# Dasatinib-Induced Perforating Folliculitis in a Bone Marrow Transplant Patient

**Nagendran Prabhakaran[#], Pallerla Sri Divya, Sivaranjini Ramassamy, Debasis Gochhait[1]**

*Departments of Dermatology and [1]Pathology, Jawaharlal Institute of Post Graduate Medical Education and Research, Puducherry, India*

*[#]Currently working as Assistant Professor in the Department of Dermatology in All India Institute of Medical Sciences, Mangalagiri*

Sir,

The appearance of follicular papules post bone marrow transplantation is a matter of concern as this could be a presentation of acute follicular graft-versus-host disease (GVHD).[1] However, a few mimics should be borne in mind while addressing such cases and dermoscopy offers the advantage of arriving at the diagnosis in certain instances.[2] Here, we report a 9-year-old child with chronic myeloid leukemia (CML) post non-myeloablative allogeneic hematopoietic stem cell transplantation (HSCT), who developed a pruritic follicular rash all over the body. It was diagnosed as perforating folliculitis with the aid of dermoscopy and later confirmed histopathologically.

A 9-year-old boy with history of CML in myeloid (megakaryoblastic) blast crisis presented with history of scattered pruritic eruption over the inner aspects of both the knees on day 2 after undergoing allogeneic HSCT following non-myeloablative conditioning with fludarabine and busalfan. The skin lesions then progressed to involve whole of the lower limbs. There was no history of fever, breathlessness, or diarrhea. For GVHD prophylaxis, the child was started on tacrolimus and mycophenolate mofetil (MMF). After 10 days of transplant, tacrolimus was changed to cyclosporine. Other medications included acyclovir, posaconazole, meropenem, teicoplanin, and colistin. The child underwent haplotransplant with father (6/10 HLA with mismatch at A, C, DRB, DQB1). Six months ago, when the initial diagnosis of CML was made, the patient had been started on imatinib. He had grade 3/4 neutropenia and thrombocytopenia, imatinib intolerance with fluid retention. He was continued on imatinib post 1 month with regular interruptions due to neutropenia. At the end of 2 months, patient had the appearance of blasts (26%) in peripheral smear and increase in platelets (8.2 lakhs/mm$^3$) and hence shifted to dasatinib 70 mg OD. The child tolerated well with grade 3 neutropenia.

Cutaneous examination revealed multiple erythematous to brownish predominantly follicle-based keratotic and erythematous papules over bilateral knees, thighs, and legs with relative sparing of face and trunk [Figure 1]. There were no erythematous or violaceous macular rash, vesicles, pustules, or bullae. Oro-genital mucosa, palms, and soles were normal. On day 3 post HSCT, laboratory examination revealed a white blood cell count (WBC) of 270 cells/mm$^3$ (Neutrophils-63%, Eosinophils-14%, and Lymphocytes-18%), hemoglobin level of 8.1 g/dL, and platelet count of 60000/mm$^3$. On day 4, WBC count was 290 cells/mm$^3$ and platelet count was 90000/mm$^3$, without transfusion. Results of serum biochemical analysis were normal. The differential diagnosis considered were eosinophilic folliculitis, perforating folliculitis, follicular psoriasis,

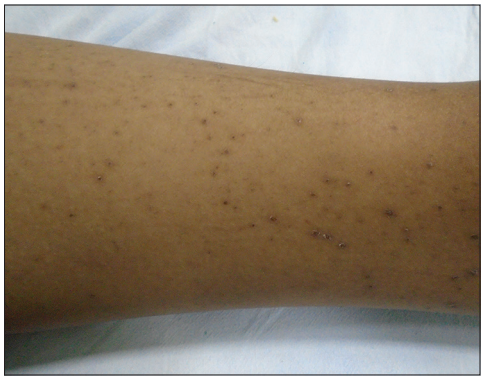

**Figure 1: Multiple discrete reddish-brown follicular papules over left thigh**

**How to cite this article:** Prabhakaran N, Sri Divya P, Ramassamy S, Gochhait D. Dasatinib-induced perforating folliculitis in a bone marrow transplant patient. Indian Dermatol Online J 2020;4:635-8.

