Case Report

Follicular Graft Vs Host Reaction: A Rare Presentation

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Abstract

Graft versus host disease (GVHD) is a unique entity wherein the donated marrow cells (graft) view the hosts as foreign and attack various body organs. Skin is the most frequently affected organ followed by mucosa, eyes, gastrointestinal, respiratory, musculoskeletal system, and other organs. The incidence of GVHD varies from 25 to 80%. Cutaneous involvement can present as exanthem, epidermolysis, lichenoid eruptions, erythroderma, ichthyosis, pityriasis rubra pilaris like lesions, psoriasiform lesions or just pruritus. Asymptomatic truncal follicular eruptions as the major presentation is rare. We report a case of aplastic anemia that developed extensive truncal folliculocentric papules 10 months following an allogeneic hematopoietic stem cell transplantation. Histopathological examination of the follicular lesions revealed perifollicular inflammatory infiltrate comprising of lymphocytes, plasma cells and histiocytes at the dermo-epidermal junction. Basal cell vacuolization, pigment incontinence in the upper dermis and few apoptotic keratinocytes in the follicular epidermis were also seen. The patient responded satisfactorily to tapering doses of steroids.

Keywords: *Graft versus host disease, hematopoietic stem cell transplant, lichenoid follicular papules*

Introduction

Graft versus Host disease (GVHD) is a unique disease wherein the donated marrow cells (graft) view the hosts as foreign and attack various body organs. Skin is the most frequently affected organ followed by mucosa, eyes, gastrointestinal, respiratory, musculoskeletal system & other organs.[1]

GVHD was earlier classified into acute and chronic based on time interval after the allogeneic graft. Acute GVHD manifested within the first 100 days of transplant and manifestation beyond that was classified as chronic GVHD. However, according to the 2014 National Institutes of Health (NIH) Consensus criteria, chronic GVHD is now classified based on the classical presentation and the duration of onset may be before or after 100 days of the hematopoietic stem cell transplant (HSCT). Chronic GVHD can be mild, moderate, or severe with high mortality rates observed in patients with severe GVHD.[2]

Cutaneous manifestations of GVHD include maculopapular rash, bullous lesions, lichenoid lesions, hyperpigmentation, keratosis pilaris, mucosal ulcerations and erosions, Stevens–Johnson/toxic epidermal necrolysis (SJS-TEN), etc. However, lichenoid follicular eruptions as the major presenting feature of chronic GVHD is very uncommon.[3] Herein, we describe a post HSCT patient who developed an asymptomatic follicular eruption 10 months post HSCT.

Case Report

A 26-year-old male patient with aplastic anemia was treated with allogeneic HSCT HLA-matched related donor (6/6, younger brother) after conditioning with fludarabine and cyclophosphamide for 09 days. Thereafter, Valganciclovir (for 1.5 months), Cyclosporine for (08 months and stopped thereafter due to azotemia), Mycophenolate mofetil (for last two months), Acyclovir 400 mg twice daily, Penicillin 400 mg twice daily was given as GVHD prophylaxis, orally.The patient had no involvement of skin or any other organs for the first 10 months after which he started developing multiple asymptomatic dark follicular lesions over the body. Examination showed multiple discrete lichenoid folliculocentric papules on the trunk and arms, involving ~30%

How to cite this article: Vashisht D, Kothari R, Baveja S, Neema S, Sengupta P, Sandhu S. Follicular graft vs host reaction: A rare presentation. Indian Dermatol Online J 2020;11:988-90.

Received: 19-Feb-2020. **Revised:** 06-Apr-2020. **Accepted:** 04-Jun-2020. **Published:** 19-Sep-2020

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Access this article online

Website: www.idoj.in

DOI: 10.4103/idoj.IDOJ_87_20

Quick Response Code:

body surface area. Dermoscopy of the lesion showed diffuse folliculocentric hyperpigmented pattern [Figure 1a and b]. Oral examination showed violaceous pigmentation over the hard palate [Figure 2]. Nails showed longitudinal melanonychia and diffuse hyperpigmented to violaceous pigmentation of the proximal nail fold.

Histopathological examination of the follicular lesions over the trunk revealed predominantly perifollicular inflammatory infiltrate comprising of lymphocytes, plasma cells, and histiocytes at the dermo-epidermal junction; basal cell vacuolization, pigment incontinence in the upper dermis and few apoptotic keratinocytes in the follicular epidermis [Figure 3a and b]. However, biopsy lacked parakeratosis, hypogranulosis, eosinophils, and civatte bodies.

A diagnosis of lichenoid follicular chronic GVHD was made according to the criteria of the National Institutes of Health (NIH) consensus project as the patient lacked any evidence of organ involvement and had normal hematological and biochemical parameters. The clinical picture was consistent with mild grade chronic GVHD. The patient was initially managed with topical steroids and later shifted to tapering doses of oral steroids (starting at 0.75mg/kg) in view of suboptimal response and gradually progressive lesions, following which there was complete resolution of lesions over next 08 weeks.

Discussion

GVHD is a major multiorgan complication of allogeneic HSCT resulting from the action of the donor-derived immunocompetent T cells against the immunosuppressed recipient. The incidence varies from 25 to 80%.[4,5] As the classical presentations of acute or chronic GVHD may not follow the previously defined time period, the NIH consensus project has emphasized on classifying GVHD based on the clinical manifestations.

