Sulfasalazine induced lichen planus in a patient of rheumatoid arthritis

Sir,

Lichen planus (LP) is a fairly common inflammatory skin disorder that affects skin, mucous membranes, nails, and hair. Overall incidence has been estimated between 0.14 and 0.80% worldwide.[1] Classical lesions of LP are characterized by shiny, violaceous, flat topped polygonal papules, which can be closely aggregated or widely distributed, especially on the flexures of wrist, lumbar region, and around ankles.[1] Drug induced LP or lichenoid drug eruption (LDE) can appear identical to classical lesions of idiopathic LP; however, the former is usually less pruritic, more psoriasiform, rarely involves oral mucosa and tends to be more widespread with variable desquamation.[2] The eruption usually appears symmetrically on the trunk and extremities, unlike the flexural distribution of classic LP and lacks Wickham's striae. Differentiating drug-induced LP from classical LP is sometimes difficult and most evidence is based on de-challenge and re-challenge with the implicated drug [Table 1].[3]

There is an ever-increasing list of drugs causing lichenoid drug eruption. Few of the most commonly attributable drugs are gold, mepacrine, penicillamine, demeclocycline, thiazide diuretics, amlodipine, etc.[2,4,5] However, sulfasalazine-induced lichen planus deserves a separate mention and reporting because sulfasalazine has been concluded as a successful therapeutic option for cutaneous lichen planus, constituting an alternative to corticosteroid and retinoids.[6,7] The mechanism by which drugs induce a lichenoid tissue reaction are unknown, but they may develop as a result of autoreactive cytotoxic

Table 1: Differences between classical lichen planus and lichenoid drug eruption

	Classical lichen planus	Lichenoid drug eruption
History	Insidious onset.	Insidious or sudden onset, after weeks to months following drug intake.
Distribution	Lesions are usually distributed symmetrically and bilaterally over the extremities, involving the flexures of the wrists, lumbar area, arms, and legs and around ankles.[1]	Widely and symmetrically on trunk and extremities. Photodistribution is often seen.[1]
Mucosal involvement	Oral or genital mucosal involvement may be seen in 60-70% cases.[1]	Less commonly involved.[1]
Morphology	Flat topped violaceous plaque and papules with typical Wickham's striae.[2]	More eczematous or psoriasiform morphology. No Wickham's striae seen.[2]
Symptoms	Intensely pruritic.[2]	Less pruritic.[2]
Histopathology	Hyperkeratosis, wedge shaped hypergranulosis, saw-tooth pattern elongation of rete ridges, civatte bodies at the dermo-epidermal junction, liquefactive degeneration of basal layer with a band like lymphocytic infiltrate in the papillary dermis abutting epidermis, and melanin incontinence.[1,2]	Features that may be seen in lichenoid drug eruption but not in lichen planus include focal parakeratosis, hypogranulosis, presence of cytoid bodies high in the stratum corneum, less intense lymphocytic infiltrate with presence of abundant plasma cells and eosinophils in the infiltrate.[3]
Prognosis	Unpredictable course, persisting for 1 to 2 years with a chronic relapsing course.[1]	Resolves following withdrawal of the offending drug. Lesions become asymptomatic within weeks and disappear within 3 to 4 months of withdrawal of the causative drug.[1]
Recurrence	Recurrence rate is 15-20%.[1]	Recur if exposed to same drug or same genre of drugs.[3]

T cell clones directed against a drug class II MHC-antigen complex, such that native keratinocytes and Langerhan's cells are viewed by the immune system as 'non self'.[2]

Fifty five-year-old lady, a known case of rheumatoid factor positive rheumatoid arthritis for three years, presented to us with progressively increasing number of moderately itchy pigmented lesions on bilateral forearms, chest, and forehead. Her arthritis was being managed with non steroidal anti-inflammatory drugs (NSAIDs) until three months back, when she was put on sulfasalazine with a dose of 500 mg twice daily. This was done in view of her peptic ulcer disease, which was suspected to be NSAID-induced, and also due to an increased severity of arthritis, which was no longer responding to NSAIDs. She tolerated sulfasalazine well and her arthritis improved within one week of introduction of this drug, but she started to develop itchy pigmented skin lesions on face and limbs over last four weeks. She denied any similar eruptions in past. There was no history of oral ulcers or hair loss or nail changes along with the skin eruption.

On examination, patient had multiple violaceous to hyperpigmented, flat topped, discrete papules and plaques over photo-exposed sites, namely the extensors of bilateral forearms, v-area of chest, upper back, and forehead [Figure 1 a-d]. On oral examination, bilateral buccal mucosa showed irregular hyperpigmented plaques without any ulcerations or white lacy pattern. Nail plates had no abnormalities and there was no involvement of scalp hair follicles. On general examination, patient was otherwise healthy except for typical bony deformities of bilateral hands and feet [Figure 2 a and b]. Large joints clinically appeared normal. Routine blood investigations were all within normal limits. Rheumatoid factor was positive with a titre of 1:32. Erythrocyte sedimentation rate (ESR) was 12 mm in first hour and C- reactive protein was positive. There was no evidence of hyperuricaemia. On the basis of these findings, a provisional diagnosis of drug-induced lichen planus was made and sulfasalazine was withdrawn for this patient. Rheumatology opinion was sought for an alternative medication. Histopathology of a representative skin lesion showed hyperkeratosis, focal parakeratosis, wedge-shaped hypergranulosis, and liquefactive degeneration of basal cell layer with interface dermatitis [Figure 3a-c]. Patient did not consent for the re-challenge test after being informed about the nature and the method of the test. However, she reported marked improvement in her pruritus and flattening of cutaneous lesions with topical steroid and oral antihistaminics within two weeks following the withdrawal of sulfasalazine. She was followed up for the next two months to monitor recurrence of similar episodes.

