case Report

A 47-Year-old man presented with a 25-year history of increasing low backache and two sided sciatica.

The patient was first admitted to a university hospital when he was 37 years old, with a 15-year history of increasing low backache and two sided sciatica. Forward flexion of the spine, and left and right straight leg raising were limited. Hypalgesia was present at the both side of L₅ dermatome. There had been no sphincteric dysfunction. Pantopaque myelography showed no disc protrusion. CSF protein was 0.35 g/l. and the fluid was acellular. No surgical intervention was considered.

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The second hospitalization occurred 10 years later in our clinic, when the patient was aged 47 years. He presented with a two months history of disabling back pain and sciatica, and a ten days history of urinary hesitancy. The lumbar lordosis was increased and extreme paravertebral muscle spasm was present. Forward flexion of the spine was nearly diminished. Straight leg raising was bilaterally limited. Hypalgesia were present at the L₅ and S₁ dermatomes at both sides. There were depression of both ankle reflexes. The remainder of the neurological examination was normal. X-ray showed minimal pantopaque remnant at the L₅ and S₁ root levels. Omnipaque myelography revealed a wide dural sac with flattening on the both side at the L₄-S₁ area. The root shadows were not visualized. CSF protein was 0.40 g/l. All the laboratory studies were normal.

Operation: Hemilaminotomy was performed and the extradural exploration of disc spaces revealed no pathology. Therefore, bilateral laminectomy of L₅ and S₁ was done. On opening the dural layer, a grayish white membrane was seen covering the structures underneath, but no adherence was noted, and arachnoidal layer could not be identified. The roots in the caudal canal were surrounded by, but not firmly adherent to, a hard bony substance. The osseous material was broken off by a microsurgical technique and removed totally. The dura and wound were closed in layer.

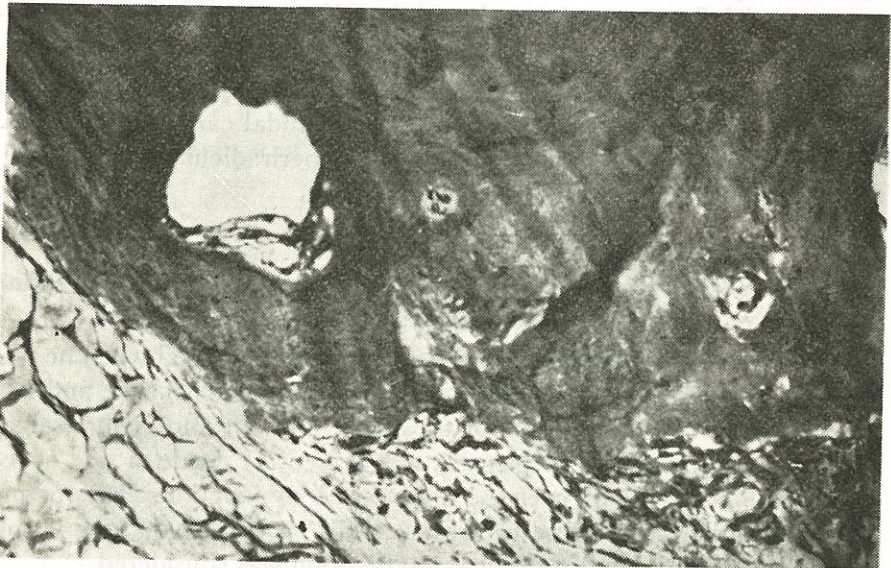


Figure 1

Photomicrograph of resected osseous material. Compact bone is shown surrounded by fibrous connective tissue. HEx160

Postoperative course: Hypalgesia in the perianal region was present postoperatively which slowly cleared. He had dense weakness in the right, and minimal in the left ankle, and urinary incontinence. There was no significant complaints of pain. When examined 18 months after the operation, the pain was almost relieved, the weakness was improved, and there was marked improvement in the motion of the lumbar spine and gait. But, he still had unsatisfactory control of bladder function.

