Case Report

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Myeloperoxidase Deficiency: Case Reports of Two Patients with Different Clinical Presentations

Babak Nejati, Shalaleh Aghaei*, Gholamreza Ravaei

Hematology and Oncology Research Center, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

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ABSTRACT

Myeloperoxidase (MPO) deficiency is a rare genetic disorder affecting neutrophil and monocyte function. It can present with diverse clinical manifestations, from recurrent infections to unexplained systemic symptoms. Here, we present two cases of MPO deficiency with distinct presentations: a 47-year-old female with recurrent pneumonia and a 25-year-old male with pruritus. Both patients were found to have neutropenia, leading to further hematologic evaluation and confirmation of MPO deficiency. This report highlights the variability in clinical manifestations and underscores the importance of considering MPO deficiency in patients with unexplained neutropenia.

Introduction

Myeloperoxidase (MPO) deficiency, an autosomal recessive inherited disorder, presents with a heterogeneous clinical phenotype and constitutes the most common primary phagocytic defect [1]. This condition arises from mutations in the MPO gene, located at 17q22-23, resulting in either hereditary or acquired forms, with the former being more prevalent and exhibiting variable expression and penetrance [2]. Pathogenic germline variants disrupt MPO biosynthesis through defective posttranslational processing or pretranslational defects due to mutations in the regulatory region [3]. Notably, loss-of-function mutations correlate with neutrophilia and inflammatory pustular dermatoses [4]. Acquired MPO deficiency has been observed in hematologic malignancies, such as myelofibrosis, wherein the precise mechanism remains elusive [5], although homozygous calreticulin mutations have been implicated in some Philadelphia chromosome-negative myeloproliferative neoplasms [6].

MPO, a 150 kDa tetramer composed of two heavy and two light chains and two iron atoms, is synthesized in neutrophils and monocytes and stored in azurophilic granules [7]. It catalyzes the conversion of hydrogen peroxide to hypohalous acid, amplifying the respiratory burst against pathogens

* **Corresponding Author:**
Shalaleh Aghaei
Address: *Hematology and Oncology Research Center, School of Medicine ,Tabriz University of Medical Sciences, Tabriz, Iran.*
E-mail: *shalalehaghaei@gmail.com*

[8] and contributing to neutrophil extracellular trap formation [9]. While the majority of individuals with MPO deficiency are asymptomatic, studies suggest impaired fungicidal activity against Candida albicans and Aspergillus fumigatus [10, 11]. Furthermore, associations with chronic inflammatory diseases, including polyarthritis, lupus nephritis, and diabetes mellitus, have been reported [12]. Paradoxically, evidence suggests a potential protective role against cardiovascular, chronic kidney disease, and skin injury due to an acute inflammatory response [13, 14].

Here, we report two cases of MPO deficiency with different presentations. The first case involves a middle-aged woman with recurrent pneumonia and neutropenia, while the second case describes a young man with unexplained pruritus who was ultimately diagnosed with MPO deficiency. These cases emphasize the necessity of considering MPO deficiency in patients with atypical presentations and unexplained neutropenia.

Case Presentation

Case 1:

A 47-year-old female presented with a history of recurrent pneumonia. She has experienced these infections since early childhood, and they have persisted throughout her life. She had no significant past medical history apart from occasional mild upper respiratory infections. Notably, there is no familial history of similar diseases, and there are no reports of similar conditions in other family members. The patient was referred to a hematologist after routine blood tests revealed neutropenia, prompting further hematologic evaluation. A comprehensive clinical assessment of the patient revealed a generally stable and well-appearing individual without any overt health concerns. There were no indications of neurological symptoms, and no cutaneous manifestations were noted. Furthermore, the patient's vital signs, including heart rate, blood pressure, and body temperature, were all within the normal range during the examination.

The patient's tests were repeated to avoid a laboratory mistake (Table 1). The patient had populations of "large unstained cells" in the automated differential counts that were not borne out by manual performance of the differential count. Upon observing the decreased number of neutrophils despite normal WBC counts (Figure 1), a peripheral blood smear (PBS) was performed. It revealed reduced neutrophil granulation (Figure 2). Flow cytometry was performed on the bone marrow primarily to evaluate lymphomatous cells or blast. Immunophenotyping of bone marrow aspirate by flow cytometry showed a normal T and B cell population and less than 5% CD34+/CD117+ blast. There was no flow cytometry evidence of T or B cell lymphoma or acute leukemia.

