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CASE REPORT

Leptomeningeal carcinomatosis: a rare phenomenon in neurology?

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ABSTRACT

Leptomeningeal involvement may be caused by various conditions, and patients may present with different clinical findings. The causes of this condition may be carcinogenic, infectious, inflammatory and autoimmmunity. The prognosis is dependent upon the underlying cause.

We present three cases of leptomeningeal involvement with different diagnoses and clinical findings.

Keywords: leptomeningeal involvement, leptomeningeal carcinomatosis, rheumatoid arthritis, neuroendocrine tumour, magnetic resonance imaging

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INTRODUCTION

The leptomeninges contain the arachnoid and pia layers, and the pachymeninges contain the dura. Leptomeningeal carcinomatosis (LC) is the infiltration of the cerebrospinal fluid and the leptomeninges of the brain and spinal cord with tumour cells [1-3]. Leptomeningeal metastasis (LM) is seen in 4-15% of solid tumours. It is the first sign of metastasis in 10% of cases [1]. Rarely, primary involvement of the leptomeninges has also been reported in diseases such as lymphoma, glioma, melanocytosis and amyloidosis. In addition, the leptomeninges may be affected by autoreactive T-cell traffic in autoimmune diseases such as systemic lupus erythematosus (SLE), sarcoidosis and rheumatoid arthritis (RA) [1,2]. Patients may present with headache, vomiting, cranial nerve deficits, seizures, loss of strength and sensation, gait abnormalities, incontinence and hydrocephalus [2,3]. Contrast enhancement on computed tomography (CT) or magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) cytology are important in the diagnosis [2,3].

In this study, we aimed to discuss three cases with different diagnoses and different clinics in which leptomeningeal involvement was found in the light of the literature. Written informed consent was obtained from patients for publication of this case report and any accompanying images.

CASE-1

A 53-year-old man presented with complaints of stuttering in his speech and involuntary movements in his right arm and leg for one month. On neurological examination, the patient was observed to be cooperative and oriented. Cranial nerve examination was normal, cerebellar tests on the right were unsuccessful, and tandem gait was impaired. Additionally, myoclonic jerks were present on the right. Electroencephalogram showed bifrontal epileptiform activity. Contrast-enhanced cranial MRI showed left parietal leptomeningeal involvement (Figure 1). No significant pathology was found on direct examination, biochemistry, culture, and cytology of CSF. Blood tests for vasculitis showed elevated levels of C-reactive protein at 25mg/dL (<5mg/dL), rheumatoid factor at 128.7 IU/mL (<20IU/mL), and anti-cyclic citrullinated peptide at >500 IU/mL(<15IU/mL). Tumour markers were negative. Following rheumatology consultation, the patient was diagnosed with rheumatoid arthritis. Valproic acid 2x500 mg and intravenous methylprednisolone (1000 mg/day) were added to the treatment for myoclonies for 7 days. Follow-up treatment was planned with oral methotrexate tablet (15 mg/week), methylprednisolone (4 mg/day) and valproic acid (2x500 mg). After this treatment he had no active complaints.

CASE-2

A 49-year-old man with no known chronic disease, presented with a generalised tonic-clonic seizure. The patient had a 4-month history of progressive girdle pain and gait disturbance. He had been bedridden for 2 months, had double vision and hoarseness for 1 month. On neurological examination, the patient was observed to be cooperative and oriented. Cranial nerve examination was normal, while motor system examination revealed muscle strength of 4/5 in all extremities. Deep tendon reflexes (DTR) were globally absent. Lumbar MRI showed multiple bone metastases and contrast-enhanced brain MRI showed leptomeningeal involvement (Figure 2). Lumbar puncture revealed that the protein level was 242mg/dL (15-45 mg/dL), the glucose level was 46,2 mg/dL in the CSF, no cells were found. No significant pathology was found in CSF culture and cytology results. Intravenous methylprednisolone (1000 mg/day) and levetiracetam (2x500 mg) were administered. The bone marrow biopsy, performed as a screening for malignancy, was consistent with a small cell neuroendocrine tumour. The patient who was planned to be referred to medical oncology for chemotherapy, was referred to intensive care unit due to his poor general condition. He died two months after admission to the hospital.