Pathological examination: Histological examination of the resected specimen revealed compact bone and dense fibrosis. There was no evidence of inflammatory, neoplastic, or hemorrhagic changes, and no relationship could be established between the ossification and the pia-arachnoid (Figure 1).

Discussion

Incidental arachnoidal calcification and ossification is a frequent age-related process of no clinical significance. This is thought to be related to the redundancy and trabeculation of the arachnoid, and to calcific degeneration of arachnoidal cell clusters that are found in this region.¹⁻³ Symptomatic arachnoiditis ossificans is, however, a separate clinico-pathological entity and several factors may be involved in its pathogenesis.

Arachnoiditis may be a sequela to repeated lumbar puncture, contrast myelography, surgery, trauma, vascular or neoplastic lesions, and infections.^{1, 4-7} The ossification may be secondary to adhesive arachnoiditis from any of these factors, and it may represent the end point of focal reactive adhesive arachnoiditis.^{7, 8} Endocrinological factors and genetic disposition may also be contributory.⁸

The pantopaque remnant from previous myelography could be blamed for triggering the ossifying process. But, the long standing symptoms could not be explained by this finding. Probably the ossification was responsible for the initial symptoms.

Histological examination of resected osseous material is not contributory in clarifying aetiology. Wise and Smith⁹ stated that arachnoiditis ossificans is a rare variation of arachnoiditis in which there is a deposition of bone within an inflammatory process, and Whittle et al⁸ found an extensive arachnoidal fibrosis surrounding the bony tissue, but some cases may be classified as ossification of the spinal arachnoid, because no inflammatory changes could be demonstrated^{2, 7, 10} as it is the case in our patient. In the present case, the grayish white membrane seen beneath the dura, which may represent a thickened arachnoidal layer,

was not adherent to the bony substance or the roots in the area. Therefore it is difficult to share the suggestion of Whittle *et al*⁸ that focal reactive adhesive arachnoiditis is a precipitating factor for ossification. Consequently, the term "intradural periradicular ossification" suggested by Varughese⁷ seems to be an appropriate term for such cases.

The surgical experience with these cases is too limited to come to a conclusion. Varughese⁷ stated that in spite of surgical decompression, symptomatic relief on a long term basis may not be seen. Nevertheless persistent pain after surgery may be due to insufficient decompression. On the other hand, in spite of meticulous microsurgical technique, the ossified material may be difficult to remove without damage to the roots.

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Systemic Sepsis and Omental Abscess Developed in Splenic Autotransplantation

A Rare Complication

Zafer Ferahköşe, M.D.* / Atilla Engin, M.D., Ph.D. / Şükrü Bozkurt, M.D.*****

Summary

Splenic autotransplantation is a procedure that can be undertaken in order to preserve the functional splenic tissue after splenectomy. Omental abscess and systemic sepsis are extremely rare complications of splenic autotransplantation.

In this present study, a case with systemic sepsis and omental abscess due to the splenic implant placed into the omentum following an elective operation is discussed.

Key Words: Systemic sepsis, omental abscess, splenic autotransplantation.

Introduction

It was reported that the sepsis and mortality rate is 0.66 percent following splenectomy and it is found to be 58 fold higher in adults in comparison to the mortality rate in the general population.^{1, 2, 3} Splenic salvage^{4, 5, 6} and splenic autotransplantation,^{4, 5, 6, 9} are the two advisable methods for the continuity of the immunological functions of the spleen after splenic rupture followed by splenectomy.

Systemic sepsis due to abscess in the implantation pouch is an extremely rare occurrence in spleen autotransplanted patients.¹⁰ The case

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discussed below, presented with systemic sepsis due to abscess in the omental pouch following splenic autotransplantation.

