Graft versus host disease localized to striae distensae: An example of locus minoris resistentiae

Sir,

Allogeneic stem cell transplantation is frequently used in the treatment of hematologic malignancies. Graft versus host disease is among the common morbid complications that affect transplant recipients and is caused by the recognition of host antigens as foreign by the transplanted cells.[1] Locus minoris resistentiae is a Latin term denoting a skin segment that presents lesser resistance to the development of disease as compared to the rest of the skin.[2] This enhanced susceptibility of some cutaneous segments to develop a dermatosis is explained by the interplay of various cutaneous, immunological and neurological factors. Herein, we report a case of chronic graft versus host disease preferentially involving the sites of striae distensae as an example of locus minoris resistentiae.

A 13-year-old girl, with a prior diagnosis of acute myeloid leukemia, presented with itchy, erythematous papules on her back on day 128 of myeloablative, haploidentical hematopoietic cell transplantation. Her past history was significant for the development of acute cutaneous graft versus host disease and steroid-refractory, severe acute liver and gut graft versus host disease 1-month post-transplant, which had responded to antithymocyte globulin.

Examination revealed multiple fragile, erythematous to violaceous, scaly papules and plaques on her back, prominently localized to atrophic striae distensae, conforming precisely to their topography [Figure 1]. Her back also showed diffuse background post-inflammatory hyperpigmentation, reminiscent of acute cutaneous graft versus host disease. Nails and mucosae were normal. The rest of the skin was normal, and there was no obvious poikiloderma or sclerosis elsewhere on the skin. At that point of time, the patient was on tapering doses of prednisolone and mycophenolate mofetil. A diagnosis of late acute graft versus host disease (recurrent type) and chronic lichenoid graft versus host disease was considered, and skin biopsy was obtained from the papulosquamous lesions located on the striae.

Histopathology from a skin biopsy obtained from the lesions on the back showed hyperkeratosis, mild hypergranulosis and dense interface dermatitis with multiple apoptotic bodies, foci of satellite cell necrosis, pigment incontinence and fragmented collagen fibers [Figures 2a-c]. A diagnosis of lichenoid chronic graft versus host disease was confirmed. She was advised topical mometasone furoate 0.1% cream and tacrolimus 0.1% ointment for local application. The dose of prednisolone was increased. Sirolimus was added to mycophenolate mofetil and the lesions resolved within a month.

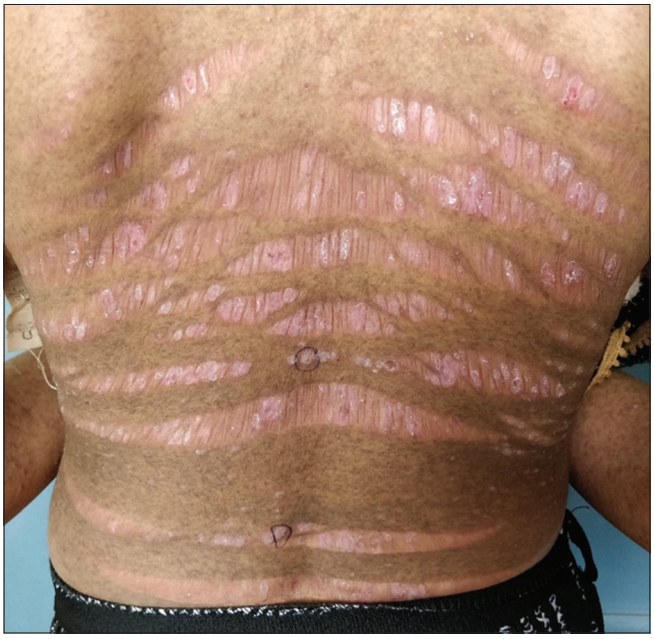

Figure 1: Graft versus host disease localized to striae distensae. Multiple fragile, erythematous to violaceous, scaly papules and plaques are present on the back, prominently localized to atrophic striae distensae. Diffuse background post-inflammatory hyperpigmentation is reminiscent of acute cutaneous graft versus host disease

Graft-versus-host disease represents one of the most common complications of allogeneic hematopoietic stem cell transplantation.[1] Its classification was previously based on the time point of 100 days (acute 100 days); though this was later revised to include cases of acute graft versus host disease that occurred beyond this time-point (persistent, recurrent

How to cite this article: Bishnoi A, Lad D, Ashraf R, Banerjee N, Saikia UN, Vinay K. Graft versus host disease localized to striae distensae: An example of locus minoris resistentiae. Indian J Dermatol Venereol Leprol 2021;87:555-7.