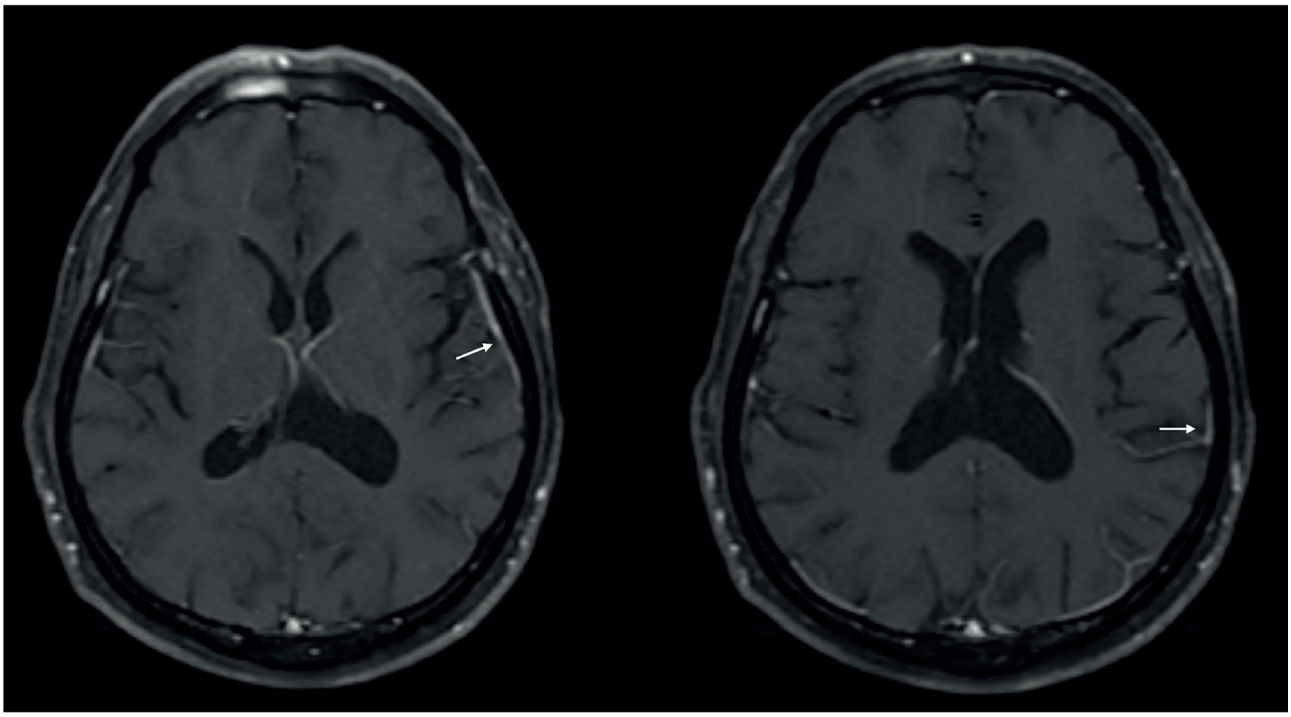

Figure 1. Case-1. Contrast-enhanced MRI of brain. Contrast-enhanced T1-weighted axial image. Showed left parietal leptomeningeal involvement (white arrow).