**Received:** 07-Dec-2019. **Revised:** 01-Mar-2020. **Accepted:** 08-Apr-2020. **Published:** 13-Jul-2020.

***Address for correspondence:***
*Dr. Sivaranjini Ramassamy, Department of Dermatology, Jawaharlal Institute of Post Graduate Medical Education and Research, Dhanvantari Nagar, Puducherry - 605 006, India.*
*E-mail: siva11rsamy@yahoo.com*

**Access this article online**

**Website:** www.idoj.in

**DOI:** 10.4103/idoj.IDOJ_592_19

**Quick Response Code:**

perforating granuloma annulare, acute follicular GVHD, and disseminated fungal infection.

Dermoscopy (using Heine delta® 20 T nonpolarized dermatoscope) of skin lesions showed comedo-like openings surrounded by reddish-brown pigmentation with few white dots (eccrine openings) and hair shaft piercing the center. Pigtail hair was also seen. There was occasional reddish area but there was no telangiectasia [Figure 2]. A biopsy of the skin papule from thigh showed dilated follicular infundibulum with basophilic debris, orthokeratosis, and parakeratosis. Underlying dermis revealed degenerated collagen entering the perforation. Cross-section of hair was noted in the follicular plug. There were no eosinophils or demodex mites in the section studied [Figure 3]. Periodic acid Schiff stain was negative for fungal organisms. Hence, the diagnosis of perforating folliculitis was made. Application of cream containing combination of precipitated sulphur and benzoyl peroxide led to complete resolution of skin lesions.

Folliculocentric disorders are a group of diseases with varied differentials. Their appearance in the setting of post bone marrow transplantation could be a harbinger of sinister conditions like acute GVHD or disseminated fungal infections.[1] In most of the instances, histopathology gives a clue to the diagnosis. However, dermoscopy is a noninvasive diagnostic tool which can help in an earlier diagnosis of follicular lesions as in our case. Perforating folliculitis usually presents as erythematous or hyperpigmented follicle based keratotic papules over trunk and extremities in patients with chronic renal failure, diabetes mellitus, or medications (like TNF-alpha inhibitors or sorafenib).[3,4] Receptor tyrosine kinase inhibitors like sorafenib and nilotinib have been associated with perforating disorders possibly due to their harmful effects on hair follicle disrupting infundibular keratinization.[4] In our case, dasatinib, which also belongs to the class of kinase inhibitors could have probably triggered perforating folliculitis.

Under polarized dermoscopy, the lesions of perforating dermatoses are seen as bright white clods indicative of dilated hair follicle with keratin debris surrounded by brownish pigmentation which could be possibly due to increased melanin pigmentation in surrounding rete ridges due to inflammation.[3,5] Similarly, in the current case, pigmentation was seen surrounding the hair follicle. Also described in the literature is the "three zone" pattern on dermoscopy with an additional gray rim between yellow clods and brown zone corresponding to the epidermal invagination.[5] Histopathology showed dilated follicular infundibulum which corresponds to the comedo-like openings in dermoscopy.

Nevertheless, other differentials considered were ruled out using histopathology. Acute GVHD presenting as follicular pattern was considered in our case as there was evidence of engraftment with platelet count improving without