Table 1. CBC of patients (Case 1 and Case 2)

CBC	Number of cells		Reference	Unit
	Case 1	Case 2		
WBC	8.76	9.13	4.0 – 11.0	10^3/µL
RBC	4.54	5.62	4.0 – 6.2	10^3/µL
HBG	14.0	17.3	12 - 18	g/dL
HCT	39.1	51.1	37 – 54	%
MCV	86.1	91.0	80 – 99	fL
MCH	30.8	30.8	26.0 – 32.0	pg
MCHC	35.8	33.9	31.0 – 36.0	g/dL
CHCM	34.3	34.9	33.0 – 37.0	g/dL
RDW	12.3	13.9	11.5 – 14.5	%
HDW	2.87	2.92	2.2 – 3.2	g/dL
PLT	294	334	130 – 450	10^3/µL
MPV	9.0	8.8	5.5 – 11.1	fL

WBC DIFF	Case 1	Case 2	Reference	Case 1	Case 2	Reference
	%	%		10^3/µL	10^3/µL	
Neutrophils	50.9	1.1	37 – 65	0.03	0.10	1.9 – 8
Lymphocytes	25.9	43.5	25- 40	3.15	3.97	0.9 – 5.2
Monocytes	10.9	18.1	3.4 – 9	1.83	1.66	0.16 – 1
Eosinophils	1.1	2.3	0 – 7	0.10	0.21	0 – 0.8
Basophils	0.3	1.6	0 – 1.5	0.02	0.15	0 – 0.2
LUC	11.8	33.3	0 – 4	3.63	3.04	0 – 0.4
NRBC	0	0	0.0 – 2.0	0	0	0.0 – 0.20

CBC: complete blood count; WBC: white blood cell count; RBC: red blood cell count; HBG: hemoglobin; HCT: hematocrit; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; CHCM: cellular hemoglobin concentration mean; RDW: red cell distribution width; HDW: Hemoglobin distribution width; PLT: platelet count; MPV: mean platelet volume; ml: microliter; LUC: large unstained Cells; NRBC: nucleated RBC; g/dL: grams per deciliter; fL: femtoliter; pg: picograms; %: percent.

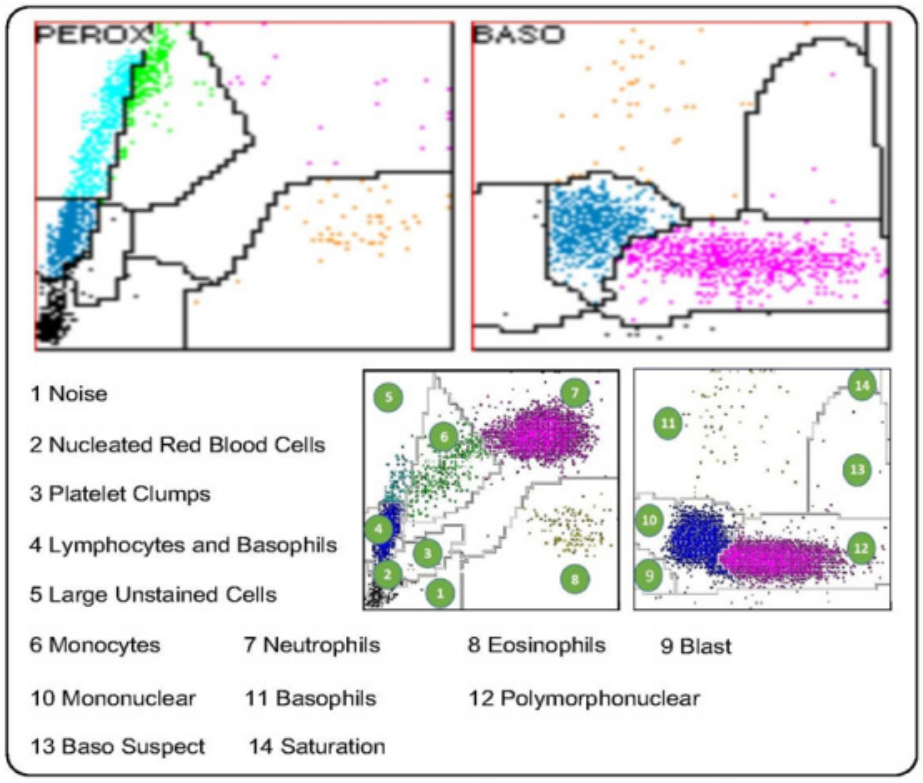

Fig. 1. Case 1 automated hematology analyzer scatterplots illustrating white blood cell differential classification across PEROX and BASO channels. Cell populations are identified and labeled (1–14).

