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CASE REPORT

Pelger-Huët anomaly: a pediatric case report

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Abstract

The Pelger-Huët anomaly (PHA) is a benign, hereditary, usually autosomal dominant condition characterized by bilobulated or completely non-segmented granulocytes and excessive chromatin aggregation that can be mistaken for band cells. PHA is a condition still poorly investigated in the medical literature, especially in developing nations. Errors in diagnosing PHA might cause wrong interpretation of leukograms. In this case, a pediatric patient (age 6) sought medical assistance due to a fever associated with diarrhea. After complete blood cell count (CBC), which showed an important left shift, PHA was suspected. The disease was confirmed with a new CBC and then followed by the family investigation for this anomaly. The younger brother and the mother were found to have the PHA. The father and the older brother were negative for the disease, thus indicating an autosomal dominant genetic transmission.

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INTRODUCTION

The Pelger-Huët anomaly (PHA) is a congenital, hematological manifestation characterized by a detrimental segmentation of the neutrophil nucleus, with a coarse nuclear chromatin. It was first described by the Dutch physician Karl Pelger in 1928 and recognized as an autosomal dominant Mendelian trait by the pediatrician G. Huët in 1932. Dr. Pelger observed changes in the peripheral blood smear of two severely ill patients with widespread tuberculosis. He attributed a bleak prognostic value to this morphology, as the patients studied soon succumbed to the disease. Dr. Huët, while working with a 7-year-old girl with severe tuberculosis, observed a left shift with similar neutrophilic morphology as Pelger had previously described. To his surprise, the patient responded favorably to treatment and made a full recovery. During follow-up visits, the peripheral blood smear continued to show hyposegmented neutrophils. Huët then deduced that there was a possibility that this left shift was not a response to the infection but had a genetic association.

The heterozygous form of PHA is asymptomatic and has no clinical significance while the homozygous form is rare and can be lethal[1]. The pseudo PHA can occasionally be observed in cases of granulocytic leukemia, myeloproliferative diseases, in some infections, and after exposure to certain drugs. The presence of characteristic morphological findings in the blood smears of other family members is essential to establish the hereditary origin of the PHA. Its proper identification consists in differentiating between the "deviation to the left", common in some infections, and the hereditary condition[2-4].

Although it is known as a morphological variant of white blood cells, the PHA anomaly might sometimes be confused with other hematological disorders with similar leukocytic changes. Thus, the anomaly may induce the physician to misinterpret laboratory findings, possibly implying unnecessary treatment. For this reason, our objective is to report a case of a pediatric patient with the PHA and the family investigation of the anomaly. In the discussion, a brief literature review is presented. We also illustrate the importance of familial investigation for an accurate clinical diagnosis.

CASE REPORT

The data from this study were obtained through a review of the medical records from a pediatric private clinic in Brazil. Ethical approval was obtained from the Western Parana State University Research Ethics Committee (approval number 2,788,001). J.C.G.A., a male patient, 6 years and 9 months old, is an offspring of second pregnancy. In 2018, he came to the doctor's office for investigation of a fever associated with diarrhea lasting two days, presenting mucus in the feces. The patient was born by c-section, weighed 3,150g, 44cm long, cephalic perimeter measuring 38cm, APGAR 10 - 10. His parents were healthy, not inbred. Patient's growth and development markers were within the normal percentiles for his age. At the time of the consultation, his weight and height were 22,750g and 119cm, respectively.

The patient presented a good general condition and his physical examination did not reveal any particularities. An outpatient CBC was requested. After the result of the examination, in which a significant left shift was found (increase in band cells), treatment for acute gastroenteritis with sulfamethoxazole 400mg + trimethoprim 80mg 7.5ml was started orally, every 12 hours for five days. According to the suggestion of the laboratory and the suspicion of PHA, the CBC was repeated after two days (Tables 1 and 2). After the diagnosis of PHA was made, family investigation continued. CBCs were requested for the patient's parents and siblings. According to these results, it was found that the patient's father did not have the disease, the mother presented 25% of hyposegmented neutrophils, which is compatible with PHA. The older brother was not affected by the disease and the younger brother presented 20% of hyposegmented neutrophils, again compatible with the disease.

Table 1. Patient's erythrograms at baseline and after 48 hours.

	Baseline	48 hours
Red cells in millions/mL	3.59	3.53
Hemoglobin in g/dL	10.3	10.2
Hematocrit in %	30.0	29.6
VCM in u3	83.6	83.9
HCM in pg	28.7	28.9
CHCM in %	34.3	34.5

Table 2. Patient's leukograms at baseline and after 48 hours.

