Anaplastic large cell non Hodgkin's lymphoma presenting as diffuse cutaneous hyperpigmentation

Article *in* Indian Journal of Dermatology, Venereology and Leprology · March 2018

DOI: 10.4103/ijdvl.IJDVL_646_16

8 authors, including:

Sarita Sasidharanpillai
Government Medical College, Kozhikode
81 PUBLICATIONS **504** CITATIONS
SEE PROFILE

Jishna Pulpadathil
Calicut Medical College
5 PUBLICATIONS **18** CITATIONS
SEE PROFILE

Case Letters

Anaplastic large cell non Hodgkin's lymphoma presenting as diffuse cutaneous hyperpigmentation

Sir,

Paraneoplastic dermatoses often help in the early detection of underlying neoplasms. Paraneoplastic dermatoses documented in anaplastic large cell lymphoma include diffuse erythroderma, skin ulceration, annular rash and paraneoplastic pemphigus.[1]

We report a young male with anaplastic large cell lymphoma who presented with progressive hyperpigmentation of skin.

A 29-year-old male patient attended the Department of Dermatology of Government Medical College, Kozhikode with diffuse hyperpigmentation and intractable pruritus (that did not respond to antihistamines, emollients and topical steroids) of 2 years' duration and significant weight loss for 6 months. No exacerbating factors or diurnal variation were observed for pruritus which involved his entire body. He was not on any medication prior to the onset of hyperpigmentation.

Clinical examination revealed generalized hyperpigmentation of the body [Figure 1a] and palmar creases [Figure 1c] with sparing

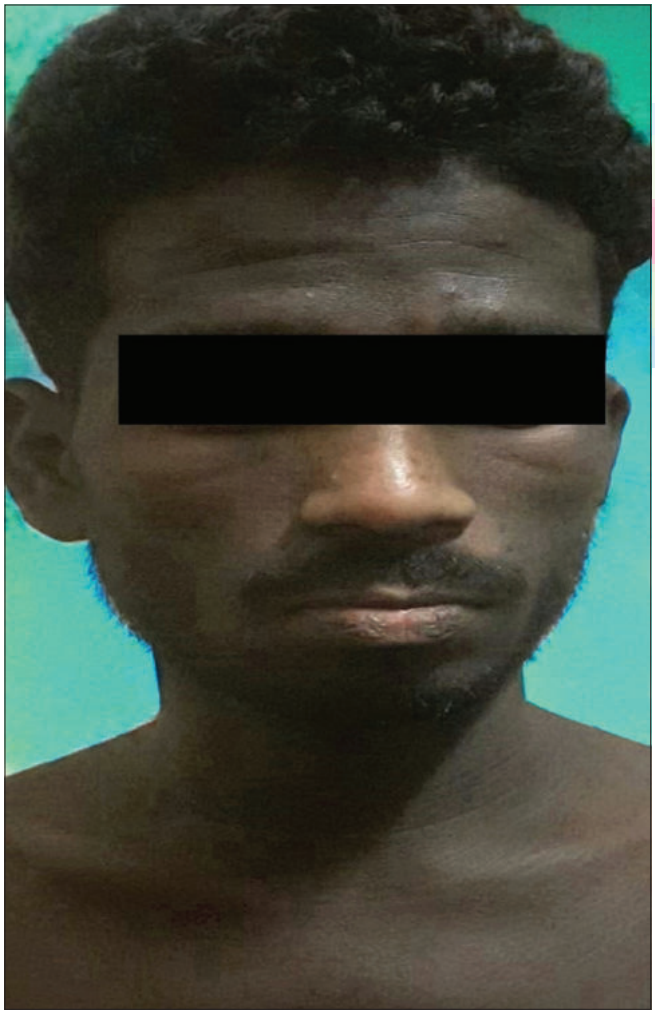

Figure 1a: Diffuse cutaneous hyperpigmentation in a patient with anaplastic lymphoma kinase negative anaplastic large cell lymphoma