Case Report

A 53 year-old woman suffering from pain in the right and left epigastrium, diffuse skin rash and itching, was admitted to the surgical department, Faculty of Medicine, Gazi University. Physical examination of the patient revealed that she had diffuse skin rash, scratches and a mass 10 x 15 cm in size in the left hypochondrium. Eosinophilia was found to be 1 % in blood smear. Abdominal ultrasonographic examination showed two cystic masses of 10 cm x 10 cm and 8 cm x 12 cm respectively in the posterior segment of the right lobe of the liver with an additional cystic mass of 20 cm x 18 cm adhering to the front of the pancreas and inferior medial of the spleen in the left abdomen. During the elective operation of the patient, all three cysts were found to be uninfected hydatid cysts. Partial cystectomy and omentopexy were performed on the two cysts localized within the liver. Cystectomy was performed on the other cyst in the left abdomen. Splenectomy was also performed due to the latter cyst being adherent to the spleen. The upper pole of the spleen was sliced into pieces of 2 cm x 2 cm x 3 cm in size. All of these slices were washed with saline and were placed in a mass into a pouch prepared in the major omentum. The pouch was closed using a 4/0 steel wire. Three sump drains were placed into the right subdiaphragmatic, right subhepatic and left subdiaphragmatic areas. Hydrothorax developed on the left side of the chest on the second postoperative day; 800 cc of fluid was removed by thoracentesis. Bacteria were not found by Gram stain and the culture was negative. The drains were removed on the seventh postoperative day. Bacterial growth was not encountered from the materials taken from the tips of the abdominal drains. Following the tenth postoperative day, the patient's temperature rose up to 40 °C and the white blood cell count was 26000/mm³. Roentgenological examination revealed a negligible amount of fluid collection on the left side of the chest. On the 18th day after the operation, a massive collection under the right subdiaphragmatic area with a size of 5 cm x 8 cm was discovered by ultrasonography. Ceftriaxone sensitive *Proteus* species were cultered in blood and ceftriaxone was prescribed daily, 2 x 2 gram intravenously. In spite of the antibiotic regimen, the patient's situation did not improve. The patient underwent a surgical intervention on the 18th postoperative day with the diagnosis of a right subdiaphragmatic abscess. However no abscess was found during the abdominal exploration of both subdiaphrag-

matic spaces. There was a mass with a size of 10 cm x 7 cm filled with pus in the splenic implantation pouch. 30 cc of necrotic material was obtained by needle aspiration. This fluctuating mass was resected totally, together with a part of the major omentum (Figure 1).

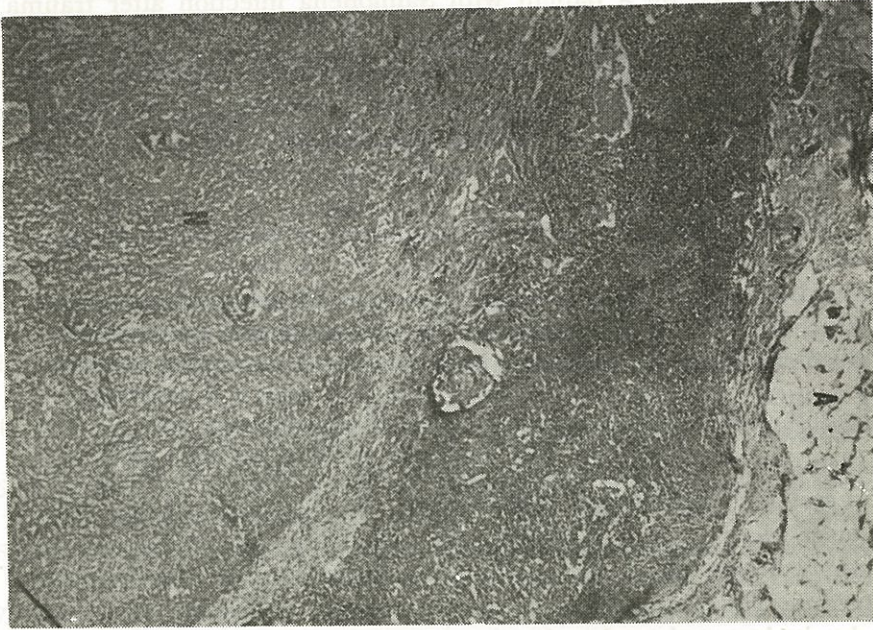


Figure 1

Histopathologic findings of the splenic implant abscess in the eighteenth posttransplantation day. (6.3 x 1.25 x 10 HE) S: Splenic tissue, A: Adipose tissue, N: Necrotic area.

