Chlorambucil-induced psoriasis: A rare entity

Sir,

Chlorambucil is a chemotherapeutic drug commonly used for the treatment of chronic lymphocytic leukemia (CLL). Despite its widespread use, cutaneous adverse drug reactions due to chlorambucil are uncommon. These range from mild reactions such as urticated erythema to severe reactions such as drug rash with eosinophilia and systemic symptoms and toxic epidermal necrolysis.[1] However, to the best of our knowledge, this is the first report of chlorambucil-induced psoriasis.

A 70-year-old male, a known case of CLL, presented with slightly itchy, erythematous scaly lesions on the body for 3 months. The patient was on chlorambucil for the last 5 months and developed skin lesions 2 months after starting chlorambucil. The lesions started from the scalp and gradually progressed to involve the forehead, trunk, and limbs [Figure 1a]. He was afebrile and had no personal or family history of similar skin lesions. He denied any comorbidity and was not on any other medication. Examination revealed confluent, erythematous scaly plaques on the scalp, forehead, and trunk with few discrete lesions on the limbs. Finger nails showed distal onycholysis. Skin biopsy showed mild orthokeratotic hyperkeratosis, focal parakeratosis containing neutrophils, hypogranulosis, and spongiform pustule [Figure 1b]. Dilated and congested capillaries in the papillary dermis along with upper dermal perivascular lymphocytic infiltrate admixed with neutrophils were seen. Chlorambucil was stopped, and the patient was started on emollients and topical steroids. Thereafter, there were neither new lesions nor progression of the preexisting ones. A diagnosis of chlorambucil-induced psoriasis was made.

Drug-provoked psoriasis can either be drug induced or drug aggravated. The commonly implicated drugs are antimalarials, beta-blockers, lithium, nonsteroidal anti-inflammatory drugs, tetracycline, etc. Drug-induced psoriasis occurs de novo in those without a personal or family history of psoriasis and withdrawal of drug stops disease progression. These patients require only topical antipsoritics and emollients and have a better prognosis. Drug-aggravated psoriasis is seen in individuals with a history of or genetic predisposition to psoriasis and progresses even after the offending drug is discontinued.[2] Such patients require systemic antipsoriatic therapy in addition to drug withdrawal. The latency period is variable, and correct diagnosis requires a high index of suspicion. Plaque type is the most common morphological variant of drug-related psoriasis. Though there are no clear morphological differences between drug-induced and classical psoriasis, psoriasis forms lesions have been described in the former. Drugs implicated in the causation of psoriasis can act via cyclic adenosine monophosphate, inositol monophosphate, transglutaminase or cyclo-oxygenase pathways, and modulation of levels of pro-inflammatory cytokines. Certain drugs such as tumor necrosis factor-alpha inhibitors have been implicated in the paradoxical induction of psoriasis.

Chlorambucil belongs to the class of nitrogen mustards. Few reports have shown the therapeutic effect of oral and topical nitrogen mustards in psoriasis.[3,4] Their therapeutic effect is attributed to their local anti-inflammatory effect and interference with sulfur metabolism, leading to reduced epithelial proliferation. However, these drugs can also increase pro-inflammatory cytokines and chemokines including interferon-gamma and interleukin-22, which are responsible for altered keratinocyte proliferation and differentiation.[3] Cyclophosphamide, also a nitrogen mustard, is known to decrease the number of CD4+ CD25+ regulatory T cells and also decreases their suppressive activity.[6] These cells are considered to be key players in maintaining immune tolerance. Thus, drug-induced alteration in cytokine milieu and decreased number of T regulatory cells might possibly have induced psoriasis in our patient. In view of the frequent use of chlorambucil as a chemotherapeutic drug, physicians should be aware of this rare cutaneous side effect of chlorambucil.

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.

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Conflicts of interest
There are no conflicts of interest.

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