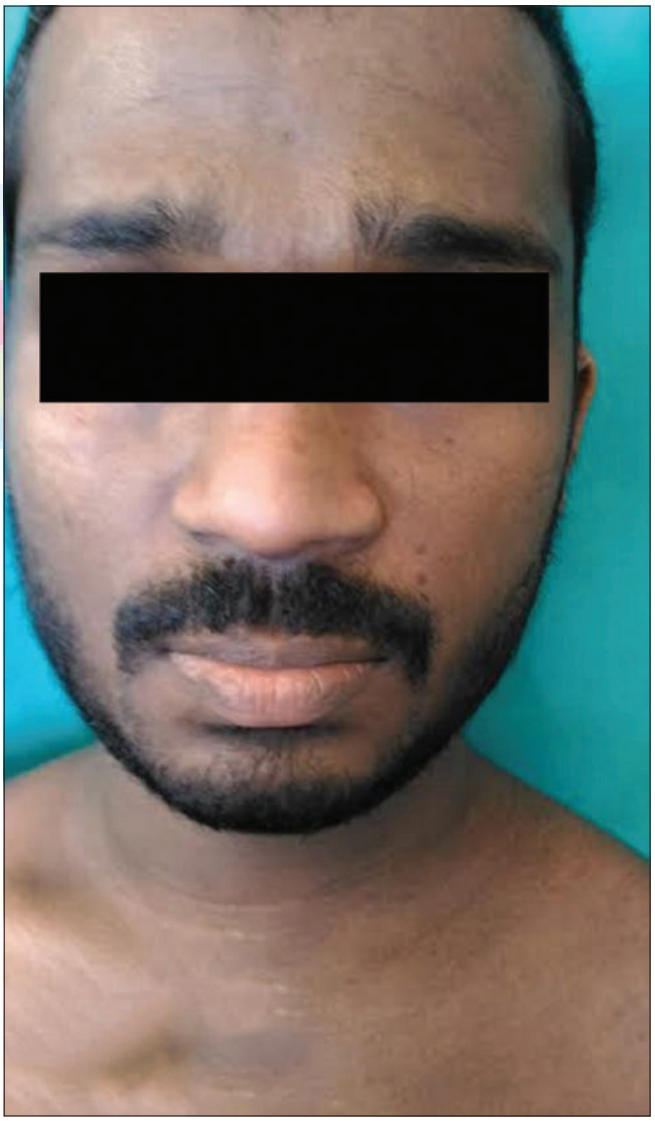

Figure 1b: Partial resolution of hyperpigmentation after chemotherapy

of mucosae and nails. A single, firm, nontender and mobile lymph node of 2 cm × 2 cm was detected in the right axilla. He had low hemoglobin (10 g%), raised erythrocyte sedimentation rate (100 mm/aefh), hypochromic microcytic anemia on peripheral smear analysis, and elevated serum lactate dehydrogenase. Mantoux test and sputum examination for acid fast bacilli were negative. Serum levels of cortisol, ferritin, transferrin, and vitamin B12 were within normal limits. Ultrasonogram and computerized tomogram evaluation of the abdomen and pelvis and magnetic resonance imaging of the brain detected no abnormality. The probable differential diagnoses of diffuse hyperpigmentation such as drug intake, vitamin B12 deficiency, tuberculosis, human immunodeficiency virus infection, adrenal pathology, adrenocorticotropic hormone secreting tumors (normal serum cortisol and brain imaging), and hemochromatosis were ruled out. Chest radiography showed a homogenous opacity in the left lung field sparing the apical and lower zones.

High-resolution computerized tomogram of thorax detected an anterior mediastinal soft tissue density lesion (8.3 × 7.7 × 12.5 cm) with calcification infiltrating the chest wall and great vessels [Figure 2].

Biopsy from the hyperpigmented skin of upper arm showed increased pigmentation of basal layer of epidermis without any pigment incontinence [Figure 3a]. Prussian blue staining failed to detect hemosiderin deposition.

Computerized tomogram-guided biopsy from the mediastinal lymph node showed a neoplasm with atypical lymphocytes, multinucleated giant cells with wreath-like nuclei, and mixed inflammatory infiltrate composed of eosinophils and neutrophils [Figure 3b]. Immunohistochemistry found the cells to be positive for CD3, CD30 [Figure 4a], and epithelial membrane antigen (EMA) and negative for CD20, CD15, anaplastic lymphoma kinase [Figure 4b], and paired box (PAX) 5 [Figure 4c] confirming the diagnosis as anaplastic large cell non-Hodgkins lymphoma- stage 2B as per Ann Arbor staging system (International prognostic index score was 1) with generalized hyperpigmentation and pruritus as a paraneoplastic phenomenon.[2] Presently, 2 months after completion of chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisolone, the patient has attained complete resolution of neoplasm and pruritus, marked improvement in cutaneous hyperpigmentation and has gained weight [Figure 1b].

