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PYODERMA GANGRENOSUM: A SKIN MARKER MASQUERADING MYELODYSPLASTIC SYNDROME - A RARE CASE REPORT

Dermatology

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ABSTRACT

Pyoderma gangrenosum is a rare non-infectious neutrophilic dermatosis commonly associated with underlying systemic disease. We report a case of pyoderma gangrenosum with myelodysplastic syndrome.

KEYWORDS

Pyoderma gangrenosum, Myelodysplastic syndrome

Introduction:

Pyoderma gangrenosum was first described by Brocq in 1916 and later named by Brunsting et al[1] in 1930. Pyoderma gangrenosum is an uncommon inflammatory neutrophilic dermatosis characterized by cutaneous ulcerations often associated with an underlying systemic disorder like myelodysplastic syndrome. Immune dysfunction with neutrophil trafficking and activation is thought to play a role in the pathogenesis of pyoderma gangrenosum. We report a 26 year old male who was diagnosed with myelodysplastic syndrome.

Case report:

A 26 year old male patient came to the skin OPD with complaints of multiple ulcers over the right leg for the past 6 months. Patient gave a history of trauma 6 months back after which he developed a small ulcer of size 1x2 cm which progressed to the current size. It was associated with pain, swelling and serosanguinous discharge. History of burning sensation was present over the skin surrounding the ulcer which was aggravated on exposure to sunlight. Patient gave history of standing for long duration. Patient was diagnosed with myelodysplastic syndrome 5 years back and is on medication. Patient underwent blood transfusion to maintain haemoglobin levels. History of weight loss was present. Patient doesn't give any history of other comorbidities.

On general examination there was pallor and right sided pedal edema. Systemic examination was normal.

Dermatological examination revealed two ulcers of size 3x4cm and 2 x 3 cm present over the medial malleolus and the lateral side of the right leg respectively, with serosanguinous discharge(figure 1&2). There was severe scaling over the surrounding skin. Pigmentation was present over both legs with a line of demarcation. There was edema over the right leg.

Patient's CBC with smear study showed decreased number of RBC's, which were predominantly microcytic hypochromic with presence of few normocytic normochromic RBC's and macrocytes (figure 6).There were decreased number of eosinophils and neutrophils with elevated ESR. Hemoglobin was 4.6gm/dl and platelet count was very low (0.14lakhs/cumm).Urine analysis was normal. Bone marrow biopsy showed hypoplastic marrow with few atypical mononuclear cells. Bone marrow aspiration cytology reported hypoplastic myelodysplastic syndrome. Biopsy from the lesion revealed hyperkeratosis with irregular elongation of rete ridges, dilated vascular spaces surrounded by necrotic keratinocytes and presence of neutrophils. All these findings are suggestive of pyoderma gangrenosum (figure 3,4,5).

Discussion:

Pyoderma gangrenosum is a reactive, non-infectious neutrophilic dermatosis characterized by solitary or multiple painful necrolytic ulcers of the skin with irregular, violaceous, undermined borders surrounded by a halo of erythema. Pyoderma gangrenosum usually starts as small, tender erythematous papules and plaques which later evolve into the characteristic painful ulcers healing with typical cribriform scarring. The variants of pyoderma gangrenosum are classical, bullous, pustular and vegetative, of which the bullous variant is most commonly associated with hematological malignancies. Pyoderma gangrenosum is most commonly seen over the lower extremities while the bullous variant is seen commonly over the upper limbs. In addition to myelodysplastic syndrome, pyoderma gangrenosum can also be associated with other systemic disorders like inflammatory bowel disease, rheumatoid arthritis, other hematological malignancies, SLE, AIDS, sarcoidosis, Takayasu's arteritis, complement deficiency, hepatitis C viral infection, hypogammaglobulinemia, hyperimmunoglobulin E syndrome, hidradenitis suppurativa, acne conglobata and many more. Pyoderma gangrenosum exhibits the pathergy phenomenon where skin trauma produces lesions at the site of injury. Skin biopsy is taken to rule out other causes of ulceration because of non specific findings on pathology.

Typical histopathology findings include central necrotizing suppurative inflammation with dermal-epidermal neutrophilic infiltration, usually with ulceration. There may be a perivascular and intramural lymphocytic infiltration with or without fibrin deposition or mural necrosis.

Pyoderma gangrenosum should be differentiated from other inflammatory disorders, vascular occlusive or venous disease, vasculitis, bacterial, fungal or atypical mycobacterial infection, drug induced or exogenous tissue injury and other opportunistic infections. Skin biopsy is not diagnostic for pyoderma gangrenosum. Culture for bacteria, atypical mycobacteria, virus and fungi, blood count, biochemical profile, chest x-ray, endoscopy, bone marrow aspirate , CT scan are some investigations which should be done to rule out other conditions that mimic pyoderma gangrenosum as well as diagnose any associated conditions.