Received: April, 2020 Accepted: November, 2020 Published: June, 2021

DOI: 10.25259/IJDVL_396_20 PMID: ***

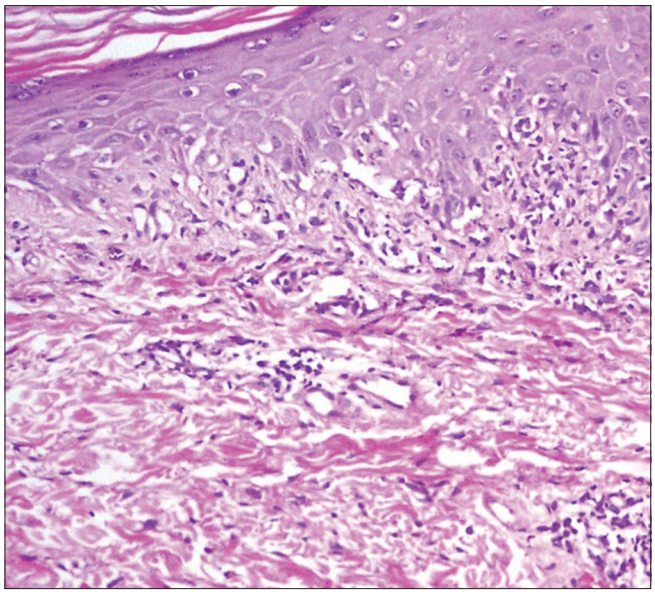

Figure 2a: Histopathological findings of skin biopsy of lesion on the back. The epidermis shows spongiosis with diffuse basal cell vacuolization and perivascular lymphocytic cell infiltration in the superficial dermis (H and E, ×100)

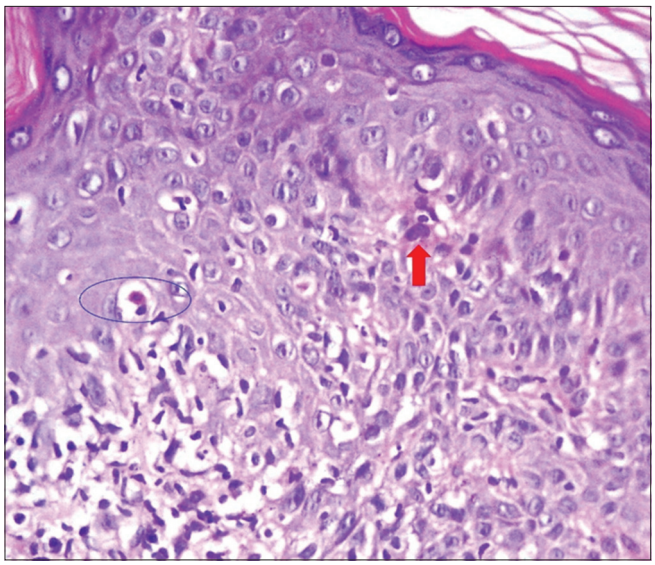

Figure 2b: Histopathological findings of skin biopsy of lesion on the back. The epidermis shows dyskeratotic keratinocyte (red arrow), satellite cell necrosis (blue circle) and lymphocytic exocytosis in the epidermis (H and E, ×200)

and de-novo). Though acute graft-versus-host disease can be usually diagnosed clinically depending upon skin, liver and gastrointestinal manifestations, the same is not true for chronic graft versus host disease, where diagnosis relies on the presence of either *diagnostic* manifestations (classical lichen planus, poikiloderma or sclerosis), or *distinctive* manifestations that are subsequently proven to be chronic graft versus host disease on histopathology (lichenoid or sclerotic features in the skin).[3] For our patient, since she presented on day 128 post-transplant, and the lesions were not very suggestive of classic lichen planus; both diagnoses were considered; that is, late acute (recurrent) or chronic lichenoid graft versus host disease, and histopathology established the diagnosis to be chronic lichenoid graft versus host disease.

