Generalized asymptomatic erythematous nodules and plaques

A previously healthy 49-year-old male was referred to our department with the complaint of asymptomatic reddish swellings of 1 year duration. The lesions first developed on the extensor aspect of his right leg which gradually increased in size and thereafter more lesions appeared on the face and trunk. He had no fever or weight loss. There was no lymph node enlargement or sternal tenderness. Physical examination revealed multiple, firm, erythematous plaques and nodules on the face, trunk and right lower limb [Figure 1a-c]. There are not any abnormal cells detected in peripheral blood, BM smear and BM biopsy. Bone marrow cell morphology examination revealed medullary proliferative activity. Whole body positron emission tomography and computed tomography (PET-CT) scans revealed multiple enlarged lymph nodes in armpit and groin, which demonstrated the evidence of lymphoma involvement. A punch biopsy from on one of the nodules on the anterior chest was performed. Skin biopsies of the lesion on the anterior chest showed a diffuse and nodular infiltrate of medium-sized monomorphic tumor cells throughout the dermis and subcutaneous tissues [Figure 2a and b]. The results of immuophenotyping showed a high positive expression of CD123, CD4, CD56, CD68, CD43, LCA and TDT (60%+), while stains for MPO, Mum-1, EMA, CD20, CD79α, CD30, ALKp80, TIA-1, CK and EBER were negative [Figure 3a-c]. The positive range of Ki-67 was 90% [Figure 3d]. Clonal T-cell receptor gene rearrangements were negative.

Question

What is your diagnosis?

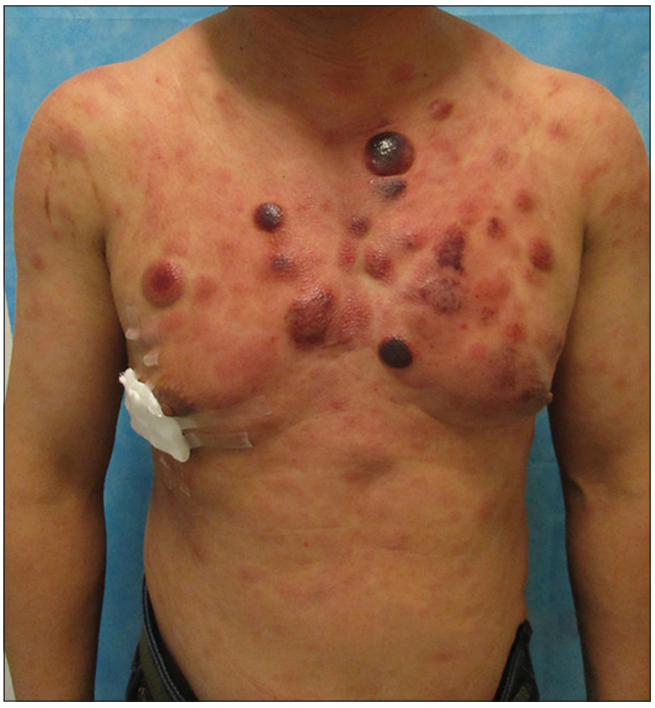

Figure 1a: Multiple erythematous plaques and nodules on the anterior aspect of trunk

How to cite this article: Chen XF, Zhan Y, Li YP, Zhang J, Zhou Y, Zhang GY. Generalized asymptomatic erythematous nodules and plaques. Indian J Dermatol Venereol Leprol 2022;88:119-22.

Received: April, 2019 **Accepted:** December, 2019 **EPub Ahead of Print:** February, 2021 **Published:** December 2021