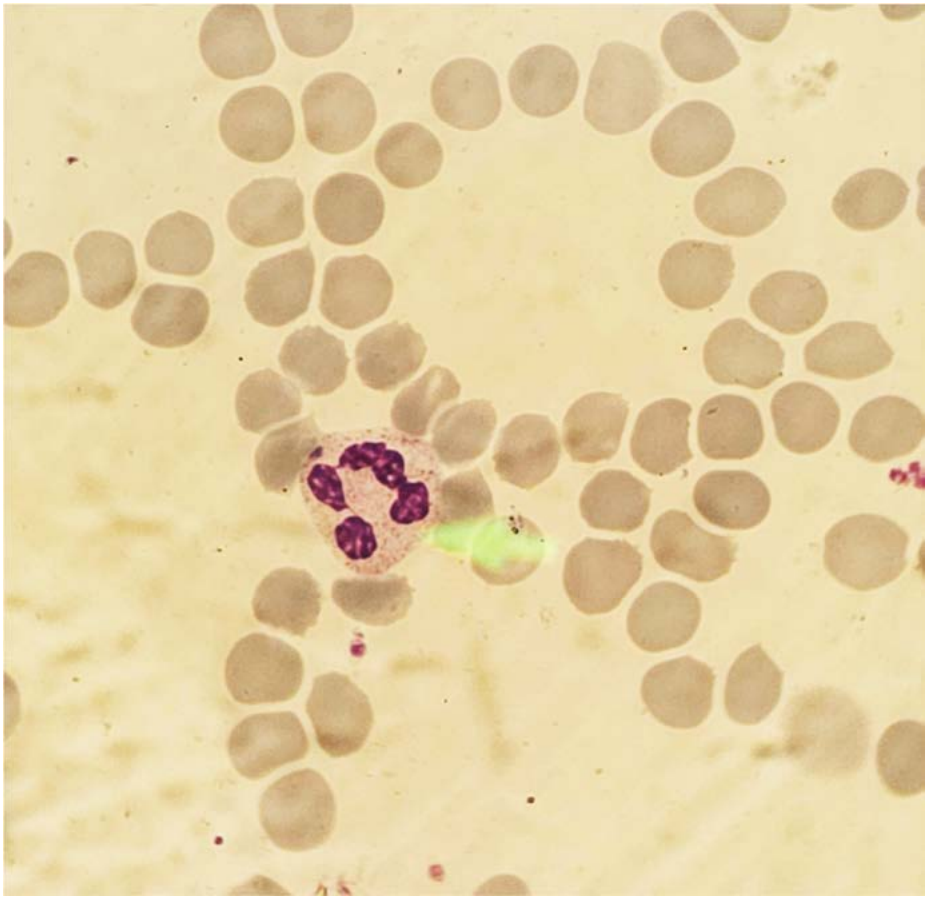

Fig. 2. Case 1 peripheral blood smear

Based on the clinical history, and laboratory findings, the patient is diagnosed with MPO deficiency.

Case 2:

A 25-year-old male presented with intermittent pruritus affecting the entire body for the past year. No dermatologic abnormalities were observed. The patient's tests were reported in Table 1. The patient had undergone extensive evaluations, including liver and renal function tests, thyroid function tests, and imaging studies, all of which were unremarkable. The decreased number of neutrophils despite normal WBC counts in CBC H1 (Figure 3), hypogranulated neutrophils in PBS (Figure 4), and normal flow cytometry confirmed the MPO deficiency diagnosis.

