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Laboratory Diagnosis of Myeloperoxidase Deficiency: A Case Report.

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Abstract:

Myeloperoxidase deficiency is a common disorder featuring deficiency, either in quantity or function of Myeloperoxidase. The patients are misdiagnosed because majority of individuals with Myeloperoxidase deficiency show no signs of immunodeficiency. Myeloperoxidase deficiency is noted even before the diagnosis is suspected because the machines that perform automated leukocyte differential counts rely upon neutrophil Myeloperoxidase activity to enumerate these cells. This report describes two cases of myeloperoxidase deficiency that were diagnosed after reassess of the hemograms.In one case ,we got to the diagnosis after the patient went under Bone marrow Aspiration for ruling out leukemia.

Keywords: Myeloperoxidase, neutrophil.

Introduction:

Automated Blood Cell Counters have affected the preliminary approach to hematologic problems and have unmasked many subclinical hematological abnormalities, as well. Using counters with cell differentiation ability broadened their usage in clinic to facilitate controlling of the patients during treatment whereas they have caused false positive diagnosis that can be reduced with good operating of the machines and adequate information of mechanism of action of such apparatus. This report describes two cases of myeloperoxidase deficiency that were diagnosed after reassess of the hemograms. In one case, we got to the diag-

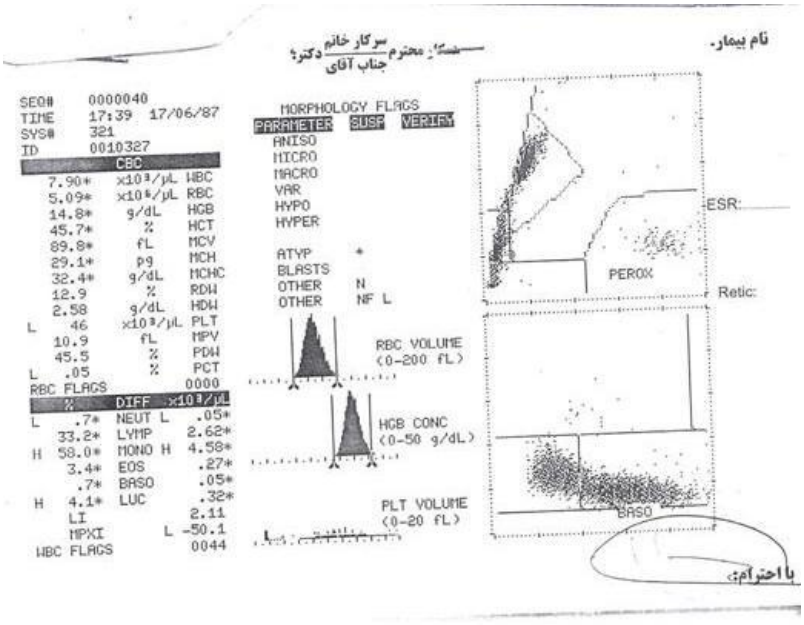
nosis after the patient went under Bone marrow aspiration for ruling out leukemia.

Case Presentation

Case 1: A 25 years old woman presented with a history of menorrhagia from two months ago and referred to haematologist. The patient had an

ecchymosis on right leg and admitted the Hematology ward. Laboratory

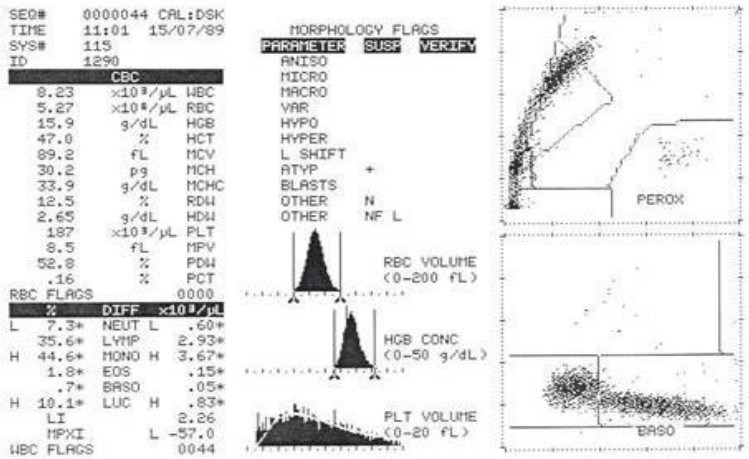
Tests were as below:

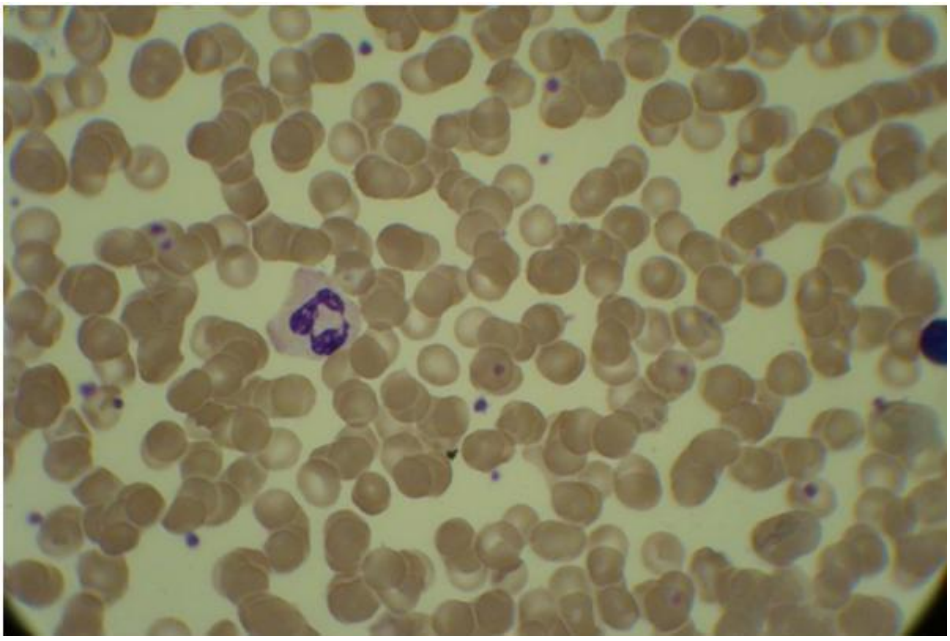


With the impression of ITP, BMA was performed and iron deficiency anemia was considered.

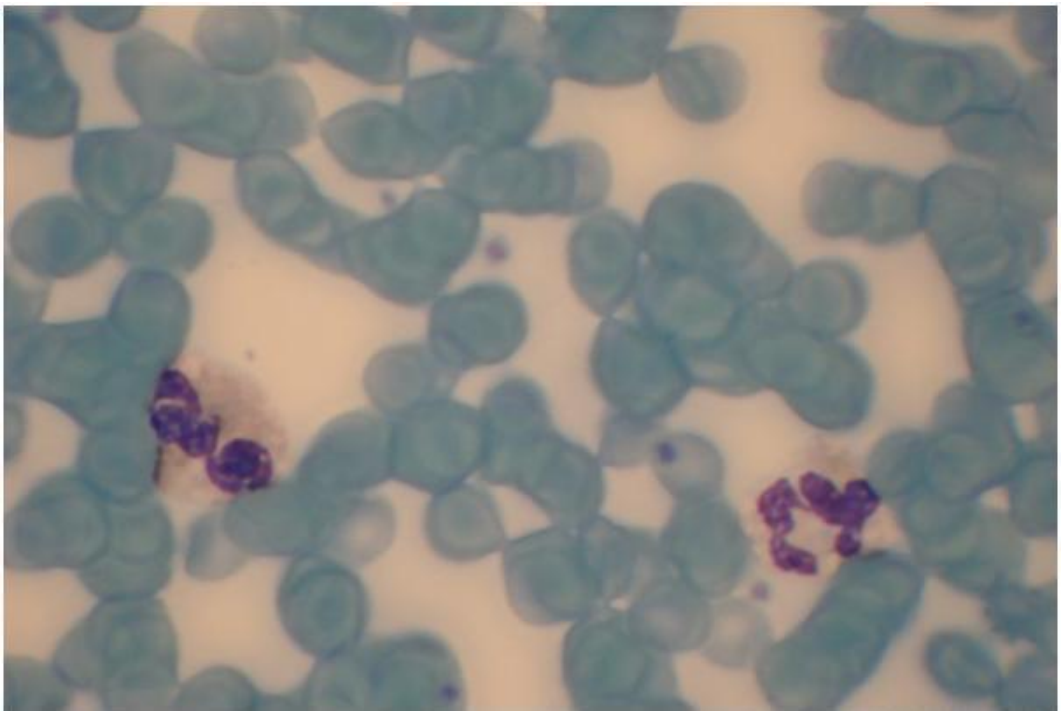
CBC done by Bayer cell worker (H1)and neutropenia was detected which was followed by bone marrow aspiration for rule out leukemia.

