acta medica

CASE REPORT

Pelger-Huët Anomaly (PHA) Case Report

Hamza Sümter[1]
ORCID: 0000-0002-0224-9438

[1] Uşak Training and Research Hospital, Clinic of Hematology, Uşak, Türkiye

Corresponding Author: Hamza Sümter
E-mail: hamzasumter@gmail.com

ABSTRACT

Pelger-Huët anomaly is a rare benign hematological disorder. It was first described in the 1920s. It is inherited in an autosomal dominant manner. Nuclear hypolobulation, which can also be seen in other leukocytes, especially neutrophils, is a characteristic feature. This morphological change does not cause a defect in the immune system. It should be differentiated clinically from pseudo-Pelger-Huët anomaly (PPHA). In this study, Pelger-Huët anomaly is presented which is noticed in the peripheral smear of a 22-year-old female patient who came to the hematology outpatient clinic due to her sibling having Hodgkin's lymphoma. The family members of the case were also evaluated in this respect.

Keywords: Pelger-Huët anomaly, benign, hyposegmentation, lamin B receptor, Pince-Nez.

Received: 24 February 2024, Accepted: 14 July 2024, Published online: 30 September 2024

INTRODUCTION

Pelger-Huët anomaly (HPA) is known as hypolobulation in leukocytes. A well-prepared peripheral smear and careful evaluation is essential for diagnosis. While the incidence of the mono allelic form of Pelger-Huët anomaly is 1 in 6000, the biallelic form is much more rare [1,2]. Hypolobulation in neutrophil nuclei can be bilobed (2-lobed) as well as non-lobulated (1-lobed). In the two-lobed nuclear structure, the lobes are connected by a thin chromatin. This change in the neutrophil nucleus can also be seen in eosinophils, lymphocytes and monocytes [3]. Neutrophilia is not expected in the blood count. In studies, the immunological functions of PHA cells were found to be normal [3]. Although different prevalence rates were reported due to its asymptomatic nature, the real frequency of this hematological disorder cannot be known [4].

CASE REPORT

A 22-year-old female patient, who applied for examination due to her sibling's history of Hodgkin lymphoma, was evaluated at the hematology outpatient clinic. The patient's anamnesis showed no medical or herbal drug use. She had no known systemic disease. No lymphadenopathy was detected on physical examination. B symptoms(fever, weight loss, night sweats) were not present. Biochemical tests (transaminases, renal function tests) were within the normal range. Complete blood count: Leukocyte (WBC): 6160/ µL, Neutrophil(ANC): 3640/µL, Hemoglobin(Hgb): 14.2 g/dL, Platelet: 409000/ µL. Peripheral smear examination reported 60% neutrophils, 35% lymphocytes, 5% monocytes. Neutrophil classification was as follows: 80% 2-lobed, 10% 1-lobule (nonlobule), 10% band formation (Figure 1-4). Peripheral blood smear was performed every 2-3 months for approximately 8 months and it was observed that hypolobulation continued at similar rates. In the genetic study conducted for the LBR gene, p.Leu177(c.530T>G) mono allelic was detected. Ten people were contacted as close relatives (mother, father, sibling, 5 aunts, 1 cousin, 1 uncle) and evaluated for Pelger-Huët anomaly. However, their peripheral smears were found normal.