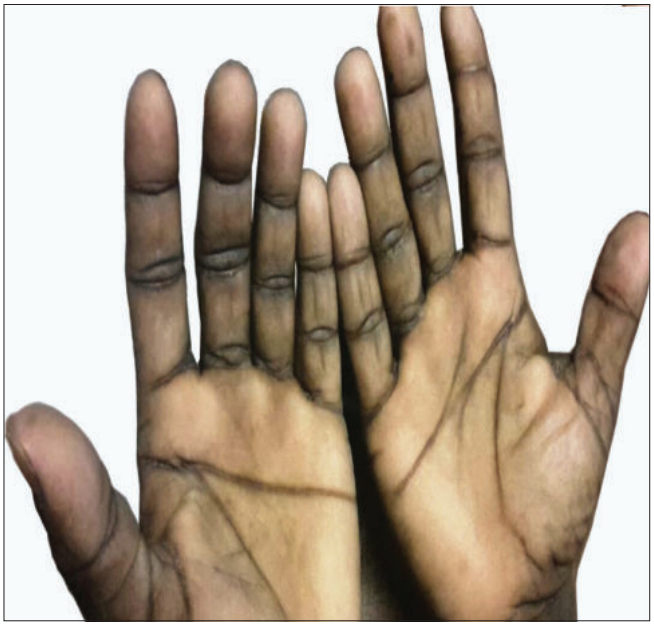

Figure 1c: Hyperpigmentation of palmar creases at the time of diagnosis.

Anaplastic large cell lymphoma is categorized into anaplastic lymphoma kinase-positive and negative anaplastic large cell lymphoma and primary cutaneous anaplastic large cell lymphoma.[3] anaplastic lymphoma kinase positive anaplastic large cell lymphoma has better prognosis compared to anaplastic lymphoma kinase negative anaplastic large cell lymphoma.[3]

Lymph node histology and immunohistochemistry including negative staining for PAX 5 in our patient favored anaplastic lymphoma kinase negative anaplastic large cell lymphoma over Hodgkin's lymphoma which could also present with addisonian-like pigmentation without mucosal involvement.[3,4] T cell gene rearrangement study, another important tool to distinguish Hodgkin's lymphoma, was not performed due to financial constraints. Angioimmunoblastic lymphoma and peripheral T cell lymphoma, not otherwise specified, were unlikely because they express less number of CD30 positive cells.[3]

Though the common age at diagnosis for anaplastic lymphoma kinase negative anaplastic large cell lymphoma is 40–65 years, it is occasionally reported in young individuals (as our patient).[3]

Clinical picture and skin biopsy findings in our case ruled out lichen planus pigmentosus, scleroderma, acanthosis nigricans and direct cutaneous involvement by anaplastic lymphoma kinase-negative anaplastic large cell lymphoma and pointed to diffuse hyperpigmentation and pruritus appearing as paraneoplastic phenomenon.

Relatively earlier stage of the disease (stage IIB) and a low international prognostic index score of 1 detected at the time of diagnosis could be a reflection of the cutaneous symptoms prompting the patient to seek early medical aid.[3]

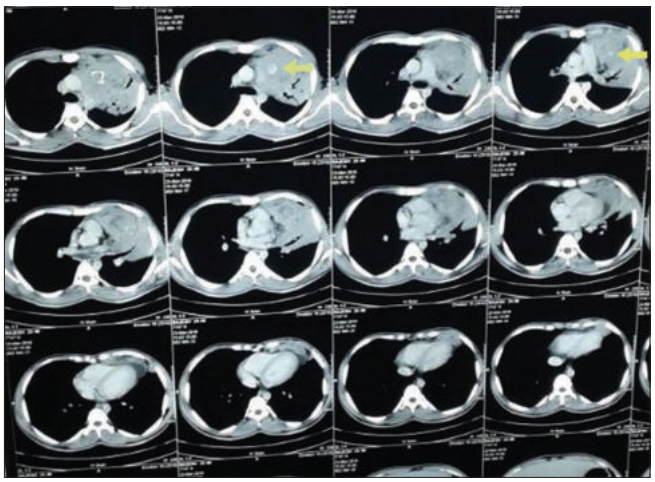

Figure 2: High resolution computerized tomogram of the thorax showing an anterior mediastinal mass with calcification (arrow on left side) infiltrating the chest wall and great vessels (arrow on right side)