DOI: 10.4103/ijdvl.IJDVL_85_19 **PMID:** 32643633

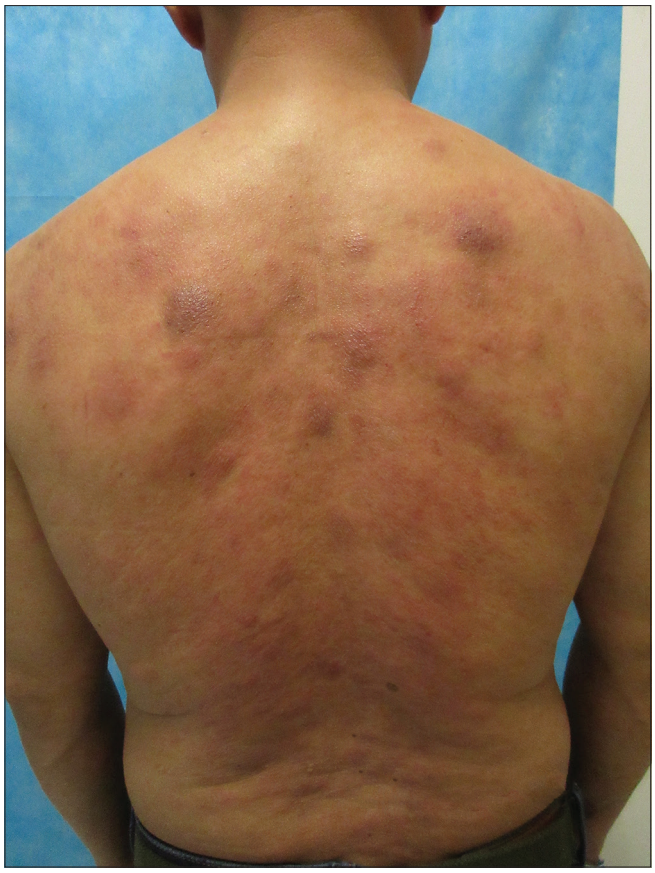

Figure 1b: Multiple erythematous plaques and nodules on the back

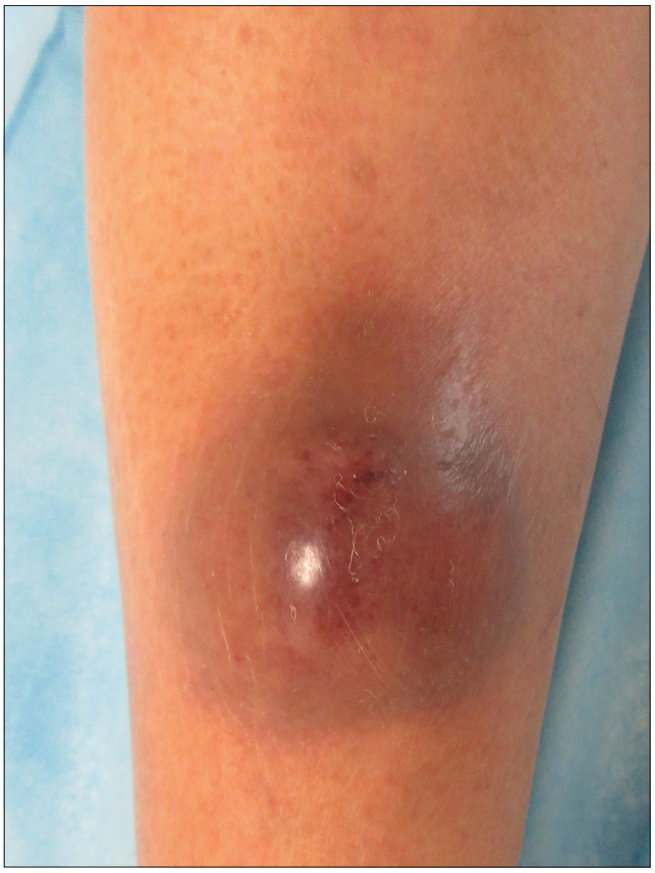

Figure 1c: An erythematous nodule on the extensor of the right leg

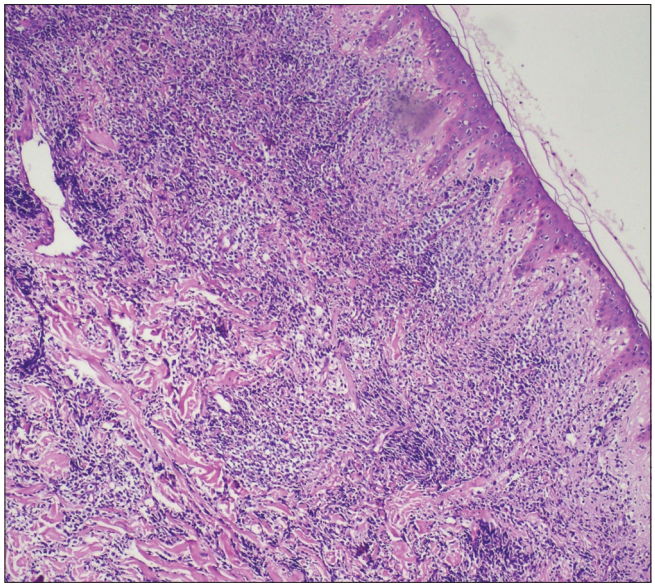

Figure 2a: A diffuse and nodular infiltrate of medium-sized monomorphic tumor cells throughout the dermis and subcutaneous tissues with a relatively normal epidermis (Hematoxylin and eosin, ×100)