Sulfasalazine is a disease-modifying drug used to

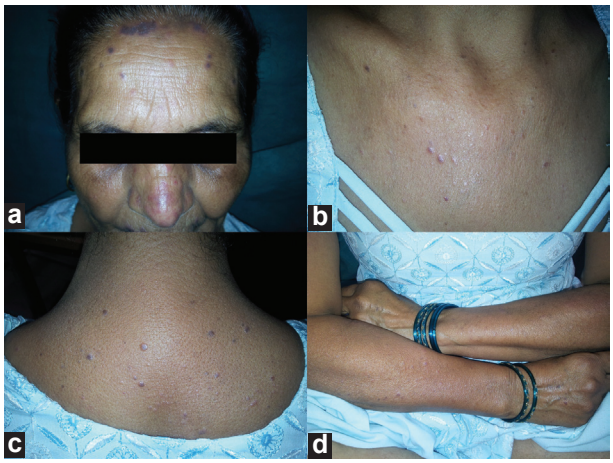

Figure 1: (a) Multiple violaceous well-defined flat topped papules and plaques suggestive of lichen planus on forehead and nose Similar papules on V area of neck (b) Lichen planus on photoexposed part of upper back (c) Lichen planus papules on extensor side of arms

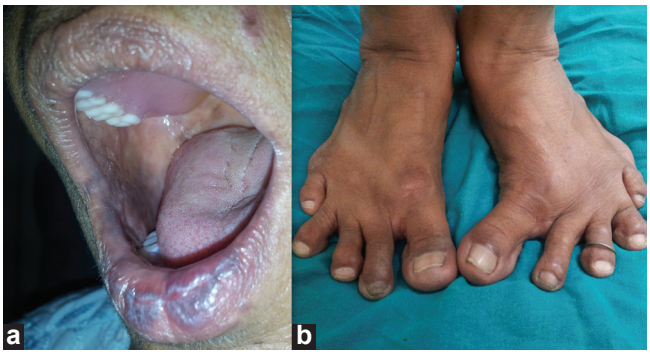

Figure 2: (a) Ill-defined violaceous plaques on buccal mucosa and lower lip (b) Bilateral feet showing typical bony deformity of Rheumatoid arthritis

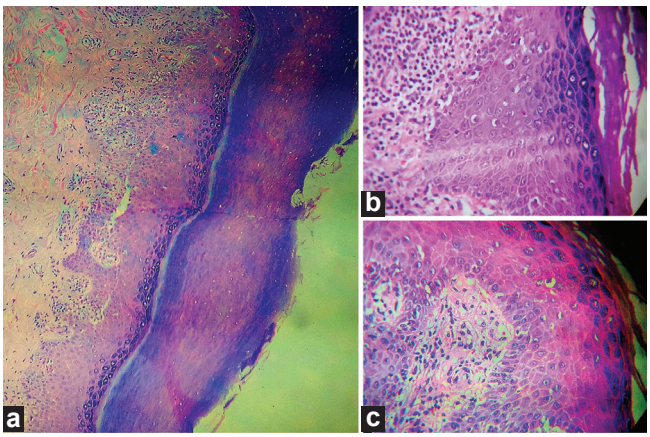

Figure 3: (a) H and E: 10X view showing hyperkeratosis, focal parakeratosis, liquefactive degeneration of basal layer, less intense lymphocytic infiltration in papillary dermis abutting epidermis (b) H and E: 40X view showing hyperkeratosis, wedge shaped hypergranulosis, saw toothing of rete ridge, with liquefactive degeneration of basal layer, and interface dermatitis with lymphocytic infiltration of papillary dermis with occasional plasma cells and eosinophils (c) H and E: 40X showing a different view of the same slide

treat rheumatoid arthritis, psoriatic arthritis, crohn's disease, ulcerative colitis, etc. Dermatologists prescribe this medicine in psoriatic arthritis and lichen planus. Sulfasalazine is a combination of an aspirin-like anti-inflammatory component and a sulfur antibiotic-like component. It appears to have anti-inflammatory effects and also reduces the activity of immune system. Gastrointestinal side effects like loss of appetite, nausea, and abdominal pain are most common. Though skin rash and oral ulcers are rare, they are known side effects of this drug.[8,9] But reports of lichen planus as a side effect of this drug are scarce in the literature.[10] The aminosalicylic moiety has been held responsible for inciting LDE in the few reported cases that are assumed to be sulfasalazine induced.[10,11]

In this case, though the patient also received NSAIDs before starting sulfasalazine, there was a considerable gap of three months after NSAIDs were stopped and before the first cutaneous eruption appeared. Although spontaneous remission could occur in the course of LP and there are a few isolated case reports of idiopathic lichen planus associated with RA; in our patient, the typical photodistribution of the lesions and prompt resolution of LP after withdrawal of the suspected drug, along with lack of recurrence, are arguments in favor of lichenoid drug eruption.[12]

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