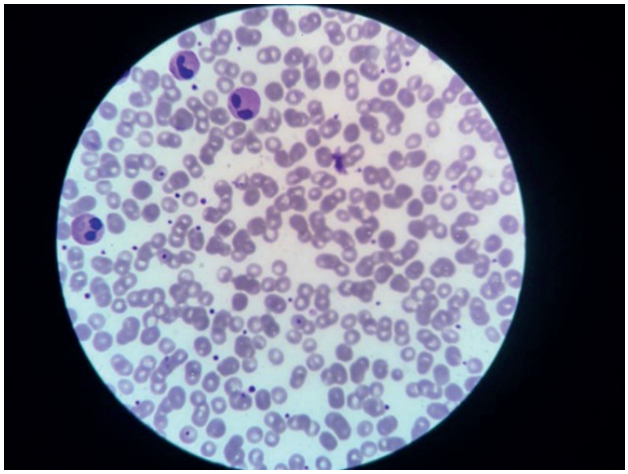

Fig. 1

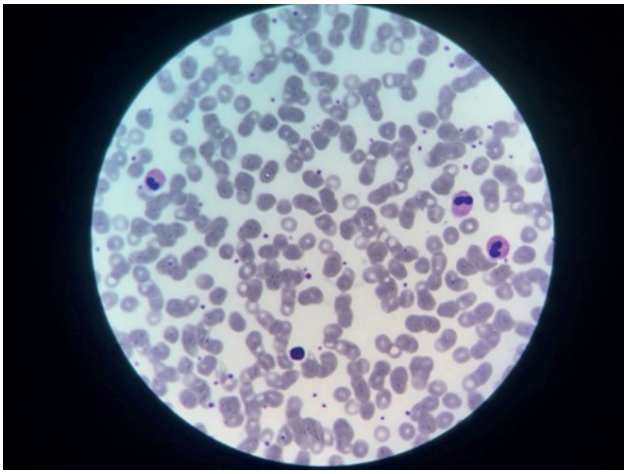

Fig. 2

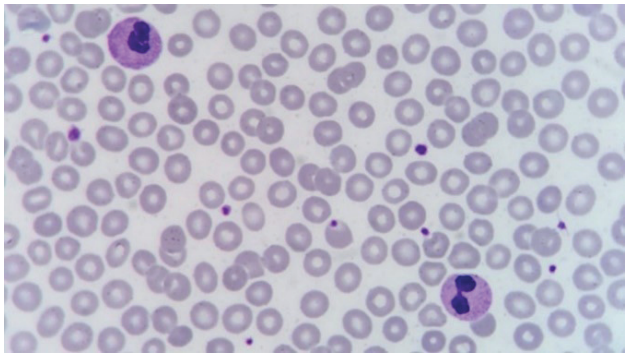

Fig. 3

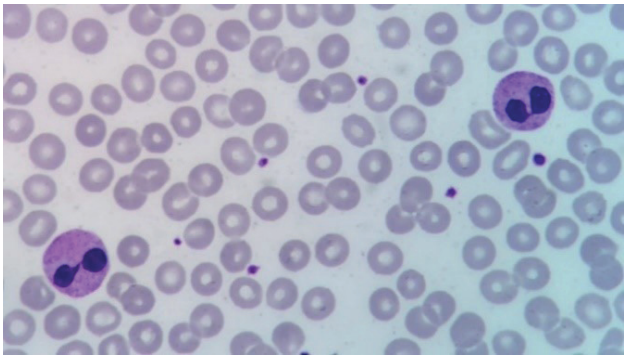

Fig. 4

DISCUSSION

In a normal peripheral blood smear, the majority of neutrophils (approximately 70-75%) have 3-4 segments, while a small number of cells may have more than 4 or less than 3 segments [1].

Pelger-Huët anomaly (PHA) was first described in 1928 by the Dutch doctor Pelger in a tuberculosis patient. This anomaly was considered to have a poor prognosis since the patient died during clinical follow-up [5,6]. It was also described in 1932 by the Dutch pediatrician Dr. Huët in another tuberculosis patient. However, since the patient recovered during the follow-up, it was concluded that this malformation in the leukocytes did not have a bad prognosis [7].

Autosomal dominant transmission is seen in PHA. The mutation is in the gene encoding the lamin B receptor (LBR) protein. This gene is located on the long arm of chromosome 1 (1q41-43). Deficiency in the amount of lamin B receptor (LBR) protein is associated with neutrophil hyposegmentation[8]. Peripheral smear findings may differ in biallelic and mono allelic interactions. Bilobulation is predominant in neutrophils in the mono allelic form. In the biallelic form, non-lobulated neutrophil morphology is more prominent [3,7]. The nuclear structure in non-lobulated cells may be round, oval or peanut shaped [3,7]. In homozygotes, in addition to hyposegmentation in blood cells, mental retardation, epilepsy, developmental delay, skeletal anomalies, macrocephaly with prominent forehead, ventricular septal defect, and metacarpal shortness may occur[8]. In experimental studies, it was observed that the lifespan and immunological functions of PHA cells were normal [1,2]. Although the studies conducted in animals lead to different results, in humans no mortality risk was detected in Pelger-Huët anomaly [5].

Biallelic PHA, which is much less common compared to the mono allelic form, was first described in rabbits. biallelic rabbits have severe chondrodystrophy, skeletal anomalies, and increased prenatal and postnatal mortality (>80% mortality) [5, 8]. The biallelic form was first described in humans in 1952 in a Dutch girl. Convulsions (familial convulsions), psychomotor and mild physical developmental delay were observed in

this patient. In the peripheral smear of the same patient, it is detected that 94% of the neutrophils were round-shaped, non-lobulated neutrophils [6]. Biallelic PHA is known to be very rare in humans, in fact even in a study conducted in 2021 as to biallelic PHA, it was reported that there were fewer than 10 known cases [3]. In a few cases identified as biallelic in humans, congenital anomalies were rarely reported [5]. Although the neutrophils in rabbits and humans are structurally similar, it was concluded that the biallelic disorder does not cause death and skeletal disorder in humans [5].

