REPORT OF A CASE OF MULTIPLE NODULAR FACIAL PSEUDOLYMPHOMA INDUCED BY AMITRYPTILENE

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Abstract:
Pseudo-lymphoma of the skin is a rare eruption with clinical and histological features similar to malignant lymphoma. We report a case of skin pseudo-lymphoma apparently caused by amitryptilene therapy, as there was improvement when the drug was discontinued. There was still no recurrence after eight months and we suggest that withdrawal therapy should be considered as the first simple step in the treatment of drug induced pseudo-lymphoma cutis.

Introduction:
Pseudolymphoma of the skin is a descriptive term for a group of benign conditions characterized by a lymphocytic infiltrate [1-3]. The condition, which has no identifiable cause, usually presents as nodules or plaques and has a chronic course [4]. Biopsy specimens of enlarged lymph nodes display a spectrum of histopathological changes ranging from benign hyperplasia to apparent malignancy [6-10].

Therapy is usually simple, topical and intra-lesional corticosteroids, x-ray therapy and anti-inflammatory medication. The case that we report was treated by discontinuing various drugs one by one until regression was noticed. We also reviewed the literature in respect of the spectrum of cutaneous reaction to various drugs and conditions [6]. [Table 1]

Case Report:
A 33-year-old white woman presented with 32 violaceous red asymptomatic cutaneous nodules on her face, which had appeared first seven months before. (Fig. 1-2). Because she suffered from migraine headaches she had been taking amitryptilene (50 mg/day orally) and ergotamine (2 mg/day) for two years. Her husband and all seven children were healthy and had no similar lesions.

The nodules were only on her face and were reddish-brown, sparse monomorphic with a diameter of 1-1.5cms. There was no lymphadenopathy or hepatosplenomegaly and no history of fever or exanthema. An excision biopsy of a facial nodule showed hyperkeratosis of a thin epidermis and diffuse and follicular lymphocytic infiltration in the dermis extending to the hypodermal fat. Mitotic figures were rare. Foreign body granulomata were seen. A diffuse dermal infiltrate was composed of small round to irregular and also large lymphoid cells of which the atypical cells were suspected by T-cells. Focally the infiltration obliterated adnexal structures. Pautriers micro-abscesses were not seen. Special stains for bacteria, including acid-fast bacilli, were all negative. The amitryptilene was discontinued and over eight months, there was complete improvement with no recurrences.

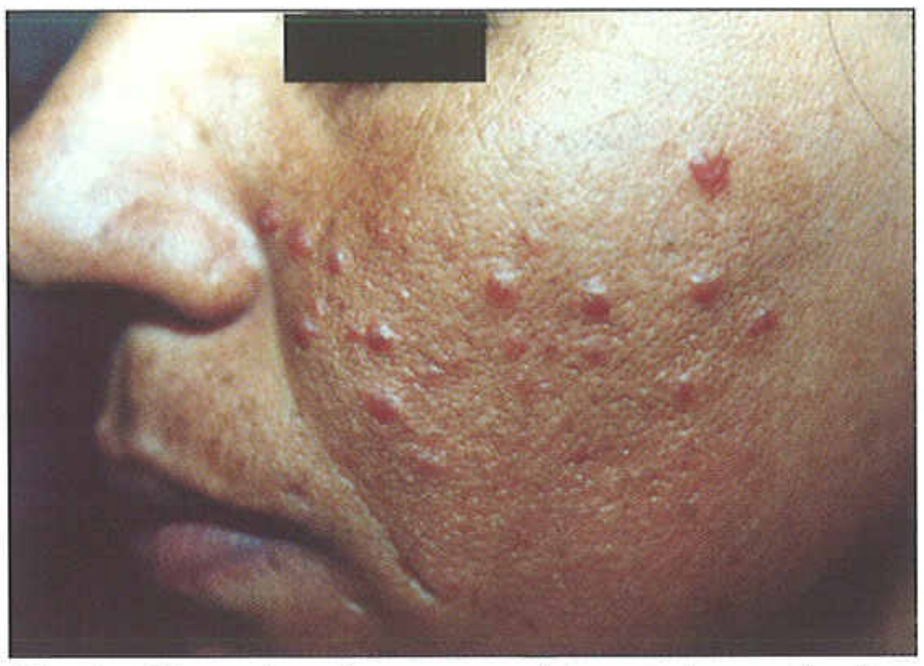

Fig. I: Fire colored monomorphic papules on the face of a case with drug induced pseudolymphoma