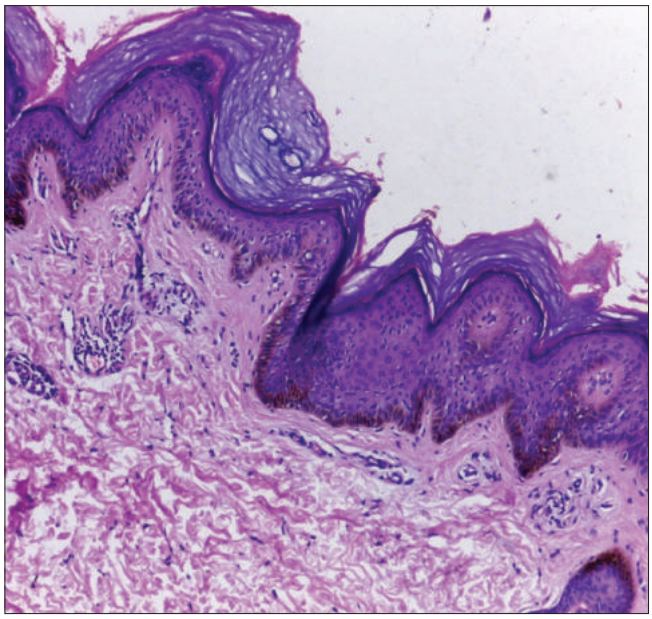

Figure 3a: Biopsy from the hyperpigmented skin of upper arm showing mild hyperkeratosis, increased pigmentation of basal layer of epidermis and mild perivascular lymphocytic infiltrate (H & E, x100)

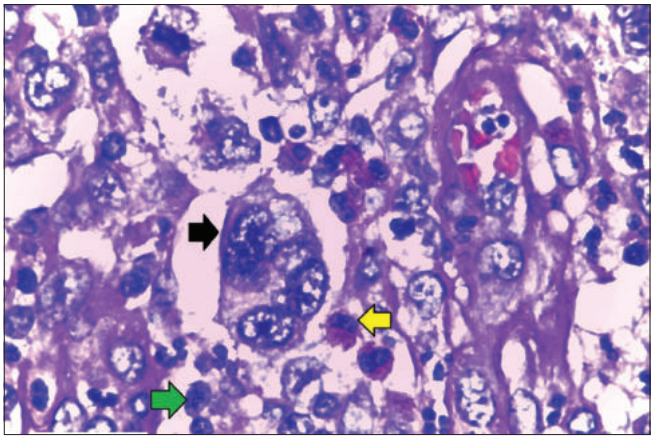

Figure 3b: Computerized tomogram guided biopsy from the mediastinal lymph node showing diffuse arrangement of atypical lymphocytes (green arrow), multinucleated giant cells with wreath like nuclei (black arrow) and mixed inflammatory infiltrate composed of eosinophils (yellow arrow) and neutrophils (H & E, x1000)

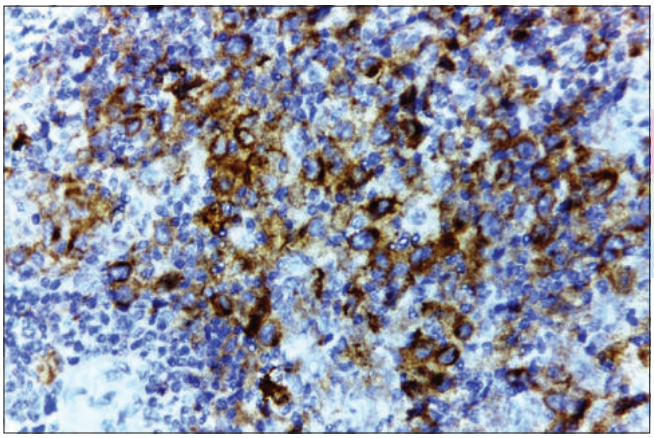

Figure 4a: Immunohistochemistry of the mediastinal lymph node biopsy specimen showing CD30 positivity (x400)