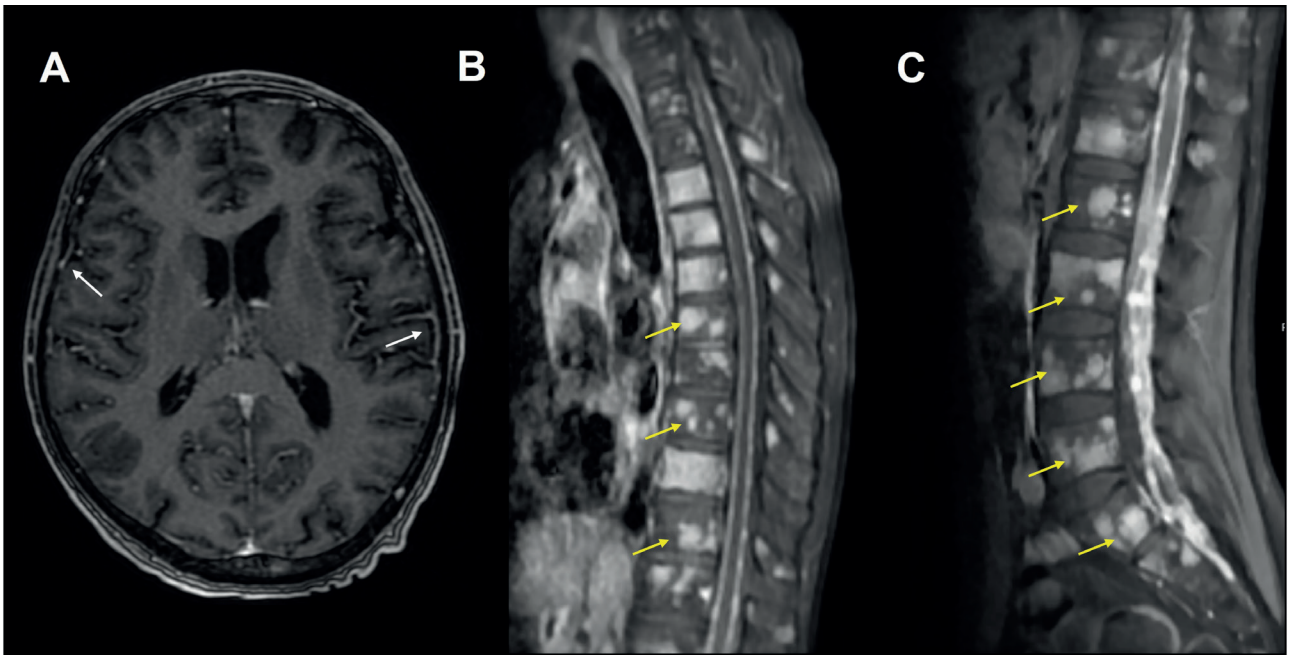

Figure 2. Case-2. (A) Contrast-enhanced MRI of brain. Contrast-enhanced T1-weighted axial image. Showed leptomeningeal involvement (white arrow). (B) Contrast-enhanced thoracic spine MRI. T1-weighted sagittal image (yellow arrow). (C) Contrast-enhanced lumber spine MRI. T1-weighted sagittal image. Showed multiple bone metastases (yellow arrow).