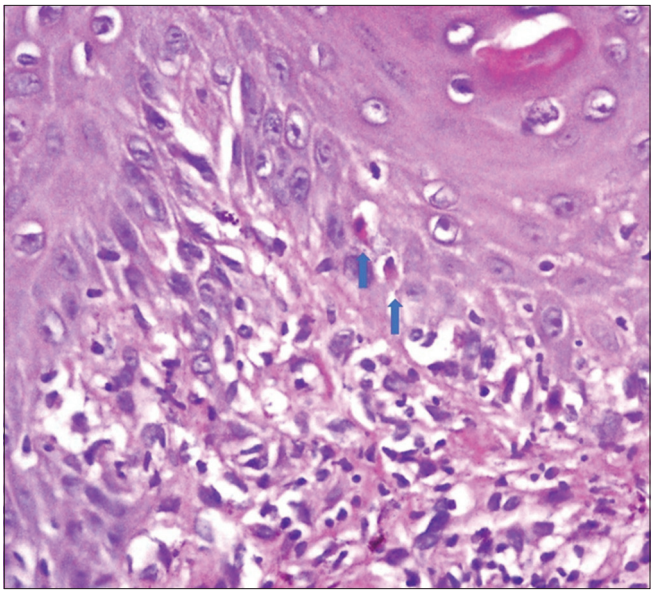

Figure 2c: Histopathological findings of skin biopsy of lesion on the back. Interface changes accompanied by basal cell vacuolization and apoptotic keratinocytes are seen in the epidermis (arrows) (H and E, ×400)

The index patient had also developed classic acute graft versus host disease (affecting skin, liver and gut) initially (after 1 month of transplant); following which she gradually developed extensive striae distensae probably because of the concomitant pubertal growth spurt and intake of systemic corticosteroids. Striae distensae represent traumatized dermal collagen zones, and their selective affliction by chronic lichenoid graft versus host disease in the index patient aptly demonstrates the phenomenon of locus minoris resistentiae. An easy transit and access of lymphocytes to cutaneous antigens through the damaged dermal matrix in the striae might be a plausible explanation for this occurrence. Chemotherapy-induced skin eruptions localized to radiotherapy site[4] and melanoma metastasis;[5] as well as infective conditions like verruca[6] and tinea barbae[7] localized to verrucous epidermal nevus and scar tissue, respectively, are other examples of locus minoris resistentiae. Fixed drug reaction secondary to minocycline localizing to areas of herpes zoster and burn scars has also been described.[8] Vitiligo,[9] psoriasis,[10] plane xanthomas,[11] drug-induced exanthems[12] leukemia cutis[13] and lichen sclerosus[14] are some of the other dermatosis that have been reported to localize to striae distensae.

Though graft versus host disease is a systemic affliction, the skin is affected preferentially; in both acute and chronic forms. Atypical cutaneous variants have been previously described [Table 1][15-18] highlighting the effect of the microenvironmental and constitutional factors on the final presentation of the disease. Blaschkoid (both acute and chronic)[19] and chronic sclerotic graft versus host disease conforming to the sites of the waistband, radiotherapy, needle sticks and healed herpes zoster has been previously reported.[20] Lichenoid graft versus host disease localizing to striae has been sparingly reported before.[21] All these cases highlight previously described Wolf's isotopic or Koebner's isomorphic response; both of which can now be

Table 1: Atypical cutaneous manifestations of graft-versus-host disease[15-18]

Acute graft-versus-host disease	Chronic graft-versus-host disease
Psoriasiform	Psoriasiform
Follicular erythema/lichenoid	Follicular erythema/lichenoid
Contact dermatitis	Acral keratosis
Type-II pityriasis rubra pilaris-like	Pityriasis rosea-like
Hand-foot-mouth disease-like	Annular scleroderma-like plaques
Localized to tattoo skin	Eczematoid
	Atopic dermatitis-like
	Exfoliative dermatitis
	Dermatomyositis-like
	Lupus erythematosus-like
	Hypertrophic lupus erythematosus-like
	Erythema multiforme-like
	Total body leukoderma
	Koebner isomorphic pattern
	Blaschko-linear
	Black hairy tongue
	Nodular/keloidal scleroderma-like

clubbed into the unifying concept of an immunocompromised cutaneous district or the locus minoris resistantiae,[22] which the index case aptly represents, though for a rarer disease.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Anuradha Bishnoi, Deepesh Lad[1], Raihan Ashraf, Nirmalya Banerjee[2], Uma Nahar Saikia[2], Keshavamurthy Vinay

Departments of Dermatology, Venereology and Leprology, [1]Clinical Haematology and [2]Histopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Corresponding author:
Dr. Keshavamurthy Vinay,
Department of Dermatology, Venereology and Leprology, Postgraduate Institute of Medical Education and Research, Sector 12, Chandigarh - 160 012, India.
vinay.keshavmurthy@gmail.com