Discussion

MPO deficiency is a rare condition with highly variable clinical manifestations [1]. The majority of affected individuals remain asymptomatic, while others experience recurrent infections or unexplained systemic symptoms [15]. The two cases presented in this report highlight the diverse presentations of MPO deficiency: recurrent pneumonia in a middle-aged female and unexplained pruritus in a young male.

When comparing our findings with previous reports, the majority of documented cases of MPO deficiency have emphasized recurrent infections, particularly in immunocompromised patients [1]. Our cases expand this spectrum by highlighting non-infectious presentations, such as pruritus. While recurrent infections remain a hallmark of symptomatic MPO deficiency [2], our findings suggest that dermatologic manifestations may also warrant further investigation in MPO-deficient patients. Furthermore, previous studies have noted that neutropenia in MPO deficiency does not always correlate with increased infection rates, suggesting a more complex interplay between MPO function and immune defense mechanisms [16].

Regarding the second case, which involved a patient

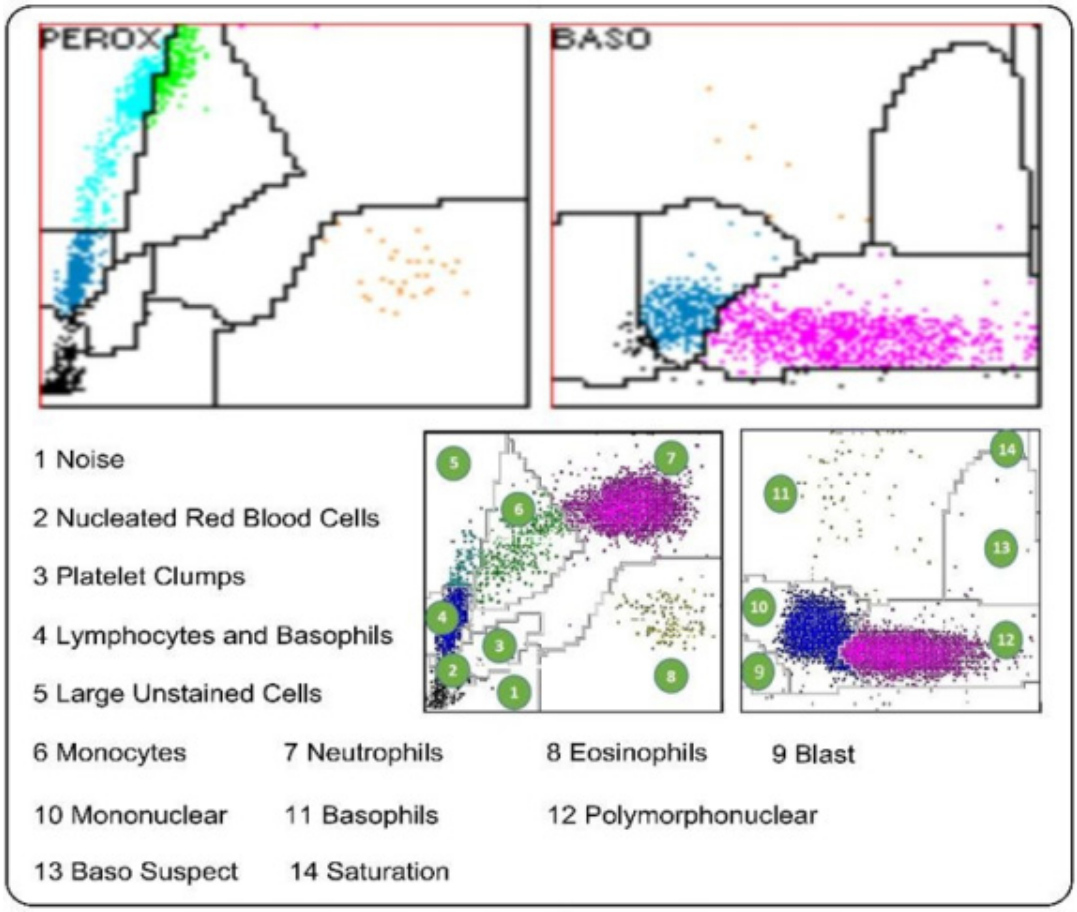

Fig. 3. Case 2 automated hematology analyzer scatterplots illustrating white blood cell differential classification across PEROX and BASO channels. Cell populations are identified and labeled (1–14).

