NOTES

Myeloperoxidase Deficiency Manifesting as Pustular Candidal Dermatitis

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Myeloperoxidase deficiency is the most common neutrophilic lysosomal enzyme deficiency. Case studies indicate that individuals with myeloperoxidase deficiency are not susceptible to serious infection in the absence of coexisting conditions such as diabetes mellitus. We present a case of myeloperoxidase deficiency manifesting as disseminated pustular candidal dermatitis in a non-diabetic male. Ceftriaxone therapy was administered to the patient for 8 days after he received a closed head injury and the development of fever and pustular dermatitis. Candida albicans was isolated from the skin lesion. His neutrophils demonstrated a qualitative lack of myeloperoxidase. Patients who develop rapidly disseminated fungal dermatitis while they are receiving antimicrobial therapy that is relatively limited in coverage should be evaluated for myeloperoxidase deficiency.

Myeloperoxidase is a lysosomal hemoprotein found in azurophilic granules of neutrophils [1]. It acts as a major mediator in the oxygen-dependent killing of bacteria, fungi, viruses, and malignant cells. It is also one of the modulators of neutrophilic inflammatory response [1–3]. Myeloperoxidase deficiency is a common functional disorder of neutrophils and has been classified into two general categories: hereditary vs. acquired. Affected individuals are generally asymptomatic in the absence of predisposing systemic illnesses such as diabetes mellitus or hematologic malignancies [1, 2].

We describe a case of myeloperoxidase deficiency (MPOD) manifesting as disseminated pustular candidal dermatitis in a host who was not predisposed to this disorder and who was receiving therapy with ceftriaxone. A review of the MEDLINE database revealed no other similar cases in which the patient presented in this manner.

Case Report

A 20-year-old male was admitted to the neurosurgery service after sustaining a closed head injury in a motorcycle accident. He had been healthy except for the nontherapeutic use of anabolic steroids for body building 6 months before admission. The initial physical examination revealed a well-developed, well-nourished male who appeared to be his stated age. Pertinent vital signs included a blood pressure of 180/90 mm Hg, a pulse of 204 beats/min, and a temperature of 103.6°F. Blood was present in the left auditory canal, and minor skin abrasions were noted on his left shoulder and hip. His neurological deficits included a dysconjugate gaze and decorticate posturing.

His WBC count was 35,000/mm³ with 74% segmented neutrophils and 2% band neutrophils. His initial hemoglobin level was 14.4 g/dL, and his platelet count was 337,000/mm³. A CT scan of the head revealed a significant intracranial hemorrhage. Examination of peritoneal lavage and subsequent peritoneal fluid specimens did not reveal an infectious or hemorrhagic process. A urine drug screen was negative.

Empirical therapy with ceftriaxone was initiated on hospital day 1 because of fever and leukocytosis. The patient’s temperature decreased over the next several days along with his WBC count. Ceftriaxone therapy was discontinued on day 8. The results of a test for Candida antigen were negative on hospital day 7. He did not receive therapy with dexamethasone or any other corticosteroids after his admission.

On hospital day 10, he became acutely tachypneic and had decreased consciousness. His temperature increased to 105.4°F, and his WBC count rose to 19,000/mm³. At this time, he developed a generalized pustular eruption (figure 1). Gram stain of an aspirate of these pustules showed many budding yeasts and neutrophils. Cultures of skin specimens were positive for Candida albicans. Cultures of blood and CSF were negative for fungal growth. Because of these findings, IV fluconazole therapy was initiated for probable disseminated candidiasis. He also received therapy with ceftriaxone and gentamicin for concomitant nosocomial urinary tract infection caused by Escherichia coli.

Because of the patient’s rapid clinical deterioration and the atypical pustular eruption, his peripheral blood smear (figure 2) was directly visualized with use of p-phenylendiamine and catechol for the cytochemical staining on hospital day 14. Figure 2a shows our patient’s neutrophil, with decreased peroxidase activity; in comparison, figure 2b shows two neutrophils from a patient with normal myeloperoxidase activity.
Our patient’s pustular dermatitis resolved by day 6 of fluconazole therapy, which was continued for 2 weeks. He did well after this episode of illness and was subsequently discharged to a rehabilitation facility on hospital day 72. On the day of discharge, he was oriented to name and place. His speech was clear but slow. Although he had some difficulty with short-term memory, he was able to perform activities of daily living and could ambulate without assistance.