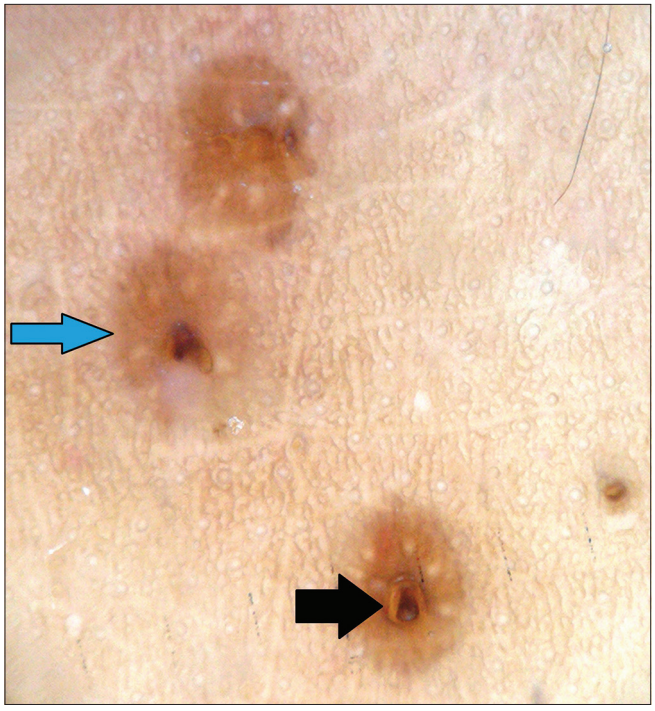

**Figure 2: Comedo-like openings surrounded by reddish-brown pigmentation (blue arrow) which is with few white dots (eccrine openings). Lower comedo-like opening shows hair shaft piercing the center (black arrow) and faint red area at 11 o'clock position. In middle comedo-like opening, one pigtail hair is present. (Heine delta®20 T non-polarised dermatoscope with 10× magnification)**

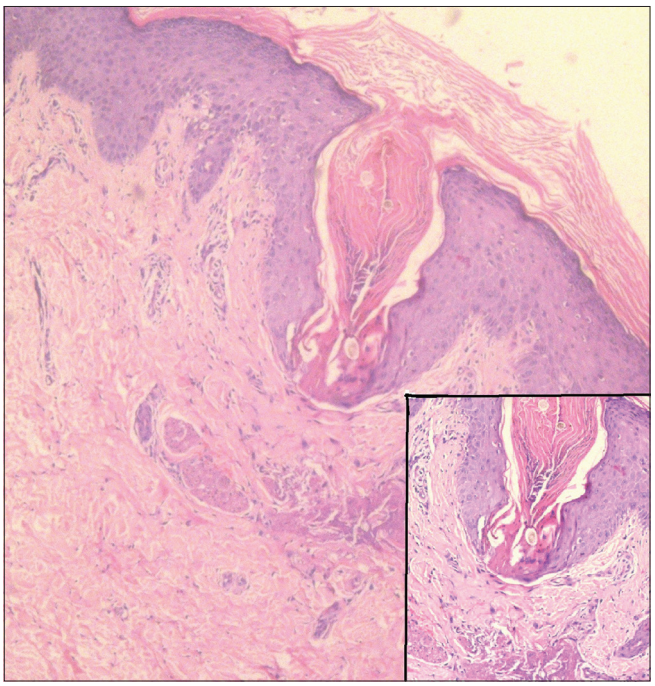

**Figure 3: Histopathology showing dilated follicular infundibulum with basophilic debris, and underlying dermis shows degenerated collagen entering the perforation. Cross section of hairs noted in the follicular plug. (H and E 100×, inset H and E 400×)**

**Table 1: Mimickers of follicular eruptions post bone marrow transplant—clinical, dermoscopic and histological findings**

| Disease | Clinical presentation | Dermoscopy | Histopathology |
|---|---|---|---|
| Acute GVHD-follicular[1,2] | Erythematous to violaceous follicular papules over trunk and extremities (Follicular type GVHD) | Multiple, telangiectatic vessels located within a pinkish or reddish background | Dilated hair follicle with keratotic plug, focal necrosis of epidermal cells basal vacuolar degeneration and sparse mononuclear cell infiltrate |
| Perforating folliculitis[3-6] | Erythematous or hyperpigmented follicle based keratotic papules over trunk and extremities | Bright white clods and a structureless gray area surrounded by brown reticular pigmentation.<br>In reactive perforating collagenosis, "A three concentric ring pattern"-central structureless brown area, surrounded by white collarette and erythematous halo has been described | Dilated follicular infundibulum with keratin plug, focal follicular disruption, degenerated connective tissue in adjacent dermis |
| Follicular psoriasis[7,8] | Follicular keratotic papules over extensors of extremities | Perifollicular scaling, multiple dotted vessels, and twisted loops | Parakeratosis with accumulation of neutrophils, hypogranulosis, and acanthosis of infundibular region |
| Eosinophilic folliculitis[6] | Intense pruritic papules in face and upper trunk | Not reported to the best of our knowledge | Eosinophilic spongiosis in the infundibular region of the hair follicle |
| Perforating granuloma annulare[9,10] | Nonfollicular papules with central umblication over extremities | Although perforating type has not been described, structureless yellowish-orange areas with dotted, branching, blurry vessels are seen in palisading histological type | Palisading histiocytic granuloma with transepidermal elimination of collagen |
| Demodex folliculitis[11,12] | Variable degree of roughness, erythema, papules, and pustules over face | Demodex tails -creamy gelatinous threads protruding out of follicular openings<br>Demodex follicular openings - light brown/grayish plugs surrounded by an erythematous halo. | Dilated follicle and the presence of dense eosinophilic material surrounding the mites |
| Malassezia folliculitis[13] | Pruritic erythematous follicular papules and pustules in upper back, shoulders, chest, and upper arms | Not reported to the best of our knowledge | Dilated hair follicle with keratin plug. PAS stain-spherical to oval yeast-like organisms |

