Perforating Folliculitis Secondary to Bendamustine-Rituximab Chemotherapy: A Case Report

Sir, 
A 64-year-old married woman was referred to us with a history of pruritic hyperpigmented lesions over the extensor aspects of her limbs, which started as black papular, umbilicated lesions and eventually gave way over a period of a few days to weeks to give rise to crateriform ulcers with a raised border, present over the lower limbs and upper limbs but sparing the trunk and genitalia [Figures 1 and 2]. She was diagnosed as a case of non-Hodgkins lymphoma (NHL) stage IV undergoing a phenomenon called transformation where indolent follicular lymphoma cells get transformed into the much aggressive diffuse large B cell lymphoma (DLBCL). The diagnosis was based upon a lymph node biopsy, a bone marrow biopsy, and the involvement of multiple internal organs such as the liver and spleen. She was started on the Bendamustine–Rituximab chemotherapy regimen (Bendamustine was given at a dose of 90 mg/m² as a 30-minute infusion on days 1 and 2, combined with 375 mg/m² rituximab on day 1, and was repeated every 4 weeks for a minimum 4 to 6 cycles). She developed the lesions soon after the second cycle of chemotherapy, which she had taken approximately 2 months after the first cycle. The delay in administering the second cycle of chemotherapy was largely owing to noncompliance on the part of the patient. However, in view of regression of disease activity and the lack of any viable and effective alternative options, the chemoimmunotherapy was continued regardless up to the sixth cycle in spite of the gradual increase in the number of lesions and the severity of pruritus associated with it. The progress of the lesions was arrested on completion of therapy, and remained status quo in terms of number and pruritic severity until the time the patient consulted with us a few weeks later. At this time, the patients’ disease was adjudged to be in regression. There was no history of pruritus prior to the onset of therapy and no history suggestive of any other dermatoses, paraneoplastic symptoms, tumour metastasis, internal organ involvement, and metabolic disorders, including evidence of kidney injury.

Skin biopsy showed a dilated follicular infundibulum, containing degenerated collagen, fragmented elastic fibres, neutrophils, lymphocytes, and nuclear debris at its centre with surrounding granulation tissue [Figures 3 and 4]. The rest of the dermis showed a perivascular and interstitial lymphocytic infiltrate. On serial sectioning, the continuity of the debris with a follicular epithelium was demonstrated.

Based on the above mentioned relevant history, clinical findings, and histopathology, a diagnosis of perforating folliculitis secondary to Bendamustine-Rituximab therapy was considered. The patient was treated with topical retinoids and the lesions decreased in number and severity over a period of 6 weeks.

Perforating disorders are characterized by transepithelial elimination of dermal structures which are usually associated with miscellaneous disease states such as chronic renal failure, diabetes mellitus, vitamin A deficiency, human immunodeficiency virus, and chronic dermatoses such as acanthosis nigricans, psoriasis, and...
Letters to the Editor

Letters to the Editor

Indian Dermatology Online Journal | Volume 8 | Issue 4 | July-August 2017

291

phrynoderma, of which our patient exhibited none. However, in terms of drugs causing perforating disorders and in particular perforating folliculitis, only a few have been reported so far, and this in particular, has been known to be a rare phenomenon. A patient with rheumatoid arthritis developed perforating folliculitis on administration of tumour necrosis factor (TNF)-alpha inhibitors such as infliximab and etanercept,\[^{1}\] suggesting a possible role in the pathogenesis for TNF-alpha. In another patient of renal cell carcinoma who was treated with sorafenib, a multikinase inhibitor, the patient developed a myriad of symptoms in the form of perforating folliculitis, angioedema, and hand-foot syndrome.\[^{2}\] Llamas-Velasco et al. presented a case in 2014 of a patient treated with nilotinib, a multikinase inhibitor, which also produced lesions of perforating folliculitis occurring after reaching a complete response of the patient’s chronic myeloid leukaemia when treated with the drug.\[^{3}\] Both drugs sorafenib and nilotinib inhibit platelet derived growth factor receptor (PDGF-R), a kinase, involved in normal hair follicle development, and as a result were cited as possible causes for perforating folliculitis.