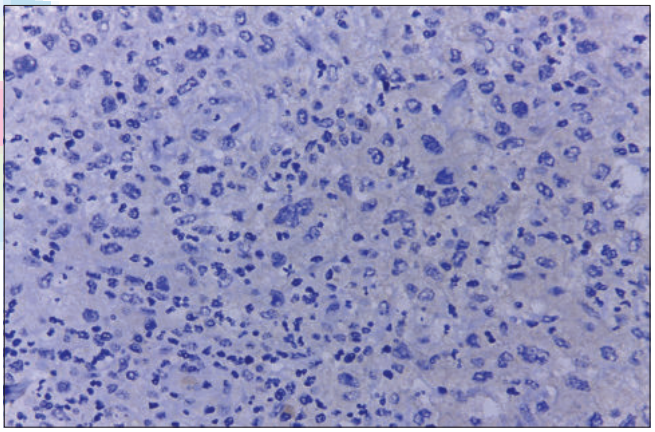

Figure 4b: Immunohistochemistry showing anaplastic lymphoma kinase negative cells (x400)

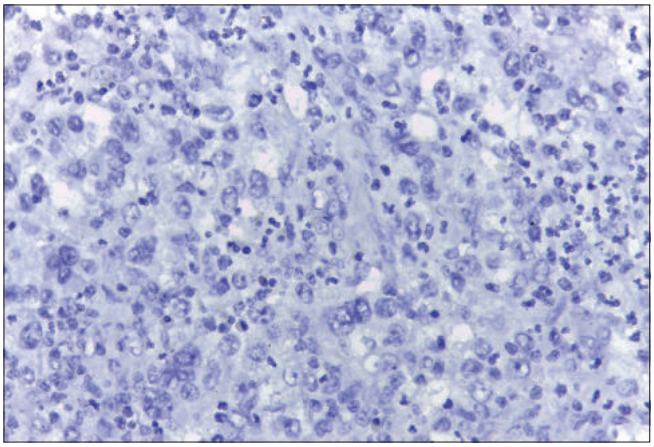

Figure 4c: Immunohistochemistry showing PAX 5 negative cells (x400)

We have come across only one other instance of anaplastic lymphoma kinase negative anaplastic large cell lymphoma manifesting with diffuse cutaneous hyperpigmentation in the literature where histology revealed hemosiderin deposition in macrophages [Table 1].[1,5-8] The absence of the same along with the increased basal cell pigmentation observed in the skin biopsy of our patient denotes a role for melanocyte stimulating substances secreted by the tumor cells.

We report this case to highlight a rare presentation of anaplastic large cell lymphoma manifesting with diffuse cutaneous hyperpigmentation and pruritus which suggests that the combination of these symptoms should raise the suspicion of an underlying malignancy.

Acknowledgement

We are grateful to Dr. Neena Mampilli, Pathologist, Baby Memorial Hospital, Kozhikode for the invaluable help in carrying out the immunohistochemistry analysis.

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.

Table 1: Paraneoplastic dermatoses associated with anaplastic large cell lymphoma