transfusion. Rare atypical presentations of deep fungal infections like fusariosis were ruled out by PAS stain on biopsy. Eosinophilic folliculitis was considered though not in typical distribution as there was relative eosinophilia concurrently.

The clinical mimickers of acute GVHD presenting as folliculocentric papules like follicular psoriasis, perforating folliculitis, perforating granuloma annulare, eosinophilic folliculitis, demodex folliculitis, and malassezia folliculitis with their dermoscopy and histological findings are summarized in Table 1.

To conclude, the present case highlights the role of dermoscopy in patients undergoing HSCT presenting with follicular eruptions. As a clinical mimicker of acute GVHD, perforating folliculitis must also be included in the differentials, especially in the setting of *c-kit* inhibitor intake.

## *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.

## References

1. Tani M, Adachi A. Acute follicular graft-versus-host disease. Dermatol Basel Switz 1992;185:281-3.
2. Kaminska-Winciorek G, Czerw T, Kruzel T, Giebel S. Dermoscopic follow-up of the skin towards acute graft-versus-host-disease in patients after allogeneic hematopoietic stem cell transplantation. BioMed Res Int ;2016:4535717.
3. Ramirez-Fort MK, Khan F, Rosendahl CO, Mercer SE, Shim-Chang H, Levitt JO. Acquired perforating dermatosis: A clinical and dermatoscopic correlation. Dermatol Online J

2013;19:18958.
4. Llamas-Velasco M, Steegmann JL, Carrascosa R, Fraga J, García Diez A, Requena L. Perforating folliculitis in a patient treated with nilotinib: A further evidence of c-kit involvement. Am J Dermatopathol 2014;36:592-3.
5. Errichetti E, Stinco G. Dermoscopy in general dermatology: A practical overview. Dermatol Ther (Heidelb) 2016;6:471-507.
6. Weedon D. Diseases of cutaneous appendages. In: Weedon D. editor. Weedon's Skin Pathology. 3rd ed. China: Elsevier; 2010. p. 406.
7. Souza BC, Bandeira LG, Cunha TD, Valente NY. Follicular psoriasis: An underdiagnosed entity? An Bras Dermatol 2019;94:116-8
8. Behera B, Gochhait D, Remya R, Resmi MR, Kumari R, Thappa DM. Follicular psoriasis-dermoscopic features at a glance. Indian J Dermatol Venereol Leprol 2017;83:702-4.
9. Errichetti E, Lallas A, Apalla Z, Di Stefani A, Stinco G. Dermoscopy of granuloma annulare: A clinical and histological correlation study. Dermatology 2017;233;74-9.
10. Witkoff BM, Ivanov NN, Trotter SC. Perforating granuloma annulare appearing as psoriasiform lesion. Case Rep Dermatol 2019;11:233-238.
11. Segal R, Mimouni D, Feuerman H, Pagovitz O, David M. Dermoscopy as a diagnostic tool in demodicidosis. Int J Dermatol 2010;49:1018-23.
12. Aylesworth R, Vance JC. Demodex folliculorum and demodex brevis in cutaneous biopsies. J Am Acad Dermatol 1982;7:583-9.
13. Weedon D. Mycoses and algal infections. In: Weedon D. editor. Weedon's Skin Pathology. 3rd ed. China: Elsevier; 2010. p. 593.