Discussion

MPOD is either hereditary or acquired. Hereditary MPOD is an autosomal recessive disorder with a variable penetrance pattern. In the United States, its prevalence ranges between 1 per 4,000 individuals for total deficiency and 1 per 2,000 individuals for partial deficiency [1]. The acquired form of MPOD may occur in individuals with predisposing illnesses,
such as leukemia, lymphoma, severe or prolonged bacterial infections, pregnancy, lead intoxication, or illnesses that activate the coagulation cascade [1, 2, 4]. Sulfonamides, antihypertensive medications, phenothiazines, or ascorbic acid may interfere with myeloperoxidase activity [2].

Our patient was assumed to have hereditary MPOD because his clinical presentation and history did not demonstrate the existence of any of the previously mentioned risk factors. However, we were unable to study any of his family members during his hospitalization. As he was subsequently lost to follow up, we were unable to determine whether his MPOD was hereditary.

During the course of his hospital stay, the patient's glucose level rose to 176 mg/dL while he was receiving 5% dextrose saline intravenously. However, he had no classical signs or symptoms of glucose intolerance such as glucosuria or diabetic retinopathy. Thus, we believe that the clinical manifestation of his MPOD was due solely to the antibacterial therapy.

Although our patient's candidal pustular rash was the impetus for considering MPOD in the differential diagnosis, it is well known that use of broad-spectrum antibiotics can predispose to candidal superinfection, including dermatologic manifestations. Cutaneous candidiasis occurs in up to 13% of patients who are receiving broad-spectrum antimicrobial therapy [5, 6]. However, in patients who are receiving ceftriaxone alone, candidal overgrowth is manifested in <0.25% in otherwise healthy hosts [7]. This may be due to ceftriaxone's lack of significant anaerobic coverage [7, 8].

A case of candidal meningitis in an adult with MPOD was reported by Ludviksson et al. [9]. A 5-year-old girl received therapy with trimethoprim-sulfamethoxazole for 5 days before developing a headache, a high fever, and a stiff neck. The initial CSF analysis was compatible with aseptic meningitis, including dermatologic manifestations. Cutaneous candidiasis occurs in up to 13% of patients who are receiving broad-spectrum antimicrobial therapy [5, 6]. However, in patients who are receiving ceftriaxone alone, candidal overgrowth is manifested in <0.25% in otherwise healthy hosts [7]. This may be due to ceftriaxone's lack of significant anaerobic coverage [7, 8].

Repeated CSF cultures 19 days after admission yielded C. albicans. Evaluation of her neutrophils revealed MPOD. It is possible that the patient initially presented with aseptic meningitis because of a reaction to trimethoprim-sulfamethoxazole therapy [10] and that the subsequent candidal meningitis resulted from antibacterial therapy, findings that make this case similar to our own. Unlike our own patient, however, this patient had no dermatologic manifestations. In addition, her antibiotic regimen, specifically the chloramphenicol, provided broader anaerobic coverage than did ceftriaxone.

Classical skin lesions of disseminated candidiasis are erythematous papulonodules ranging from 0.5 cm to 1.0 cm. They tend to localize on the trunk and extremities and may become hemorrhagic if there is associated thrombocytopenia [5]. Other described cutaneous eruptions associated with disseminated candidiasis include macronodular, follicular, and necrotic lesions resembling ecthyma gangrenosum [5, 6]. Our patient's pustular eruption was atypical on the basis of our review. Oral thrush and deep mucocutaneous candidiasis have been reported in symptomatic individuals with MPOD [2, 11]. Similar oral lesions were not noted in our patient but may have been overlooked as he was not able to cooperate for an oral examination at that time.

Myeloperoxidase is a dimer, lysosomal hemoprotein [1]. Its central function lies in its role as a mediator in the oxygen-dependent killing of bacteria, fungi, viruses, and tumor cells by neutrophils. As an enzyme, it catalyzes the generation of hypochlorous acid and other long-lived oxidants that are microbicidal. It has been postulated that myeloperoxidase-deficient neutrophils are impaired in their candidicidal activity and have retarded bactericidal activity in general [1−3]. However, it is unclear why most individuals with MPOD remain asymptomatic in the absence of coexisting illnesses.

In conclusion, we present the first reported case of MPOD that was manifested as disseminated pustular dermatitis in a patient who was receiving a third-generation cephalosporin. MPOD should be considered in the differential diagnosis for individuals who present in this manner—or with the other finding(s) described above—after they have received a course of antimicrobial therapy with limited anaerobic coverage.

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References