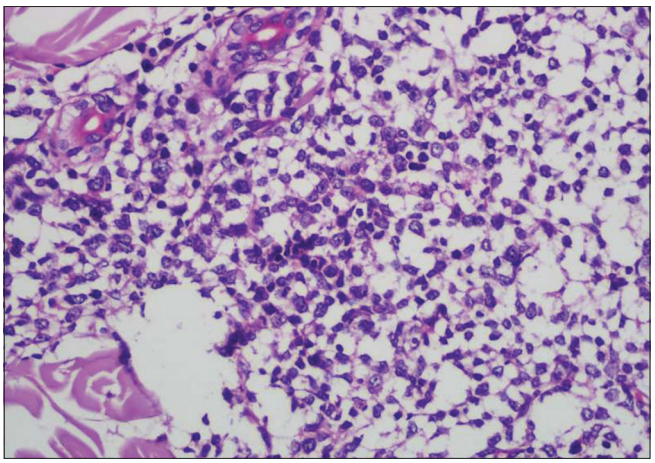

Figure 2b: Infiltrate of medium-sized monomorphic tumor cells (Hematoxylin and eosin, ×400)

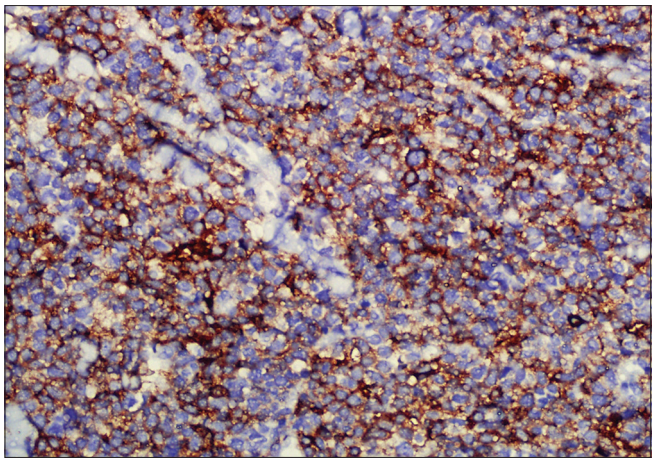

Figure 3a: Immunohistochemistry showing tumor cells positive for CD4 (×200)

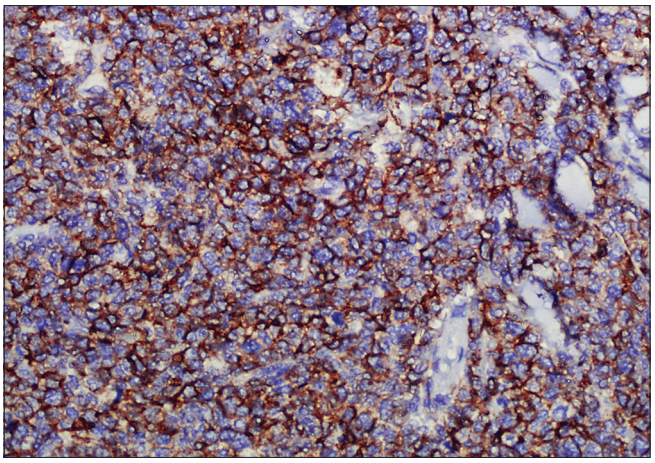

Figure 3b: Immunohistochemistry showing tumor cells positive for CD56 (×200)

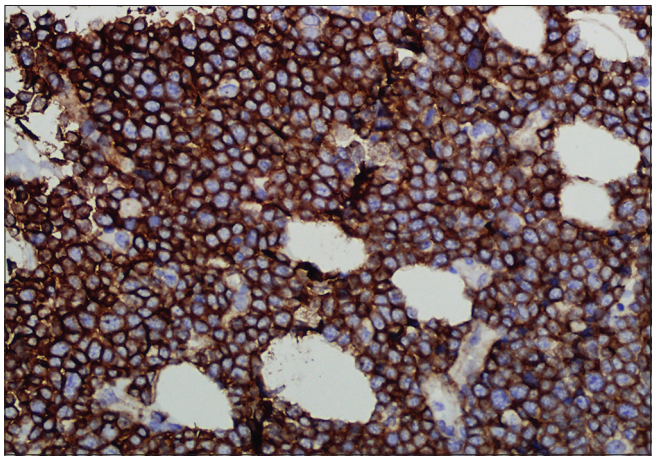

Figure 3c: Immunohistochemistry showing tumor cells positive for CD123 (×200)