Proteus was cultured from this necrotic material taken from the mass. During the second postoperative period, the patient's temperature returned to normal on the second day and the white blood cell count was 8000/cm³. Antibiotic administration was stopped on the seventh day, the patient was discharged on the 14th postoperative day.

Discussion

Infection due to immunosuppression in heterotropic kidney and pancreatic transplantation is a serious problem and infective complications in these types of transplantation procedures frequently result in graft failure.^{11, 12} Since there is no immunological response in parathyroid, islet cell pancreatic and vascular autotransplantation, infection problems have not been reported leading to graft failure.^{10, 13, 14} However, there have been several reports concerning serious intraabdominal infection and sepsis which have led to graft failure due to immunological

insufficiency until normal splenic functions were acquired even though successful splenic implantation were performed: In 1983, it was first reported that abscess developed in implant following splenic autotransplantation.¹⁵ Later in 1985, splenectomy and splenic autotransplantation were performed on a patient with *Salmonella* infection after trauma, but *Salmonella sandiego* was isolated in both blood culture and the abscess which developed in the transplantation area.¹⁶ Recently in 1988, it has been reported that abscess developed in the splenic autotransplanted omental pouch after an elective operation and staphylococcus epidermiditis was cultured from pus and blood culture.¹⁰

In the present case as mentioned above, abscess developed in the omental pouch which contained splenic slices following an elective cyst hydatid operation and proteus species were cultured from pus and blood culture. Actually, it was suggested that the implanted spleen developed either in the form of splenosis or from peripheric cell regeneration following complete necrosis of the implant during the first week of autotransplantation.^{17, 18} Abscess develop in the omental pouch due to the inadequacy of vascular formation during the operation or the existence of a systemic bacteriemia. Additionally, the placement of the implant as large pieces or as a mass into the omental pouch retards the development of the blood circulation and facilitates the development of infection. This is especially the case in patients with trauma or major abdominal operations that the development of intraabdominal abscess and systemic sepsis increases the mortality and the morbidity rate.¹⁹

In conclusion, it is suggested that the splenic implantation should not be performed in contaminated or infected situations; splenic implantations must be performed under strict sterile conditions. Also; in order to improve the blood supply of the splenic implant, the spleen slices should be placed in different omental pouches as separate and small pieces.

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Can Screening for Glaucoma be Improved?

Pınar Kırkalı, M.D.* / Bertil E. Damato, F.R.C.S., Ph.D.**

Summary

Glaucoma is one of the major causes of blindness; and prevention of blindness from glaucoma has long been one of the most important goals in ophthalmology. Patients with glaucoma are usually diagnosed when their visual handicap is imminent. Therefore, screening for glaucoma is essential for early diagnosis.

The Oculokinetic visual field test, which plots the glaucomatous visual field defects as precisely as conventional techniques, was developed for use in the community, because it is simple and economical. We believe that testing for early glaucomatous visual field loss with the Oculokinetic test-charts may shortly become as quick and routine as testing of the visual acuity and could, therefore, prove to be the key to the prevention of blindness from glaucoma.

Key Words: Glaucoma, Visual Field Test, Prevention of Blindness.

Glaucoma is one of the major causes of blindness, not only in industrialised countries¹ but also in many parts of the Third World,² and the problem is growing in the line with improvements in the life expectancy. Glaucoma tends to cause bilateral, irreversible, and, eventually total blindness which deprives individuals of their livelihood and independence their enjoyment of the visual arts, their contact with their family and friends, and sometimes also of their own sanity. The prevention of blindness from glaucoma has long been one of the most important and elusive goals in ophthalmology. This essay highlights the main reason for lack of progress and outlines a new approach to the problem.