Case2: The patient was a young man in the control group of a study who had a





Sudan black staining



Sudan-Black Staining

Myeloperoxidase deficiency

Polymorphonuclear neutrophils (PMN) represent the dominant cell in the acute response to microbial infection. Effective antimicrobial activity reflects the combined action of soluble agents in plasma with PMN-derived reactive oxygen species and granule proteins, including the azurophilic granule protein myeloperoxidase (MPO). The inhibition or absence of the MPO-H2O2-halide system results in marked reduction in PMN killing of a

variety of microbes, implicating its relative prominence in the hierarchy of PMN antimicrobial systems.[1]

Myeloperoxidase deficiency is asymptomatic and it is seldom accompanied by fungal infections

Pathophysiology

The functional and immunochemical absence of the enzyme MPO from granules of neutrophils and monocytes, but not eosinophils, is inherited as an autosomal recessive trait, with a prevalence of 1:2000. MPO, an enzyme that catalyzes the production of hypochlorous acid in the phagosome, causes microbicidal deficiency of the neutrophils early after ingestion of microorganisms. However, normal microbicidal activity is observed approximately 1 hour after a variety of organisms are ingested. Thus, the MPO-deficient neutrophil uses MPO-independent system for killing bacteria that is slower than the MPO– H2O2–halide system that eventually is effective in eliminating bacteria.[2] Myeloperoxidase ,encoded by a gene located at 17q23 and Myeloperoxidase expression is linked to a promoter polymorphism, which confers higher (G allele) or lower(A allele)activity.[3]

Acquired Myeloperoxidase deficiency

The following have been mentioned as the reasons of Myeloperoxidase deficiency in several studies. Pregnancy, lead intoxication, severe infection, Thrombotic disease, DM, Drugs (cytotoxic agents and some anti inflammatory medications), several hematologic disorders and neoplasms such as AML, CML, polycythemia vera, Hodgkin disease, iron deficiency, Aplastic Anemia, Myelofibrosis with myeloid metaplasia.[4]

In some of the cases above Myeloperoxidase deficiency is reversible with treating the underlying cause. Myeloperoxidase deficiency in acquired cases is usually transient and generally resolves once the inciting condition improves.

Clinical finding

Sometimes Family studies have shown various degrees of partial or complete MPO deficiency in first-degree relatives. Both of the above patients did not have family history and did not report any infection history, however, in other studies mild infections have been observed in some patients. severe infections are uncommon, occurring in fewer than 5% of patients with Myeloperoxidase deficiency. if infectioud disease occurs, it is usually a fungal infection(particulary candidal, such as C.Albicans or C.tropicalis) that occurs in a patient who also has D.M. patients without D.M rarely have problems. Possibly, Myeloperoxidase deficiency becomes clinically significant only in the presence of an additional defect in the host defense, or perhaps the MPO-independent system is defective in some patients with D.M. physicians should entertain the diagnosis of yeloperoxidase deficiency in cases of invasive fungal infection in a patient with no known predisposing immune defects (e.g., chemotherapy, corticosteroid treatment)or in a patient with concomitant D.M.[5]In some research studies increasing number of malignancies, especially respiratory malignancies, have been reported.