	Baseline	48 hours
Leukocytes (% / mL)	- / 6.580	- / 4.270
Neutrophils (% / mL)	77 / 5.067	51 / 2.178
Band cells (% / mL)	53 / 3.487	24 / 1.025
Segmented (% / mL)	24 / 1.579	27 / 1.153
Eosinophils (% / mL)	0 / 0	3 / 128
Basophils (% / mL)	0 / 0	1.0 / 43
Lymphocytes (% / mL)	18 / 1.184	32 / 1.366
Monocytes (% / mL)	5 / 329	4 / 384

DISCUSSION

The PHA is characterized by granulocytes that are bilobulated or completely non-segmented. The chromatin is mature and dense[5]. The heterozygous form of PHA serves as a marker for the Lamin-B receptor mutation. It is assumed that patients with this abnormality are clinically normal in relation to neutrophil function[4]. The accurate PHA diagnosis is important because it can often distort laboratory results, leading to errors in the interpretation of the leukogram. Indeed, leukocytic hyposegmentation can be confused with a left shift found in bacterial infections, or even sepsis.

This case demonstrates the importance of obtaining a complete family history from both parents, since the transmission of the disease occurs in an autosomal dominant way. In the patient studied, the hyposegmentation of neutrophils was found in the laboratory data, being initially attributed to an infectious process. Therefore, complete evaluation of the patient's history, efficient clinical examination, and laboratory data are essential for an accurate diagnosis.

Experiments performed on granulocytes with PHA in relation to their phagocytic, metabolic and bactericidal activities - as well as their motility and response to chemotactic stimuli - are equivalent to normal granulocytes[6]. However, Johnson et al.[7] observed a higher incidence of local infection in PHA carriers. This may be related to an impaired ability to migrate through small blood vessels. In the present pediatric case report study, there were no symptoms associated with poor granulocyte function, such as increased infection.

Importantly, although PHA has been recognized as a morphological variant of white blood cells, this anomaly might sometimes be confused with other hematological disorders with similar leukocytic changes. A recent case report included the misinterpretation of PHA in a suspected sepsis in a newborn with tachypnea. The anomaly was only recognized after a family history was obtained, revealing that the father, grandfather, and uncle of the case had PHA[8]. Another study showed a newborn with left shift in which invasive tests and intravenous antibiotic therapy for suspected neonatal sepsis were performed[9]. Moreover, Anand et al.[10] demonstrated a case in which PHA was misinterpreted as a possible myeloproliferative disorder, leading to a bone marrow procedure.

When evaluating blood smear in heterozygous phenotypes, Pelger-Huët cells can be identified by their classical finding. The lobes (ranging from 2 to 5) are symmetrically presented as "pince-nez" or "dumbbell", connected by a thin filament of chromatin. They are usually round with a thick, densely clustered and fully mature nuclear chromatin[11]. A small population of up to 4% of neutrophils are characterized by a non-lobulated or peanut-shaped nucleus (i.e., Stodtmeister cells). The overall size of these cells, the appearance of the cytoplasm and the staining of the granules in the cytoplasm resemble those of normal mature neutrophils. In PHA homozygosis, Stodmeister cells predominate, constituting about 95% of total neutrophils[4].

As this anomaly - in a state of heterozygosis - is considered a benign alteration with no clinical significance, there is no specific treatment for this condition. However, PHA homozygosis is associated with skeletal abnormalities and early intrauterine lethality[12]. Thus, it is important that genetic counseling is performed for heterozygous PHA carriers due to the chance of homozygosis in children and possible lethality of this condition[1].

The acquired form, sometimes called pseudo PHA, can be occasionally observed in cases of granulocytic leukemia, myeloproliferative diseases, some infections and as reactions to some drugs. In this case, the cells present oval nuclei, characteristic of cases of homozygosis[2]. Pseudo-PHA cell nuclei acquired in myeloproliferative neoplasms and myelodysplastic syndromes can be distinguished from congenital PHA by noting marked heterogeneity in nuclear lobulations, which are not symmetrical. Other myelodysplasia findings will also be present, including hypo granulation and an increased nuclear/cytoplasmic granulocyte ratio, while nuclear chromatin is not as condensed and dark as in PHA[4]. In the heterozygous state, PHA serves as a marker for the Lamin B receptor mutation state without adverse symptoms. Patients with this abnormality are clinically normal in relation to neutrophil function[1].

Although it is known as a morphological variant of white blood cells, the anomaly studied here might sometimes be confused with other hematological disorders with similar leukocytic changes. Familiarity with the classical morphological changes in granulocytes of PHA can help to avoid laboratory misinterpretation of granulocyte morphology, helping in the differentiation between PHA, leukemoid reaction, myeloproliferative neoplasia, or myelodysplastic syndrome.

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