Late-onset acute graft-versus-host disease mimicking hand, foot, and mouth disease

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ABSTRACT

Acute skin graft-versus-host disease (GVHD) classically presents as a pruritic erythematous maculopapular rash. We describe a patient who underwent allogeneic hematopoietic stem cell transplantation and presented with a hand foot and mouth disease like clinical presentation. Histopathology was suggestive of acute GVHD. This case is being reported to make dermatologists aware of this unusual presentation of GVHD.

Key words: Atypical presentation, hand foot and mouth disease, late presentation

INTRODUCTION

Graft-versus-host disease (GVHD) is a very common complication of hematopoietic stem cell transplantation (HSCT). Skin is the most common and often the first organ to be affected. It is involved in almost 80% patients.[1] Skin GVHD classically presents as a maculopapular rash in acute GVHD. Various atypical presentations of skin GVHD have been described. We present a case of late-onset acute GVHD mimicking hand, foot, and mouth disease (HFMD).

CASE REPORT

An eight-year-old boy underwent HLA-matched sibling transplant for thalassemia major. Preparative regimen was treosulfan-based myeloablative regimen. GVHD prophylaxis consisted of cyclosporine and short course methotrexate. On day 24 post-HSCT, he developed grade 4 acute GVHD (grade 4 gut; grade 2 liver), which was treated with methylprednisolone (2 mg/kg), etanercept, basiliximab while cyclosporine was continued.

By day 210 post-HSCT, immunosuppression was discontinued. The patient was on oral antibacterial and antiviral prophylaxis in the form of oral penicillin and cotrimoxazole and acyclovir. Antifungal prophylaxis was discontinued with the immunosuppression.

One week later, the patient presented with painful rash over both palms and soles as well as oral and genital mucosal lesions. On examination, he had multiple tender hemorrhagic vesicles over bilateral palms [Figure 1a] and feet. A few crusted erosions and atypical targetoid lesions were seen over the dorsa of both hands [Figure 1b], erosions on the palate [Figure 1c] and periurethral mucosa [Figure 1d] was also noted. General condition of the patient was stable and he did not have any constitutional and gastrointestinal symptoms. His liver function tests were within normal limits. Laboratory evaluation was unremarkable. The differential diagnoses considered were HFMD, erythema multiforme (EM), and cutaneous GVHD. However, there was no temporal correlation with drug intake. Polymerase chain reaction (PCR) for herpes simplex virus, coxsackie virus, and enterovirus from the vesicular fluid was negative. Skin biopsy from the foot showed vacuolar degeneration of basal cells and necrotic keratinocytes with associated lymphocytic exocytosis ("satellite cell necrosis") (grade 2 acute GVHD). No viral cytopathic effects were present [Figure 2a and b].

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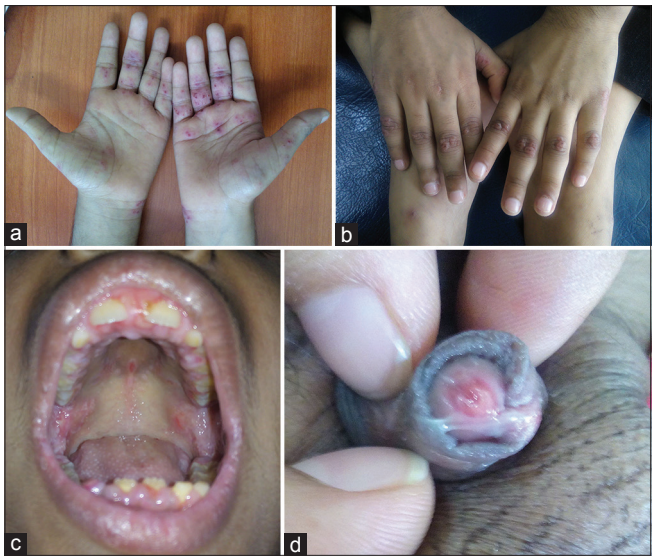

Figure 1: (a) Hemorrhagic tender vesicles over palms. (b) Erythema multiforme-like lesions over the dorsa of hands. (c) Erosions over the palate. (d) Erosions over the glans penis

The patient was diagnosed to have cutaneous GVHD based on the clinical course and clinicopathologic correlation. Cyclosporine (3 mg/kg) was restarted with topical mometasone. The patient responded promptly to this treatment.

DISCUSSION

Skin GVHD is classically described as acute or chronic. Previously, the presence of any manifestations of GVHD beyond 100 days after HSCT was called chronic GVHD. However, according to the recent NIH consensus criteria,[2] acute and chronic GVHD is distinguished based on clinical manifestations rather than time after transplantation.

Acute skin GVHD can be persistent, recurrent, or late-onset acute GVHD. Late appearance of acute GVHD is known to occur after suspending or tapering immunosuppressive drugs.[3] Hence, we considered late-onset acute skin GVHD in our patient. It is important to distinguish late acute GVHD from chronic GVHD as the latter is associated with a lower chance of recurrent malignancy and discontinued systemic treatment.[4]

Acute skin GVHD commonly presents with a characteristic pruritic erythematous maculopapular rash involving the whole body, especially palms, soles, and ear lobes.[1] Various atypical presentations of acute GVHD have been recently described like follicular type,[5] psoriasiform,[6] contact-dermatitis like,[6] type II pityriasis rubra pilaris-like,[6] eczema craquelé-like GVHD,[6] erythema-multiforme like,[7] erythematous nodules,[8] and pustular acral erythema.[9]

Factors responsible for the various phenotypic manifestations of acute cutaneous GVHD have not been studied. Similar studies

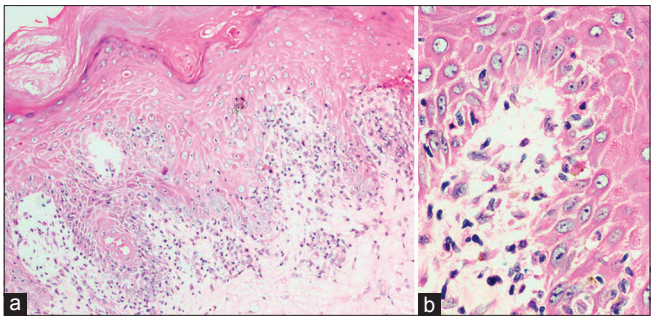

Figure 2: (a) Interface dermatitis with mild lymphocytic exocytosis and necrotic keratinocytes (H and E, ×10). (b) Basal cell vacuolation and necrotic keratinocytes with associated lymphocytic exocytosis ("satellite cell necrosis") suggestive of grade 2 GVHD (H and E, ×40)

done for chronic GVHD have found that sclerodermatous type is associated with anti-dsDNA and lichenoid rash with soluble B-cell activating factor (sBAFF).[10]

The clinical presentation of our patient is more in favor of HFMD. However, a diagnosis of GVHD is favored over HFMD in this patient due to appearance of lesions after discontinuation of immunosuppression while still on antiviral prophylaxis, subsequent clinical course, characteristic histopathologic finding, and prompt response to the immunosuppressive treatment. Apoptotic keratinocytes can be seen on the histopathology in HFMD as well, but satellite cell necrosis is a specific histopathologic finding of GVHD. The differentiation between these entities is important as immunosuppression is warranted for GVHD while HFMD is self-limiting.

Cutaneous GVHD is an important marker for GVHD involving other organs. It is important to recognise it early so that timely intervention can be initiated, preventing further progression. To the best of our knowledge, acute GVHD mimicking a hand foot and mouth disease has not been reported earlier.

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Conflicts of interest
There are no conflicts of interest.

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