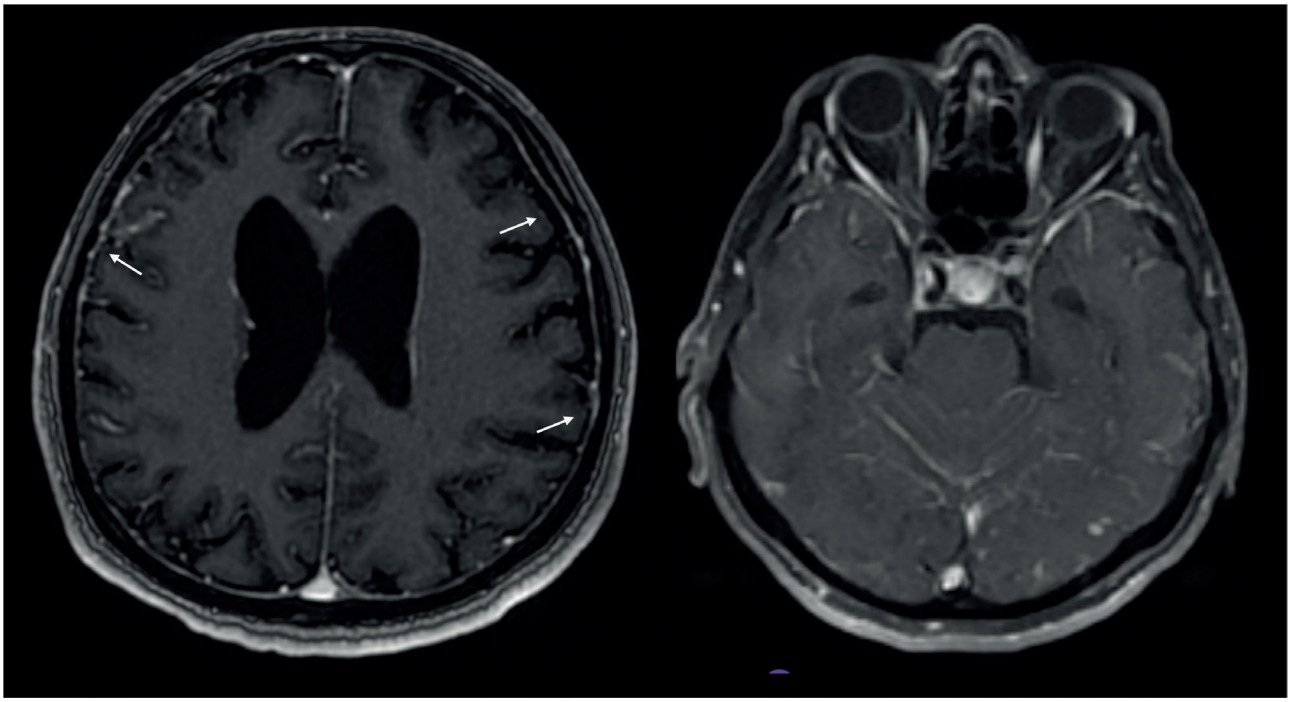

Figure 3. Case-3. Contrast-enhanced MRI of brain. Contrast-enhanced T1-weighted axial image. Showed leptomeningeal involvement (white arrow).

CASE-3

A 72-year-old male patient presented with complaints of slurred speech and difficulty walking, which developed following diarrhea and lasted for ten days. During the neurological examination, the patient was conscious, cooperative, and oriented. The patient had dysarthric speech, paralysis of the sixth cranial nerve on the right and paralysis of the central facial nerve on the left. The patient's gait was ataxic and DTR were hyperactive. The patient was diagnosed with pancreatic cancer a year ago,

and metastases in the liver and lungs were later detected on CT scans. Whole body Positron Emission Tomography-Computed Tomography (PET-CT) imaging revealed diffuse metastatic findings throughout the body, and the contrast-enhanced brain MRI showed leptomeningeal involvement (Figure 3). There was a rapid deterioration in the patient's general condition and he died within a week.

DISCUSSION

The leptomeninges, the cerebrospinal-fluid-filled tissues surrounding the central nervous system, play host to various pathologies including infection, neuroinflammation, autoimmune disease and malignancy [4,5]. Patients may present with a variety of clinical symptoms and the prognosis depends on the cause of the leptomeningeal involvement. Carcinomatous meningitis, also known LM or LC, is a rare complication of advanced cancer that occurs when the disease spreads to the meninges surrounding the brain and spinal cord, often from neoplastic causes or, less commonly, from infectious causes that disrupt the blood-brain barrier [3].

In autoimmune diseases such as SLE, sarcoidosis and RA, it is important to consider leptomeningeal involvement as a potential differential diagnosis [1,2]. Although CNS involvement is observed in SLE, aseptic leptomeningeal involvement has been reported very rarely with a rate of 1.4-2% [6,7]. This may be due to increased inflammatory molecules resulting from autoimmune pathology and dysregulation in the clearance of immune complexes [8]. Rheumatoid meningitis may present with seizures resistant to antiepileptic treatment, recurrent stroke-like episodes, or aseptic meningitis with headache, fever, and altered consciousness [9,10].

