A Case Report of Cyclic Neutropenia Associated with Pyoderma Gangrenosum

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Abstract- We present a 24-year-old female referred with non-healing wound of a few days duration on anterior aspect of her right foreleg. Biopsy of the wound was reported to be pyoderma gangrenosum on pathologic report. Further work up of the patient for high grade fever and occasional leukopenias revealed the diagnosis of cyclic neutropenia. Treatment with granulocyte colony-stimulating factor (G-CSF) resulted in patient's neutrophil counts correction and dramatic improvement in healing of her lower extremity wound.

Keywords: Cyclic neutropenia; Pyoderma gangrenosum

Introduction

Cyclic neutropenia (CN) is a rare blood disorder characterized by relatively long periods of extremely low neutrophil count, which can result in frequent opportunistic infections. These low counts typically occur every 21 days and last for about 7 days. This disorder also has the capacity to affect other blood counts. Commonly identified symptoms include fatigue, weakness, fever, malaise, and oral membrane ulcers (1). In some cases, CN has been successfully treated with granulocyte colony-stimulating-factor (G-CSF), which leads to an increase in the absolute neutrophil count (ANC) and prevents infections (2).

Pyoderma gangrenosum (PG) is a disease that causes tissue to become necrotic, resulting in deep ulcers that usually present in the lower extremities. The lesions initially present as a pustule or erythematous nodule which evolve to form deep ulcers that may progress to chronic wound infections. Although the etiology of PG is not well understood, the disease is thought to be due to immune system dysfunction, and in particular, to improper functioning of neutrophils. Therapy for PG in both localized and disseminated cases is systemic treatment with immunosuppressive agents such as corticosteroids, cyclosporine (or mycophenolate mofetil), tacrolimus, and infliximab (3). The following report presents a young lady who presented with non-healing wound in anterior shin which was proved to be PG on skin biopsy. Further work ups revealed underlying CN. Based on our knowledge, this association has not been previously documented.

Case Report

The presenting patient is a 24-year-old young single lady who was visited in a day care center eight days prior to hospitalization in infectious diseases unit due to minor blunt trauma in the anterior surface of her right foreleg, which led to edema and ecchymosis. The lesion gradually evolved to form a wound that was also accompanied by fever. A general surgeon performed two episodes of extensive wound debridement followed by administration of oral antimicrobial agents (cephalexin and cloxacillin), with no improvement, so referred to our hospital and was admitted for further work up and management.

A more detailed history revealed that, since the age of 16, the patient has had recurring postural lesions on her buttocks and thighs at the site of friction of her trousers. The lesions were associated with fatigue and weakness and lasted a few days before spontaneous healing. It was also revealed that one of the patient’s sisters (she had five sisters) died at the age 26 due to a
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severe perineal infection of unknown cause. The patient’s mother was a known case of type I diabetes but other family members were well.

Initial blood tests were all normal with the exception of slight diminution of serum IgA and relative leucopenia of a few days duration. Dermatologist consult was performed and they recommended transferring the patient to the dermatology unit. Patient was transferred to dermatology unit and on immunologist consultation intravenous immunoglobulin (IVIG) infusion was suggested due to low IgA level. During the course of hospitalization, the patient developed a small abscess at the site of the IV catheter on her right wrist. Prior to receiving the IVIG infusion, the patient developed a high-grade fever on day 29 of hospital admission, an infectious diseases specialist consultation was requested. A complete blood count (CBC) was obtained which showed leukopenia. Reviewing serial leukocyte counts and estimated ANCs indicated two nadirs and one peak of neutrophil counts in serial complete blood counts for which no underlying was found. Therefore, cyclic neutropenia was considered as the best explanation for this case given the labs, the patient’s clinical course, and her past medical and family history. Empirical treatment with granulocyte colony-stimulating factor (G-CSF) resulted in a dramatic correction in the patient’s leukocyte count and ANC, and improvement in her general condition and subsequent healing of her lower extremity wound. Serial blood counts looking for cyclic changes in leukocyte and neutrophil counts confirmed the diagnosis of cyclic neutropenia in one year follow-up after discharge.

Discussion

Cyclic neutropenia is a rare hematologic disorder characterized by recurrent episodes of severe neutropenia occurring typically at 21-day intervals which may also be associated cyclical variations in other blood components. Patients with this disease may experience malaise, stomatitis, cervical lymphadenopathy, and fever during the recurrent neutropenic episodes (3,4).

The exact cause of cyclic neutropenia is unknown. About one third of cases appear to be inherited in an autosomal dominant pattern. In other cases, the disease appears to arise spontaneously with symptoms usually beginning in infancy or early childhood. In adult patients, the disease may be acquired and occurs in association with a colonial proliferation of large granular lymphocytes (5). Long-term follow-up of these patients shows that life-threatening complications include spontaneous peritonitis, segmental bowel necrosis, and septicemia, all of which require surgical interventions (4).

Therapy for cyclic neutropenia involves local and symptomatic treatment of the recurrent mouth ulcers and pharyngitis, and antibiotics for episodes of sinusitis, pneumonia, peritonitis, or bacteremia. Therapy with glucocorticosteroids, androgens, and plasmapheresis has been efficacious in some adult patients, but no therapy has been proven to alter the cycling of blood counts in children. Despite their repetitive illnesses, patients with cyclic neutropenia grow and develop normally (5).

PG is a neutrophilic dermatosis that has an inflammatory infiltrate consisting of mature polymorphonuclear cells. The neutrophils are usually located in the dermis. It is characterized by a painful, enlarging, necrotic ulcer with bluish undermined borders surrounded by advancing zones of erythema; its clinical variants include ulcerative or classic pustular, bullous or atypical, vegetative, peristomal, and drug-induced forms (6,7). In the presented patient, skin biopsy was performed when patient was not in neutropenic episode.

To the best of our knowledge, the association between cyclic neutropenia with manifestations of PG has not been reported since before with through search in electronic data bases. Here, we presented a case with cyclic neutropenia associated with non-healing wound which was proved by skin biopsy to be pyoderma gangrenosum.

References