As the skin, gut, and liver are the major organs involved in acute GVHD, the classic triad of rash, diarrhea, and raised bilirubin levels strongly suggest the diagnosis.[6] The rash is usually an erythematous maculopapular or morbilliform eruption that starts on the face, ears, palms, and soles. Follicular erythema is a frequent early manifestation of acute GVHD, and both erythematous macular and papular rash can occur.[7] Chronic GVHD is now classified into (i) classic chronic GVHD, with the presence of at least one diagnostic or distinctive manifestation of chronic GVHD and (ii) overlap syndrome with features of both chronic and acute GVHD.[5] Cutaneous findings like poikiloderma, lichen planus-like, lichen sclerosus-like, morphea-like, and deep sclerotic eruptions establish the presence of chronic GVHD even without skin biopsy or additional tests. Distinctive manifestations such as vitiligo-like depigmentation and papulosquamous lesions, when present alone are not sufficient for diagnosis. Other nonspecific, rare, or controversial eruptions that may be seen are ichthyosis, keratosis pilaris, sweat impairment, hypopigmentation, and hyperpigmentation. The common manifestations to both acute and chronic GVHD, include erythema, maculopapular rash, and pruritus.[2]

Lichenoid follicular eruptions as the major presenting feature of chronic GVHD is not common.The exact pathogenesis of follicular GVHD is not known, however, it has been postulated that the parafollicular bulge stem cells of the hair follicle, rather than the papillary bulb tip, maybe the target.[8] It may be the initial or early presentation of severe GVHD, which has a high mortality.This patient fulfilled the diagnosis of classic chronic GVHD as he had lichen-planus like

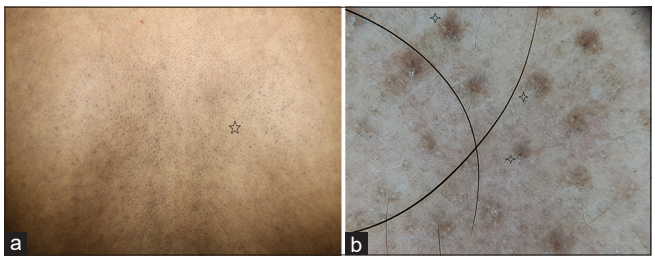

Figure 1: Follicular GVHD (a) Higher magnification of the folliculocentric lichenoid papules over the back (Empty five-point star) (b) Dermoscopy (Illuco IDS-1100, 10×) of the follicular lesions over the trunk showed diffuse folliculocentric hyperpigmented pattern (Empty four-point stars)

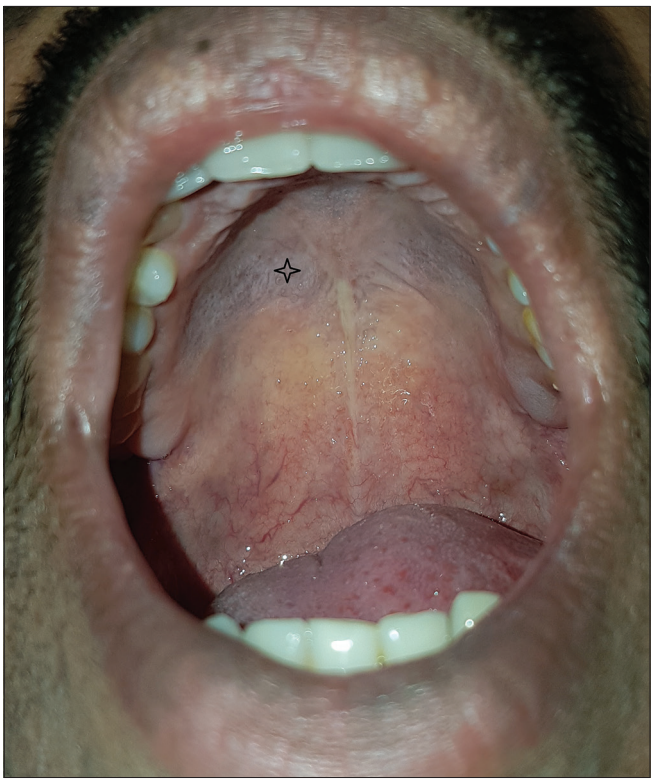

Figure 2: Oral cavity showing an ill to well-defined violaceous pigmentation over the hard palate (Empty four-point star)

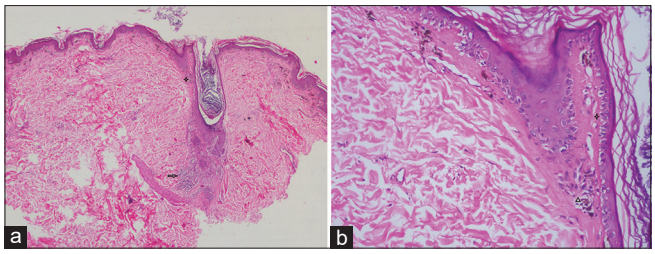

Figure 3: Histopathology of follicular GVHD (a): Perifollicular inflammatory infiltrate comprising of lymphocytes, plasma cells, histiocytes at the dermo-epidermal junction (Black empty arrow) and pigment incontinence in the upper dermis (Empty four-point star) (H & E, 40×) (b): Basal cell vacuolization (Empty four-point star), pigment incontinence (Empty black triangle) and few apoptotic keratinocytes in the follicular epidermis (H & E, 200×)

folliculocentric violaceous papules involving the trunk, violaceus pigmentation of the oral cavity and nails and lacked features of acute GVHD such as abdominal pain, diarrhea, and liver abnormalities.

Conclusions

Lichenoid follicular chronic GVHD is a very uncommon presentation of cutaneous GVHD. It may be a harbinger of severe GVHD, which has a high mortality. It is important for the clinicians to recognize this entity early and initiate appropriate therapy for a good prognosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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