Reports of paraneoplastic dermatoses in anaplastic large cell lymphoma	Anaplastic lymphoma kinase status	Pananeoplastic dermatosis	The time of appearance of lesion with respect to diagnosis of neoplasm	Stage of lymphoma at the time of diagnosis	Outcome
Tagami *et al*.[1]	Anaplastic lymphoma kinase negative	Erythematous scaly and annular rash	Skin manifestation preceded the diagnosis of neoplasm	Stage 1B	Both rash and neoplasm responded to chemotherapy with CHOP
Hanafusa *et al*.[5]	Not mentioned	Erythroderma and painful leg ulcers	Skin lesions preceded diagnosis of malignancy by 5 years	Not mentioned	Both rash and neoplasm responded to chemotherapy with CHOP
Hanafusa *et al*.[5]	Not mentioned	Erythroderma	Skin lesions preceded diagnosis of malignancy by 20 years	Stage 1	Both rash and neoplasm responded to chemotherapy with CHOP; but due to adverse effects had to change to low dose etoposide and oral etretinate. Patient responded well
Vande *et al*.[6]	Anaplastic lymphoma kinase positive	Dry red skin rash affecting hands, feet and face	Skin rash preceded diagnosis of malignancy by 6 months	Stage IIB	Both rash and neoplasm responded to chemotherapy with CHOP
Davis *et al*.[7]	Anaplastic lymphoma kinase positive	Paraneoplastic pemphigus	Skin lesions preceded diagnosis of malignancy by 7 days	Stage IV	Treated with dexamethasone, vincristine, adriamycin, and cyclophosphamide. Patient died due to septic shock
Prka *et al*.[8]	Anaplastic lymphoma kinase negative	Diffuse skin hyperpigmentation and alopecia universalis	Skin lesions preceded diagnosis of malignancy by 18 months	Stage IVB	Treated with etoposide, vincristine, doxorubicin, cyclophosphamide, and prednisone. Patient died due to septic shock
Our case	Anaplastic lymphoma kinase negative	Diffuse skin hyperpigmentation and prurutus	Skin lesions preceded diagnosis of malignancy by 2 years	Stage IIB	Both cutaneous hyperpigmentation and neoplasm responded to chemotherapy with CHOP

CHOP: Cyclophosphamide, doxorubicin, vincristine and prednisolone

The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

Sarita Sasidharanpillai, Ettappurath N. Abdul Latheef, Poovullathil Jayesh Kumar[1], Puthen Parambath Sathi[2], Shiny P. Manakkad[2], Pulpadathil Jishna, Thapron Smitha, Aparna S. Vidya

Departments of Dermatology and Venereology, [1]General Medicine and [2]Pathology, Government Medical College, Kozhikode, Kerala, India

Correspondence: Dr. Sarita Sasidharanpillai, "Rohini," Girish Nagar, Nallalom PO, Kozhikode - 673 027, Kerala, India.
E-mail: saritasclt@gmail.com

References

1. Tagami T, Alhalabi O, Ward N, Huang J. Paraneoplastic dermatosis in a patient with anaplastic large-cell lymphoma: Case report and literature review. Dermatopathology (Basel) 2016;3:39-43.
2. International Non-Hodgkin's Lymphoma Prognostic Factors Project. A predictive model for aggressive non-Hodgkin's lymphoma. N Engl J Med 1993;329:987-94.
3. Kinney MC, Higgins RA, Medina EA. Anaplastic large cell lymphoma: Twenty-five years of discovery. Arch Pathol Lab Med 2011;135:19-43.
4. Garg S, Mishra S, Tondon R, Tripathi K. Hodgkin's lymphoma presenting as alopecia. Int J Trichology 2012;4:169-71.
5. Hanafusa T, Igawa K, Takagawa S, Yahara H, Harada J, Tani M, *et al.* Erythroderma as a paraneoplastic cutaneous disorder in systemic anaplastic large cell lymphoma. J Eur Acad Dermatol Venereol 2012;26:710-3.
6. Vande Walle N, Van den Enden E, Fostier K, De Coninck A, Nieboer K, Velkeniers B, *et al.* Systemic anaplastic large cell lymphoma presenting with cutaneous manifestations in a young man: A case report. Acta Clin Belg 2012;67:127-9.
7. Davis AK, Cole-Sinclair M, Russell P. Anaplastic large cell

lymphoma presenting with paraneoplastic pemphigus. J Clin Pathol 2007;60:108-10.
8. Prka Z, Tomasovic-Loncaric C, Pejsa V, Nevajda B, Kusec R. Diffuse skin hyperpigmentation in CD30+ lymphoproliferation. Ann Saudi Med 2012;32:318-20.

Access this article online

Quick Response Code:

Website: www.ijdvl.com

DOI: 10.4103/ijdvl.IJDVL_646_16

How to cite this article: Sasidharanpillai S, Latheef EN, Kumar PJ, Sathi PP, Manakkad SP, Jishna P, *et al*. Anaplastic large cell non Hodgkin's lymphoma presenting as diffuse cutaneous hyperpigmentation. Indian J Dermatol Venereol Leprol 2018;84:316-20.

Received: July, 2017. **Accepted:** August, 2017.