Pyoderma gangrenosum in a renal transplant recipient: A case report and review of literature

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ABSTRACT

Pyoderma gangrenosum (PG) is a rare disorder of unknown etiology characterized by multiple cutaneous ulcers with mucopurulent or hemorrhagic exudate. This sterile neutrophilic dermatosis is known to occur in association with malignancy, infection, autoimmune disorders and drugs. Occurrence of PG in a renal transplant recipient, who is already on immunosuppressants, is rare. We hereby report a renal transplant recipient who developed PG 1-month after transplant and responded well to treatment with escalated dose of oral steroid.

Key words: Immunosuppressed, kidney transplantation, pyoderma gangrenosum

Introduction

Pyoderma gangrenosum (PG) is an ulcerative disorder characterized by neutrophilic infiltration of the dermis. It has been associated with malignancy, infections, autoimmune diseases, inflammatory bowel disease and drugs. The incidence is 3–10 per million population per year and peaks in 20–50 years age group.[1,2] Brocq, in 1916 gave a first description of this disease although the name PG was given by Brunsting *et al*.[3,4]

The occurrence of PG in a renal transplant recipient is rare.[5] We hereby present a renal transplant recipient who manifested lesions typical of PG.

Case Report

A 41-year-old male underwent live related renal transplant in March 2013 with sister as a donor. His native kidney disease was focal segmental glomerulosclerosis diagnosed in January 2009, on renal biopsy. For this, he was treated with prednisolone and tacrolimus but his disease progressed and eventually reached end-stage renal disease. For the transplant, he received basiliximab induction and was started on maintenance immunosuppression with tacrolimus, mycophenolate sodium, and prednisolone. The posttransplant course was uneventful, and his serum creatinine reduced to a minimum of 1.5 mg/dl.

He presented 1-month posttransplant with painful ulcerative lesion over left knee for which he had received oral clindamycin without any relief. Over next follow-up visit, similar lesions developed over both the lower limbs, back, abdomen, retroauricular region and nape of the neck. On examination, these lesions were ovoid in shape and of varying sizes. It had a necrotic center with a rim of erythema showing a tendency for the peripheral spread. Figure 1a1 and a2 show the lesions at the time of presentation. Other clinical examination was unremarkable. The immunosuppression consisted of tacrolimus 3.5 mg twice daily, mycophenolate sodium 720 mg twice daily and prednisolone 12.5 mg once daily. Other medications included oral pantoprazole 40 mg once daily and amlodipine 5 mg once daily.

Investigations showed hemoglobin 13.5 g/dL, total leukocyte count 8.2 × 10^9/L with the normal differential count, platelet count 191 × 10^9/L. Renal graft function was stable with a serum creatinine of 1.5 mg/dl and blood urea 36 mg/dl. Fasting blood sugar was 102 mg/dl.

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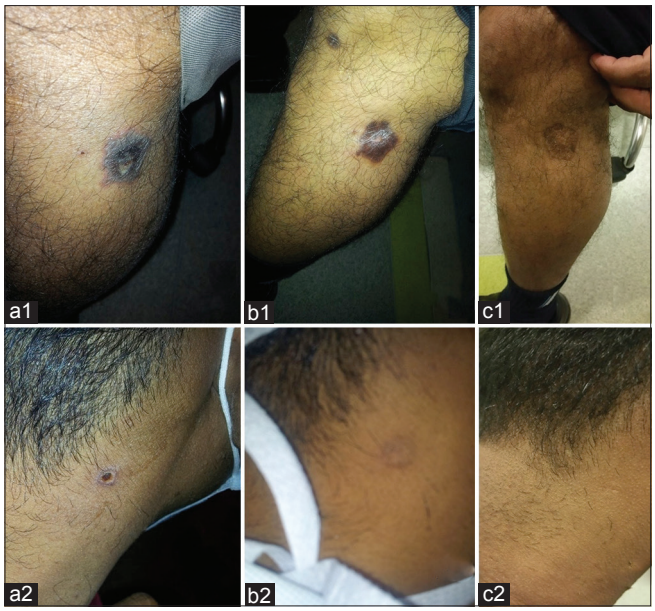

Figure 1: (a1 and a2) Lesions of pyoderma gangrenosum at the time of presentation; (b1 and b2) Lesions after 1-month; (c1 and c2) Lesions on last follow-up (19 months)

Serum calcium was 9.1 mg/dl and phosphorus was 3 mg/dl. Liver function test revealed total bilirubin of 1 mg/dl and normal liver enzymes. Trough tacrolimus level was 8.3 ng/ml. Urinalysis was normal, and urine protein creatinine ratio was 0.13. Anti-nuclear antibody and anti-neutrophil cytoplasmic antibody was negative by immunofluorescence.

Skin biopsy revealed central neutrophilic suppurative necrosis surrounded by fibrinous exudate with overlying epithelium showing partial necrosis, suggestive of PG [Figure 2].