References

1. Hymes SR, Alousi AM, Cowen EW. Graft-versus-host disease: Part I. Pathogenesis and clinical manifestations of graft-versus-host disease. J Am Acad Dermatol 2012;66:515.e1-18.
2. Ruocco V, Brunetti G, Puca RV, Ruocco E. The immunocompromised district: A unifying concept for lymphoedematous, herpes-infected and otherwise damaged sites. J Eur Acad Dermatol Venereol 2009;23:1364-73.
3. Lee SJ. Classification systems for chronic graft-versus-host disease. Blood 2017;129:30-7.
4. Noell C, Chen C, Sells R, Mikailov A, Kroshinsky D. An acneiform eruption exhibiting locus minoris resistentiae after whole-brain radiation and vemurafenib therapy. J Eur Acad Dermatol Venereol 2017;31:e209-10.
5. Donaldson M, Owen JL, Choi JN. Cutaneous eruption secondary to immunotherapy for metastatic melanoma limited to sites of locoregional melanoma metastases: A possible variant of locus minoris resistentiae. JAMA Dermatol 2018;154:846-7.
6. Ranugha PSS, Betkerur JB, Veeranna S, Basavaraj V. Appearance of verruca over linear verrucous epidermal nevus - An example of locus minoris resistentiae: A report of three cases. Indian Dermatol Online J 2018;9:334-7.
7. Sander CS, Sander O, Khatib A, Berger T. Tinea barbae spreading to locus minoris resistentiae. Eur J Dermatol 2009;19:173-4.
8. Dalla Costa R, Yang CY, Stout M, Kroshinsky D, Kourosh AS. Multiple fixed drug eruption to minocycline at sites of healed burn and zoster: An interesting case of locus minoris resistentiae. JAAD Case Rep 2017;3:392-4.
9. Yu RX, Hui Y, Li CR. Köebner phenomenon induced by striae distensae in a vitiligo patient. Ann Dermatol 2017;29:633-4.
10. Balasubramanian P, Srinivas CR. Pustular psoriasis occurring on the striae distensae: Isotopic phenomenon/Koebner's phenomenon. Indian J Dermatol 2016;61:239.
11. Baykal C, Yılmaz Z, Büyükbabani N. Diffuse normolipemic plane xanthoma on striae. J Eur Acad Dermatol Venereol 2017;31:e452-3.
12. Monteagudo B, Cabanillas M, Iriarte P, Ramírez-Santos A, León-Muinos E, González-Vilas D, *et al*. Clindamycin-induced maculopapular exanthema with preferential involvement of striae distensae: A Koebner phenomenon? Acta Dermatovenerol Croat 2018;26:61-3.
13. Ayesh Haj Yousef MH, Omari MU, Rjoub MM, Al-Khatib SM. Striae gravidarum leukaemia cutis: A rare manifestation of acute myeloid leukaemia. BMJ Case Rep 2017;2017:bcr2016218428.
14. Baykal C, Kobaner GB, Copur S, Buyukbabani N. Lichen sclerosus on the sites of striae distensae and a surgical scar in a patient with coexistent morphea. Acta Dermatovenerol Croat 2019;27:44-6.
15. Cornejo CM, Kim EJ, Rosenbach M, Micheletti RG. Atypical manifestations of graft-versus-host disease. J Am Acad Dermatol 2015;72:690-5.
16. Mahabal G, George L, Bindra M, George B. Late-onset acute graft-versus-host disease mimicking hand, foot, and mouth disease. Indian Dermatol Online J 2016;7:509-11.
17. Meade C, Halvorson C, Kao G, Makhzoumi Z. Acute graft-versus-host disease arising within tattooed skin. JAAD Case Rep 2015;1:114-6.
18. Prieto-Torres L, Boggio F, Gruber-Wackernagel A, Cerroni L. Nodular sclerodermatous chronic cutaneous graft-versus-host disease (GvHD): A new clinicopathological variant of cutaneous sclerodermatous GvHD resembling nodular/Keloidal scleroderma. Am J Dermatopathol 2017;39:910-3.
19. Gupta V, Arava S, Ramam M. Blaschkoid acute graft-vs-host disease. JAMA Dermatol 2018;154:494-5.
20. Martires KJ, Baird K, Citrin DE, Hakim FT, Pavletic SZ, Cowen EW. Localization of sclerotic-type chronic graft-vs-host disease to sites of skin injury: Potential insight into the mechanism of isomorphic and isotopic responses. Arch Dermatol 2011;147:1081-6.
21. García-Rodiño S, Sánchez-Aguilar D, Aliste C, Vázquez-Veiga H. Cutaneous acute graft-versus-host disease with isomorphic disposition over striae distensae in a 12-year-old girl. Int J Dermatol 2017;56:e37-8.
22. Lo Schiavo A, Ruocco E, Russo T, Brancaccio G. Locus minoris resistentiae: An old but still valid way of thinking in medicine. Clin Dermatol 2014;32:553-6.