Patient history (medication use, infection status) and the percentage of pelgeroid cells in the peripheral smear are important in distinguishing PHA from pseudo-Pelger-Huët anomaly (PPHA). In PPHA, three-lobed neutrophils predominate, while a small number of pelgeroid cells are present. In HPA, the predominant cells are 2-lobed. Even in biallelic HPA cases, there is a dominance of non-lobulated neutrophils. In addition to hyposegmentation in neutrophils, band form may be seen in a small number of cells. In PPHA There is a secondary cause that may cause hypolobulation in the peripheral smear. Myelodysplastic syndrome, acute myeloid leukemia, myeloproliferative neoplasia, lymphoproliferative disease, some drugs (ibuprofen, tacrolimus, ganciclovir, co-trimaxazole, itraconazole, fludarabine, rituximab, citalopram, lorezepam, valproic acid, colchicine, mycophenolate mofetil), infections (HIV, tuberculosis , mycoplasma, malaria, influenza) can cause PPHA [1,3].

Hyposegmentation in PHA cells must be distinguished from granulocyte precursors (myeloid precursor cells). While the nucleus to cytoplasm ratio is high in granulocyte precursors, this ratio is low in neutrophils with PHA[3]. While normal neutrophil segmentation is absent or minimal in congenital PHA, hypolobulation is found in a small number of cells in MDS or other acquired PPHA conditions [7]. Additionally, in hypolobulation in PPHA, the lobes are non-symmetrical [9]. A distinction should also be made between PHA cells with a single lobe (round - oval nucleus) and myelocytes. Compared to typical myelocytes, the nucleus in a HPA cell is smaller, denser and more compact. The nucleus to cytoplasm ratio is lower than the one for myelocyte [9]. Another nuclear shape, the peanut-shaped Pelger-Huët cell may resemble a metamyelocyte [7].

According to Ham's classification, neutrophils are divided into 3 groups [3]:

Type A: Nucleus more than 2 lobes

Type B: The nucleus is 2-lobed (dumbbell-shaped). Pince-nez cells consist of a symmetrical 2-lobed nucleus.

Type C: Nucleus non lobule. Round or oval shaped. They are known as Stodmeister cells.

In congenital mono allelic HPA, type B (2-lobed) neutrophils are dominant, while type A and type C are found in small numbers.

In congenital biallelic HPA, type C neutrophils are dominant, while type A and type B are present in small numbers.

In PPHA, type A neutrophils are dominant, while type B and type C are found in small numbers [3].

Mutation in the LBR gene has been identified also in Greenberg/HEM dysplasia, which can show hypolobulation like HPA in peripheral blood smear. Greenberg/HEM dysplasia results in in utero exitus. A total of 8 cases were described in the article published in 2015. HPA was also detected in the peripheral blood smear of two patients with this diagnosis [5]. However, no information was available about the peripheral smear of the other cases. For this reason, it was stated that a neutrophil morphology connection cannot be established between Greenberg/HEM dysplasia and PHA [5,7].

CONCLUSION

Pelger-Huët anomaly (HPA) is a rare hematological disorder and is caused by lobulation deficiency in the leukocyte nucleus. It is noticed by hypolobulation due to a defect in the LBR gene. Although it is stated that it is effective in the diapedesis and chemotaxis of lobulated leukocytes in the nucleus, there is no retardation in immune functions in people with HPA compared to normal people. People with HPA may not even be diagnosed since it is asymptomatic. However, it is important to distinguish it from pseudo Pelger-Huët anomaly (PPHA), which may develop due to secondary causes.

Author contribution

Study conception and design: HS; data collection: HS; analysis and interpretation of results: HS; draft manuscript preparation: HS. The author reviewed the results and approved the final version of the manuscript.

Funding

The authors declare that the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

[1] Ayan M S, et al. Case of acquired or pseudo-Pelger-Huët anomaly. Oxf Med Case Reports 2015. 2015(4): 248-50.

[2] Shah S S, et al. Familial Pelger-Huet Anomaly. Indian J Hematol Blood Transfus 2016. 32(Suppl 1): 347-50.

[3] Padmapriya B, et al. Pelger-Huet anomaly: A Rare case report. 2020. 9(4): 255-258.

[4] Konishi T, et al. Familial case of hereditary Pelger-Huët anomaly. Int J Hematol 2019. 110(2): 127-128.

[5] Oosterwijk J C, et al. Congenital abnormalities reported in Pelger-Huët homozygosity as compared to Greenberg/HEM dysplasia: highly variable expression of allelic phenotypes. J Med Genet 2003. 40(12): 937-41.

[6] Haverkamp Begemann N and A Van Lookeren Campagne. Homozygous form of Pelger-Huët's nuclear anomaly in man. Acta Haematol 1952. 7(5): 295-303.

[7] Cunningham J M, et al. Historical perspective and clinical implications of the Pelger-Hüet cell. Am J Hematol 2009. 84(2): 116-9.

[8] Hoffmann K, et al. Mutations in the gene encoding the lamin B receptor produce an altered nuclear morphology in granulocytes (Pelger-Huët anomaly). Nat Genet 2002. 31(4): 410-4.

[9] Colella R and S C Hollensead. Understanding and recognizing the Pelger-Huët anomaly. Am J Clin Pathol 2012. 137(3): 358-66.