His oral steroid was stepped up and prednisolone was changed to oral betamethasone. This was given in a dose of 4 mg once daily for 1-week followed by 3 mg once daily for another week. Thereafter, he was switched back to oral prednisolone 12.5 mg once daily. He responded well to the treatment and lesions healed within a month as seen in Figure 1b1 and b2. He has not developed any new lesions during the last 19 months of follow-up as seen in Figure 1c1 and c2.

Discussion

Pyoderma gangrenosum is a neutrophilic dermatosis. In almost 50% of the cases, it has been found to be associated with a systemic disease such as inflammatory bowel disease, myeloproliferatvie disorder, leukemia, collagen vascular diseases, arthritis, and malignancy.[6] It has also been reported to be associated with certain drugs such as isotretinoin, gefitinib, and propylthiouracil.[7,8]

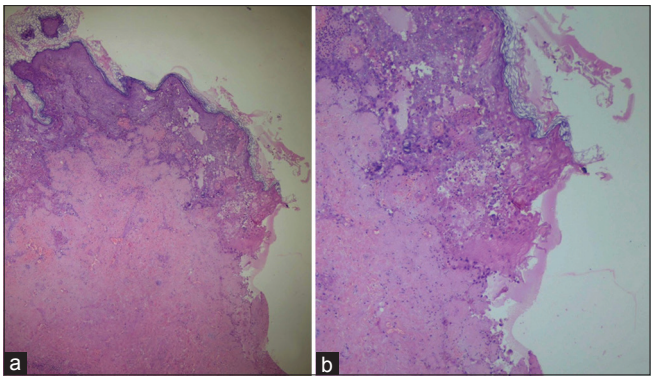

Figure 2: (a) Scanner view show intact epidermal lining at one end and other aspect show marked degeneration and necrosis of keratinocytes (H and E, original magnification ×4); (b) Medium power view further highlight necrotic epidermal lining (H and E, original magnification ×20)

Pathogenesis of PG is largely unknown. Initially, it was thought to be caused by bacterial infection.[4] Later, various putative mechanisms have been proposed, most important of which is a dysregulation of the immune system. Biopsies of such lesions have shown cutaneous vascular immune deposits suggesting immune complex disease or lymphocytotoxic reaction.[9]

Presentation of PG in a renal transplant recipient is rare. Haim and Friedman-Birnbaum had reported one such case and proposed that immunosuppressive therapy particularly drugs like antimetabolites may have an etiological role.[10] Serdar *et al*. described a case of PG developing in a patient 5 years posttransplant. He proposed that the pathogenesis in such cases depend upon the immune system defects and immunosuppressive agents as well.[11] Al-Hwiesh described a case of PG in renal transplant recipient and proposed an association with cytomegalovirus infection.[5]

Pyoderma gangrenosum usually manifests as single or multiple painful lesions distributed mainly over legs especially in the pretibial region. Lesions can also be present on other body sites such as head and neck, trunk, hand. Powell *et al*. classified PG into four clinical types: (1) ulcerative (2) pustular (3) bullous (4) vegetative.[12] In the most common ulcerative type, the lesion starts as a pustule that grows rapidly leading to necrosis of adjoining tissue forming an ulcer that has typical undermined violaceous borders. It is associated with a positive pathergy test in about 25% of patients. This refers to the appearance of new lesions at the site of trauma, surgery or venipuncture.[13] Our patient had presented with multiple skin lesions with ulcerative morphology.

Diagnosis of PG is by exclusion of other causes. As its association with various systemic disorders is well known, these should be carefully ruled out. Histopathology is nonspecific, and it is usually difficult to diagnose PG based

solely on that. Initially, there is perivascular lymphocytic infiltrate associated with endothelial swelling. As the stage progresses, necrosis can be noticed. Later on, ulceration and abscess formation sets in.[9] In our case, workup for other associated systemic illness was negative, and histopathology showed central necrosis surrounded by a fibrinous exudate.

Differential diagnosis consists of vaso-occlusive diseases, vasculitis, infections, external injury, drug reactions and other neutrophilic dermatosis such as sweet's syndrome.

Treatment mainly consists of immunosuppressant medications and steroids are the first choice drugs.[14] Other agents used in combination with oral steroids for the widespread disease are cyclosporin, tacrolimus, mycophenolate mofetil (MMF), azathioprine, dapsone, clofazimine, thalidomide, infliximab, etanercept and intravenous immunoglobulin.[1] Our patient responded well to the escalation of oral steroid therapy. He was already on tacrolimus and MMF as an immunosuppressant for renal transplantation.

To conclude, presentation of PG in a renal transplant recipient is extremely rare. Secondary causes should be looked for carefully, as the diagnosis is by exclusion. Patient usually responds to stepping up of the steroid dose and recurrence of such lesion is rare.

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