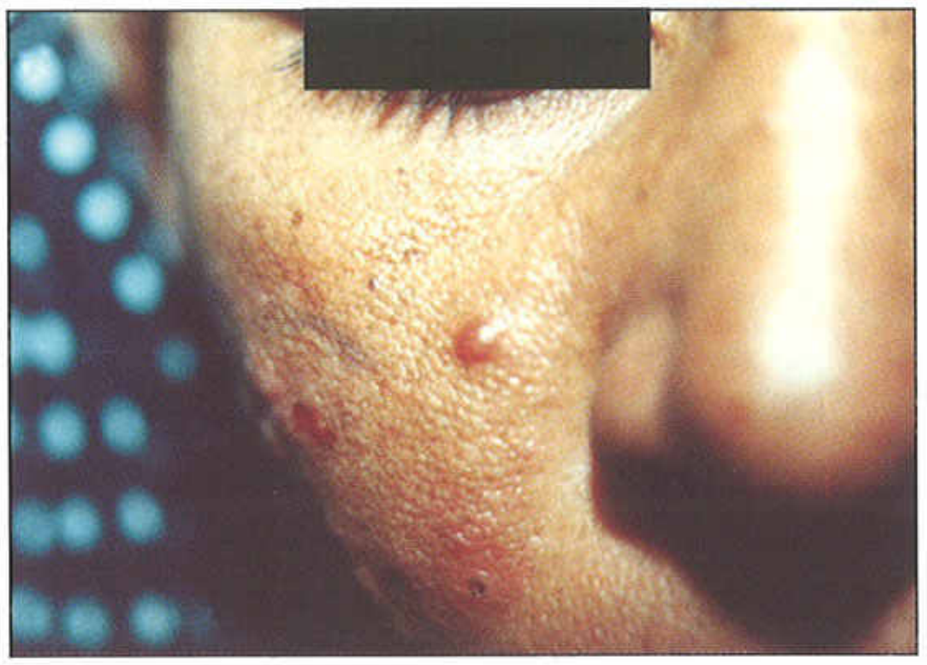

Fig. 2: A close-up magnification of one of the papules on the face of the same case

Discussion:
The pseudolymphoma in this case could have been caused by either ergotamine or amitryptilene. However we suspected that amitryptilene was the cause and the subsequent improvement and lack of recurrence following amitryptilene withdrawal suggests that we were correct in our assumption.

Cutaneous pseudo-lymphoma has been reported following the use of phenytoin [11], mephytoin, trimethadion, phenobarbitone,

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gold injections[12, 13], carbamazepin [14,16] and identical phenothiazide compounds [18,17]. Arthropod bites are another possible cause and recent reports have suggested an association with tick-borne borrellosis or Lyme disease [18,19]. Rare tumor-like lymphoproliferative infiltrations can occur intra-orally, notably in the palate, but these lack the malignant potential of lymphoma [20].

Several cases of cutaneous pseudo-lymphoma have been reported but the diagnosis has rested on the identification of Pautriers micro-abscesses in the epidermis. It can be argued that these represent spongiotic vesicles but in any case their presence is insufficient evidence for the diagnosis of cutaneous T-cell lymphoma since they can be found in other conditions including drug eruptions [21]. Severe forms and relapses occurred even after drug withdrawal.

The inducing drugs fall into two groups corresponding to drug-induced pseudo-lymphoma and the hypersensitivity syndrome. Even if the pathological findings

are similar we believe that there are two distinct entities with different clinical and biological features and outcomes. Further studies are needed to investigate this hypothesis and to evaluate the discontinuation of therapy in treating these cases[20]. A study of skin biopsies might be particularly helpful, as the lesions of drug-induced pseudolymphoma are morphologically distinctive from malignant lymphoma [22]. [Table 1]

Table 1:

Some differentiating features between benign and malign lymphoid infiltrates as compared with the present case.

Pathological Infiltration	Pseudolymphoma	Our Case	Lymphoma
Involvement	Papillary and upper reticular dermis	++	Frequently deep and incompletely excised
Heavily Involvement	At the top papules near the surface	++	Bottom of papules
Adnexals and Blood vessels and Nerves	Not involved	—	All involved
Infiltration	Lymphocytes are high Eosinophils frequent	++	Relatively monomorph

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