Bendamustine, marketed as TREANDA, is a nitrogen mustard that contains three components, namely, a mechlorethamine group, a benzimidazole ring, and a butyric acid side chain that confers it water solubility. Among these components, only the benzimidazole ring is unique to bendamustine, compared to other nitrogen mustards such as cyclophosphamide and cladribine, and it is said to provide it with possible antimetabolite-like activity. This factor could also explain the increased incidence of cutaneous interactions in relation with bendamustine, when used alone or in combination with other drugs, as compared to the other nitrogen mustard drugs. Bendamustine alone has been associated with cutaneous lesions in the form of a generalized pruritic erythematous desquamating rash, as reported by Alamdari et al.\[^{4}\] in an NHL patient, whose histopathology showed interface dermatitis with prominent basovacular alteration and numerous dyskeratotic keratinocytes.

Cases of severe drug eruptions such as Steven–Johnson’s syndrome and toxic epidermal necrolysis have been reported when bendamustine is used with rituximab, allopurinol, and other medications with the potential for severe drug eruptions, however, no explanation for this phenomenon is available as of yet.

Figure 1: Multiple circumscribed hyperpigmented papules and shallow crateriform ulcers over the lower limb

Figure 2: Multiple hyperpigmented papules over the extensor aspect of the upper limb

Figure 3: Epidermis with underlying cystic lesion containing basophilic material. (H and E, ×40)

Figure 4: Nuclear debris, neutrophils, lymphocytes and degenerated fibres. (H and E, ×400)
In conclusion, perforating folliculitis has a varied number of causative factors, mostly related to dermatitis or renal disorder, with only a few known implicated drugs having been known to cause it, as a result of which we present this case report highlighting the role of combined Bendamustine–Rituximab therapy as a potential or possible causative factor of perforating folliculitis, until more reports and evidence can be gathered.

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.

Rowan Monteiro, Ishwara Bhat, Anil Abraham, T. Rajlakshmi
Department of Dermatology and Pathology,
St. Johns Medical College, Bengaluru,
Karnataka, India

Address for correspondence:
Dr. Rowan Monterio,
Department of Dermatology and Pathology, St. Johns Medical College, Bengaluru, Karnataka, India.
E-mail: rowanmonterio89@gmail.com

References
1. Gilaberte Y, Coscojuela C, Vasquez C, Roselio R, Vera J. Perforating folliculitis associated with tumour necrosis factor-α inhibitors administered for rheumatoid arthritis. Br J Dermatol 2007;156:368-71.
2. Wolber C, Udvardi A, Tatzreiter G, Schneeberger A, Volc-Platzer B. Perforating folliculitis, angioedema, hand-foot syndrome-multiple cutaneous side effects in a patient treated with sorafenib. J Dtsch Dermatol Ges 2009;7:449-52.
3. Llamas-Velasco M, Steegmann JL, Carrascosa R, Fraga J, Garcia Diez A, Requena L. Perforating Folliculitis in a Patient Treated With Nilotinib: A Further Evidence of C-Kit Involvement. Am J Dermatopathol 2013;36:592-3.
4. Alamdari HS, Pinter-brown L, Cassarino DS, Chiu MW. Severe cutaneous interface drug eruption associated with bendamustine. Dermatol Online J 2010;16:1.

Access this article online
Website: www.idoj.in
DOI: 10.4103/2229-5178.209602

How to cite this article: Monteiro R, Bhat I, Abraham A, Rajlakshmi T. Perforating folliculitis secondary to bendamustine-rituximab chemotherapy: A case report. Indian Dermatol Online J 2017;8:290-2.

Received: May, 2016. Accepted: September, 2016.

© 2017 Journal of Pediatric Neurosciences | Published by Wolters Kluwer - Medknow