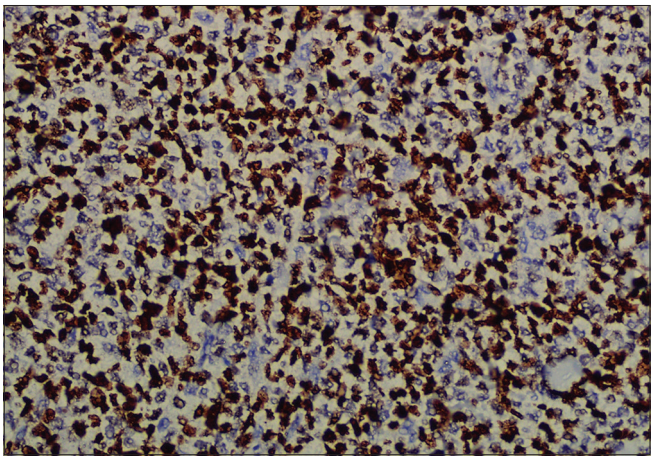

Figure 3d: Immunohistochemistry showing tumor cells positive for Ki-67 (×400)

Answer

Primary cutaneous blastic plasmacytoid dendritic cell neoplasm.

Treatment and Follow-up

The patient was referred to the hematology department and attained partial remission after undergoing 2 rounds of chemotherapeutic regiem of EPOCH (etoposide, pirarubicin, vincristine, prednisone, cyclosphamide). However, he died of severe infection at 2 months of follow-up.

Discussion

Primary cutaneous blastic plasmacytoid dendritic cell neoplasm is a rare blastic plasmacytoid dendritic cells proliferative disorder that frequently involves the skin and bone marrow.[1] Extracutaneous disease is common, including regional lymphadenopathy (55.8%), splenomegaly (44.2%), hepatomegaly (41.9%), central nervous system (9.3%) and pleural fluid (7.0%).[2] This neoplasm commonly present on the skin as asymptomatic, nonspecific solitary or multiple nodules. Typical cutaneous lesions are large purplish plaques and nodules involving the head, neck and trunk. The expected pathological findings of primary cutaneous blastic plasmacytoid dendritic cell neoplasm are dense monomorphic infiltrate of medium-sized tumor cells with fine chromatin resembling lymphoblasts throughout the dermis with a well-defined grenz zone.[3] Tumor cells express CD4, CD56 and CD123 without specific markers for myeloid, B, T and NK cells. Expression of TdT, a marker of the immature stage, significantly supported the less mature stages of primary cutaneous blastic plasmacytoid dendritic cell neoplasm.[4] Atypical immunophenotype expression may be present, making diagnosis difficult. The clinical differential diagnosis includes myeloid sarcoma, acute myeloid leukemia, T-cell lymphoblastic leukemia/lymphoma, NK-cell lymphoma/leukemia and chronic myelomonocytic leukemia with massive nodal/extranodal localization of plasmacytoid dendritic cells.[5] The median survival time of patients was 15.2 months in a large case series.[6] There is currently no consensus regarding optimal treatment for primary cutaneous blastic plasmacytoid dendritic cell neoplasm. Polychemotherapy, combination chemotherapy and radiotherapy, hematopoietic stem cell transplantation (HSCT) and target therapy are the mainstay treatments of primary cutaneous blastic plasmacytoid dendritic cell neoplasm. Pagano summarized 41 patients with induction therapy according to therapy for other hematopoietic malignancies such as acute leukemia and lymphoma.[2] Seventeen patients achieved a complete remission, however relapse occurred in six of the patients. Combination chemotherapy and radiotherapy is another treatment option. Patients usually respond to initial chemotherapy but often relapse. Allogeneic or autologous bone marrow transplantation may be a better option. Roos-Weil *et al*. retrospectively reviewed 34 of primary cutaneous blastic plasmacytoid dendritic cell neoplasm patients who underwent allogeneic HSCT.[7] 16 patients (47%) were alive at 28 months (range 4-77) of follow up and 7 patients (32%) experienced relapse at a median of 8 months (range 2-27) after allo-SCT. Target therapy as an alternative way to treat primary cutaneous blastic plasmacytoid dendritic cell neoplasm is currently underway. Falcone *et al.* summarizes the different mechanisms of some target drugs, including hypomethylating agents, interleukin 3 receptor alpha inhibition, signaling pathway inhibition and monoclonal antibodies.[8] Further clinical trials are still needed to verify therapeutic efficacy.

Declaration of patient consent

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

Acknowledgement

This research was supported by the National Natural Science Foundation of China (81500187, 81502710).

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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