The 5-year survival rate for pancreatic cancer is less than 5%. CNS and leptomeningeal involvement are rare, occurring at a rate of 0.3%, and prognosis is worse in these cases [9,11]. Neuroendocrine tumors (NETs) are a group of heterogeneous malignancies of epithelial or neural origin, with a range of histologies including low-grade carcinoid, intermediate-grade atypical carcinoid, and high-grade small cell neuroendocrine carcinoma. Small cell neuroendocrine carcinomas (SCNC) are highly aggressive and have a high recurrence rate [12]. Leptomeningeal involvement is reported as case reports in poorly differentiated NETs [13-16].

Our cases were leptomeningeal involvements with different diagnoses. Two cases were carcinomatous and one case was inflammatory. Clinical findings were widely described, including headache, speech disorder, cranial nerve findings, epileptic seizures, paresis, ataxia, and urinary incontinence [2,3]. Different clinical patterns were also observed in our cases.

CSF have an important role in the diagnosis [17]. When investigating CSF, it is important to examine cell count, pressure, protein and glucose levels, as well as perform cytological and immunohistochemical examinations and tumor marker tests [17]. Our second case showed a significant elevation in CSF protein, which is consistent with findings in the literature. The first case with leptomeningeal involvement of RA had normal CSF protein. The third case with pancreatic cancer, lung metastasis and LC could not be lumbar punctured due to rapid deterioration. It is important to note that malignant cells can be detected in the initial CSF cytology in only 50% of LC cases [18]. Therefore, repeat lumbar puncture is recommended. In addition, elevated protein level and decreased glucose level in CSF may also help in diagnosis [19]. Studies have reported that tumor markers in CSF can be detected earlier than radiological findings and are more diagnostic than those in serum.

MRI and CT are important radiologic imaging techniques for the diagnosis, prognosis, and survival of LM. Although contrast-enhanced imaging is more sensitive than cytological examination, it is not specific [17]. Studies have shown that contrast-enhanced T1-weighted sequences in MRI are more sensitive in the detection of LM [20]. In our cases, leptomeningeal contrast enhancement was also observed in MRI with contrast-enhanced T1 sequence.

The prognosis for patients with LC is poor, with limited survival of 1-4 months [1,2]. Palliative treatment options have been used to prolong survival to six months, but there have also been reports of protection against further neurological deficits [21]. It has been reported that

leptomeningeal involvement due to autoimmune causes has a better response to treatment [21]. In the Apostolidis et al. series the mean duration of survey in patients with LC was reported to be ten months [22]. In our cases, the first patient had complaints for one month, the second patient had complaints for four months, and the third patient had a diagnosis of pancreatic cancer one year ago, and a ten-day history of clinical deterioration. The second patient died two months after hospitalization, and the third patient died one week after hospitalization due to rapid progression.

In conclusion, leptomeningeal involvement resulting from disruption of the blood-brain barrier may occur as a result of malignancy, infection, autoimmune causes such as SLE, sarcoidosis, and RA. It causes a wide variety of symptoms depending on the site of involvement of the leptomeninges; therefore, clinical presentation of patients may vary. CSF examination and radiological imaging, especially MRI, play important roles in diagnosis. The prognosis of LC is poor and aggressive and palliative treatment options are used; rheumatological and infectious causes have a better prognosis. In cases with multisystemic and different neurological symptoms, leptomeningeal involvement should be kept in mind.

The limitation of this study is that it included 3 cases of leptomeningeal involvement due to solid tumor, neuroendocrine tumor and rheumatoid arthritis. This subject needs to be reviewed with larger case series or meta-analyses including multiple studies.

Author contribution

Study conception and design: BGB, ES, and SK; data collection: BGB, BCOK, PB, ES, and SK; analysis and interpretation of results: BGB, ES, BCOK, PB, SK, MGŞ, and MFÖ; draft manuscript preparation: BGB, ES, BCOK, PB, SK, MGŞ, and MFÖ. All authors reviewed the results and approved the final version of the manuscript.

Ethical approval

The informed consent was obtained from the patient for the participation and publication.

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Conflict of interest

The authors declare that there is no conflict of interest.

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