Increased incidence of malignancy: A strong association between total Myeloperoxidase deficiency and malignancies has been reported by several independent investigators. Myeloperoxidase is released from neutrophils in lung tissue in response to pulmonary insult including damage secondary to tobacco smoke exposure. Myeloperoxidase has been shown to convert the metabolites of benzopyrene from tobacco smoke into a highly reactive carcinogen. researchers have demonstrated that decreased MPO can decrease lung cancer risk.[5]

Differential Diagnoses

Conditions such as Chronic Granulomatous Disease, Glycogen-storage disease Type1, job syndrome, Kostmann Disease, Leukocyte Adhesion deficiency, Shwachman-Diamond syndrome can cause acquired Myeloperoxidase deficiency.

Laboratory studies

The easier, more reliable and more sensitive assay in the diagnosis of Chronic Granulomatous Disease is Dihydrorhodamine123 (DHR) assay – a flow cytometric assay – in comparison with nitroblue tetrazolium dye reduction assay. For screening Myeloperoxidase deficiency a DHR assay should not be used due to variable results and poor sensitivity in detecting partial Myeloperoxidase deficiency.[6] the Clinical Chemistry evaluated 4 patients with complete MPO deficiency, 2 with partial MPO deficiency, and 3 with CGD (2 without and 1 with residual NADPH-oxidase activity) and compared them, as shown in this research study total MPO deficiency can lead to a significantly reduced fluorescence signal in the DHR assay that is consistent with the results observed in some CGD patients. In contrast, cells taken from partial MPO deficiency including only nominal residual MPO activity produced fluorescence signals consistent with normal (non-CGD) individuals. To identify eosinophils by flow cytometry can be demanding and may at times allocate for differentiation between CGD and MPO deficiencies. In the latter cases, other methods can be used to identify false-positive CGD because of total MPO deficiency rapidly. In order to enable a very rapid and clear discernment between MPO deficiency and CGD simply rhMPO can be added to the assay, since cells from patients with true CGD will not be affected by rhMPO. By using a monoclonal anti-MPO antibody with conventional intracellular staining MPO deficiency can be clearly shown.[8]

Treatment

Routine treatment with prophylactic antibiotics is not recommended because most patients with Myeloperoxidase deficiency have no increased incidence of infections. Rigorous control of blood glucose is beneficial in patients with associated diabetes.[7] Avoid any treatments that might increase the likelihood of developing fungal infection.

Discussion

Even though Myeloperoxidase deficiency is a common genetic disorder but hte diagnosis remains obscured because most of involved cases are asymptomatic. Partial or complete MPO deficiency was confirmed by examination of cyto-

chemical stains, biochemical measurement of total enzymatic activity, and flow cytometry .Always, none of the patients had apparent hematologic disorders. Rarely, patients had infections; or had major systemic infections (one, candidiasis; one, bacteremia).

In assays of leukocyte function only minor defects in killing of Staphylococcus aureus by MPO-deficient cells were noted whereas killing of Candida albicans was much more impaired. The easiest technique is to perform direct visualization of neutrophils on a peripheral blood smear that has been stained for peroxidase. The clinician can ask the pathologist to examine the neutrophils for peroxidase when a peripheral smear is requested Using automated blood cell counters that have full leukocytes diff ability with utilizing peroxidase for differentiation leukocytes can facilitate the diagnosis of Myeloperoxidase deficiency. Expert operators of such machines plays an important role in diagnosis of the same cases, but having adequate knowledge of interpreting homograms of such cell counters by physicians can fix the diagnosis before causing additional embarrassment to the healthy individuals that are going under blood work for screening program or unnecessarily subjected to a costly and sometimes risky diagnostic procedure. With respect to these two cases neither of them had clinical symptoms and underwent invasive procedures and unnecessary expenses. These patients usually are asymptomatic and do not warrant any treatment, therefore careful clinical evaluation is the simplest and cheapest way for diagnosis.

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