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Glaucoma is characterised by atrophy of the retinal nerve fibres due to their interruption at their point of exit from the eye, that is, at the optic disc. This pathological process results in excessive cupping of the optic disc and progressive constriction of the visual field. This destructive process is somehow related to a high intraocular pressure, caused by a high resistance to aqueous outflow at the trabecular meshwork. The pathogenesis of this obstruction is unknown in the vast majority of cases, who are then said to be suffering from primary open angle glaucoma.

Treatment of the disease is aimed at reducing the intraocular pressure to a level at which deterioration of vision is arrested. This can successfully be achieved, in most cases, by medical, surgical or laser therapy which reduces aqueous production or which increases aqueous drainage from the eye. The safety and efficacy of such therapeutic procedures have improved greatly over the past few decades. It is a great tragedy, therefore, when a patient goes blind for lack of treatment.

Patients with glaucoma are not usually aware of their disease until they have reached the stage when severe visual handicap is imminent. This is because they do not develop any external physical signs, and do not usually experience any pain or intrusive visual defects. Because of its insidious and irreversible nature, glaucoma would seem to be a good target for large-scale screening. Unfortunately, until now, such preventive programmes could only be undertaken by ophthalmic personnel because the lack of an appropriate test has made more widespread screening un-economical, even when directed at individuals with increased risk (ie. first degree relatives and individuals suffering from diabetes mellitus, systemic hypertension).

Screening for glaucoma has been based on three tests: 1. The detection of an abnormally high intraocular pressure by tonometry, 2. The recognition of pathological cupping of the optic disc by ophthalmoscopy, or 3. The identification of typical patterns of visual field loss by perimetry. Although all three tests need to be performed to establish a diagnosis of glaucoma, none have been adequate for screening purposes. It has been shown that reliance on a single intraocular pressure measurement will miss one patient with glaucoma for every patient detected, whilst identifying about ten individuals with a high intraocular pressure, of whom only a small minority will eventually develop glaucomatous visual loss.³ Assessment of the degree of optic disc cupping is difficult, both from the technical point of view and because of the extensive variation in appearance that exists in the normal population. Screening for glaucoma by ophthalmoscopy in isolation will therefore produce many equivocal

cases, even when performed by a specialist, unless it is merely aimed at detecting very advanced disease.

Ophthalmoscopy can be enhanced by visualisation of defects in the retinal nerve fibres, using high quality photographs,⁴ or by measurement of the neuroretinal rim area in the optic disc, using computerised image analysis.⁵ It is unlikely, however, that such sophisticated research tools will ever play a major role in the community because of their cost and complexity. Measurement of colour vision⁶ and contrast sensitivity⁷ are other tests that have failed to gain widespread use. A number of studies have indicated that visual field examination is potentially the best screening test for glaucoma.⁸

Although visual field loss can be caused by other conditions, such as cataract, corneal scarring, amblyopia and macular degeneration, these can readily be identified by non-ophthalmic primary health care workers.⁹ Unfortunately, conventional perimetry is too expensive for widespread use in the community.¹⁰

In 1983, the need was recognised for a simple and inexpensive visual field test, for use in the community, and developed what came to be known as the Oculokinetic visual field test. This comprises a white tangent screen which has a central black test-stimulus and a series of numbers distributed peripherally at strategic locations (Figure 1). As the subject looks at each number in turn, from a known working distance, the image of the test stimulus impinges onto pre-selected points on the retina. Numbers associated with disappearance of the test stimulus are noted on a special record sheet, so that a plot of the defective visual field is obtained. The simplicity of the procedure is such that patients with glaucoma are also able to perform selfassessment of the visual fields without direct supervision, using a disposable and fully portable paper test chart.¹¹

Extensive evaluation performed by one of us (B.E.D.) and independently by other workers has shown that glaucomatous visual field defects can be plotted by the Oculokinetic visual field test as precisely as sophisticated and expensive conventional techniques.¹² The initial results of a study still in progress suggest that individuals with early glaucomatous visual field defects can be distinguished from age matched normal controls by means of a "dedicated," test chart containing only 10-20 numbers. If this preliminary finding is confirmed by more extensive studies in the community, then screening for glaucoma would be greatly facilitated.

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