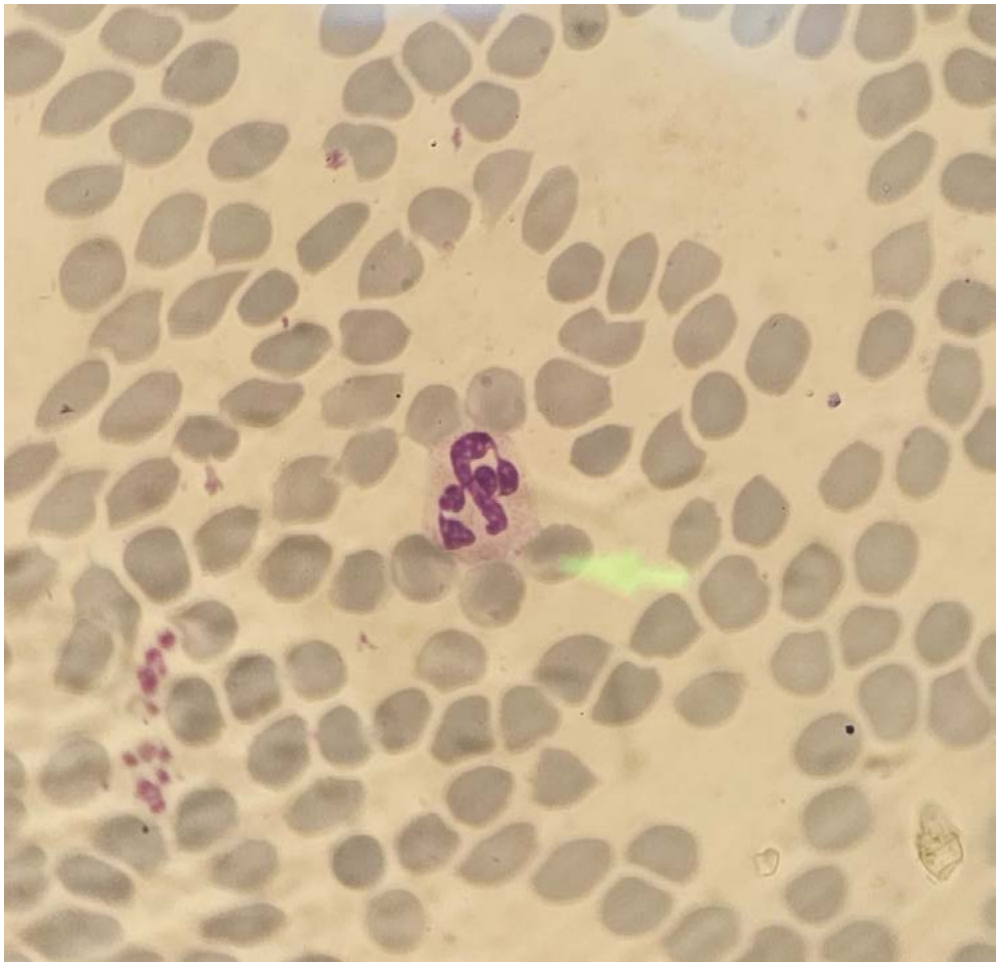

Fig. 4. Case 2 peripheral blood smear

with pruritus, the direct association between MPO deficiency and pruritus remains unclear. Pruritus can have multiple etiologies, including dermatologic, systemic, or neuropathic causes. One possible explanation regarding the relationship between MPO deficiency and pruritus is the role of MPO in modulating immune responses and oxidative stress, which could influence pruritus. Studies suggest that MPO may regulate mast cell degranulation and histamine release, both of which play key roles in pruritus pathophysiology [17].

At present, there is no specific treatment for MPO deficiency. Management primarily focuses on infection control and addressing underlying risk factors such as diabetes. Future research may provide deeper insights into the clinical implications and potential therapeutic strategies for MPO deficiency.

Conclusion

MPO deficiency is an underrecognized hematologic condition with variable clinical manifestations. These two cases demonstrate the importance of considering MPO deficiency in patients with recurrent infections or unexplained symptoms associated with neutropenia. Increased awareness and improved diagnostic techniques can aid in early detection and appropriate management of this condition.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this article.

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Conflict of Interests

The authors have no conflict of interest to declare.

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