Myelodysplastic syndrome (MDS) represents a group of heterogeneous hematopoietic disorders derived from an abnormal multipotent progenitor cell resulting in ineffective hematopoiesis, bone marrow failure and peripheral blood cytopenias. MDS may involve any or all three hematopoietic cell lineages (i.e.) erythrocyte, granulocyte and megakaryocyte resulting in anemia, leucopenia and/or thrombocytopenia. MDS is a premalignant condition and long standing MDS may progress to acute myeloid leukemia[2]. They are associated with auto-immune manifestations, such as thrombocytopenic purpura, vasculitis, chronic inflammatory demyelinating polyneuropathy and Pyoderma gangrenosum, which represent a significant cause of morbidity and mortality, and are associated with poorer prognosis[3].

The pathogenesis of the relation between PG and hematological disorders is not understood. MDS can cause alterations in antigen presentation, in T cell response or in the interaction between T and B cells, leading to an immune system imbalance[4], which would lead, in turn, to production of auto-antibodies against cutaneous antigens with perivascular immune complex deposition[5]. PG can occur concomitant to the hematological disease or during its evolution, as marker of the malignant transformation of a previously stable disease[6].

Treatment of pyoderma gangrenosum involves high-dose corticosteroids as the first choice[7]. Immunosuppressive drugs such as cyclosporine A, azathioprine, cyclophosphamide, chlorambucil, sulphasalazine, dapsone, minocycline, clofazimine and thalidomide are used in steroid-refractory cases, alone or in combination with steroids[7]. Autoimmune manifestations of MDS and pyoderma gangrenosum frequently respond to immunosuppressive agents and occasional hematological responses to steroid therapy have been reported in MDS[3].Daily wound oxygenation increases collagen production by fibroblasts to support capillary angiogenesis in pyoderma gangrenosum[8]. Thalidomide is used in pyoderma gangrenosum for its antiangiogenic and anti-inflammatory effects[7]. Thalidomide is also effective in the management of MDS[9].How thalidomide acts in MDS is not clear. It exerts heterogeneous biological effects on haematopoiesis in MDS[10]. Some data suggest several mechanisms possibly involving stimulation of erythropoiesis through activation of physiological compensative mechanisms and reduction of apoptosis[9].

CONCLUSION:

When a patient with pyoderma gangrenosum presents with peripheral blood dyscrasias, a bone marrow study should be done to rule out myelodysplastic syndrome and other haematological malignancies, as pyoderma gangrenosum may present as a skin marker for MDS.

Legends to figure:

- Figure 1& 2: Clinical picture shows two ulcers of size 3 x 4cm and 2 x 3 cm present over the medial malleolus and the lateral side of the right leg associated with discharge.
- Figure 3: Histopathological picture showing hyperkeratosis with irregular elongation of rete ridges.
- Figure 4: Histopathological picture showing irregular elongation of rete ridges with multiple dilated vascular spaces.
- Figure 5: Histopathological picture showing neutrophils, pigment incontinence and necrotic keratinocytes.
- Figure 6: Peripheral smear report.

FIGURE 1:

FIGURE 2:

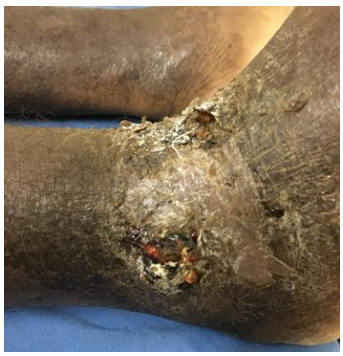


FIGURE 3:

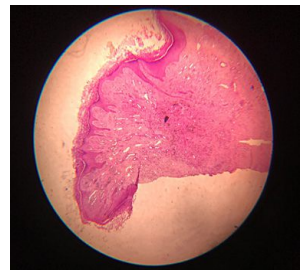


FIGURE 4:

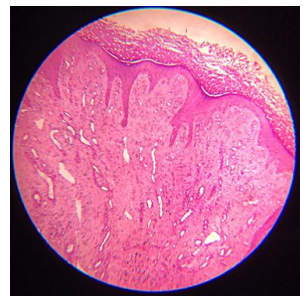


FIGURE 5:

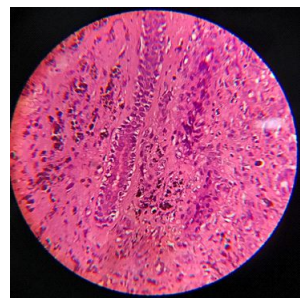
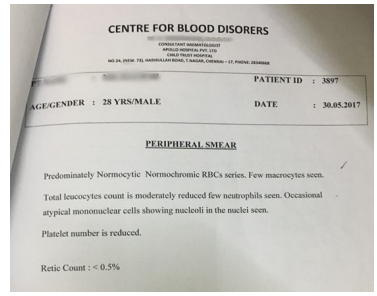


FIGURE 6:



CENTRE FOR BLOOD DISORERS

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PATIENT ID : 3897

AGE/GENDER : 28 YRS/MALE

DATE : 30.05.2017

PERIPHERAL SMEAR

Predominately Normocytic Normochromic RBCs series. Few macrocytes seen.

Total leucocytes count is moderately reduced few neutrophils seen. Occasional atypical mononuclear cells showing nucleoli in the nuclei seen.

Platelet number is reduced.

Retic Count : < 0.5%

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