

## Case Report

# Multiple autoimmune syndrome with isotopic phenomenon: association of lichen planus, vitiligo and alopecia areata with autoimmune hepatitis

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**Abstract** Multiple autoimmune syndrome (MAS) is the presence of 3 or more autoimmune disorders in the same patient, and is being increasingly reported. Here, we report a 31-year-old man who presented with lichen planus, vitiligo, alopecia areata and hepatitis. He also displayed isotopic phenomenon in the form of depigmented lichen planus lesions. Autoimmune tautology is implicated as the basis for MAS, and is supported by the findings of polyautoimmunity and familial immunity in cross-sectional studies. There are reports of dermatological and systemic autoimmune diseases co-occurring as MAS.

### Key words

Multiple autoimmune syndrome, lichen planus, vitiligo, alopecia areata, isotopic phenomenon.

### Introduction

Multiple autoimmune syndrome (MAS) is co-occurrence of three or more definite autoimmune diseases in the same patient, and is being increasingly reported.<sup>1</sup> These patients usually have one dermatological condition. Approximately 25% of patients with one autoimmune disorder tend to have other autoimmune disorders.

### Case Report

A 31-year-old man presented with the following complaints: (a) depigmented patches over hands and genitalia of 2 months; (b) erythematous itchy papules over limbs, trunk, head and neck of 3 months; (c) patchy hair loss over beard and scalp of 6 months without any prior medication.

He was a known case of idiopathic hepatitis with ANA positivity for past 3 years. There was no history of similar problems or any other autoimmune disease in family members. Clinical examination revealed nummular, non-inflamed, patches of alopecia over posterior scalp and beard (**Figure 1a, 1b**). Multiple erythematous to violaceous flat-topped papules over dorsa of hands (**Figure 1c**), neck and face (**Figure 1d**), few of which were depigmented (**Figures 1c, 2**). Lacy white striae were seen in buccal mucosa. Multiple hypopigmented to depigmented macules present over fingertips (**Figure 2**), forearms, groins and penis. Koebner's phenomenon was seen. He was diagnosed as multifocal alopecia areata, lichen planus and vitiligo vulgaris with isotopic phenomenon of vitiligo occurring over lichenoid lesions.

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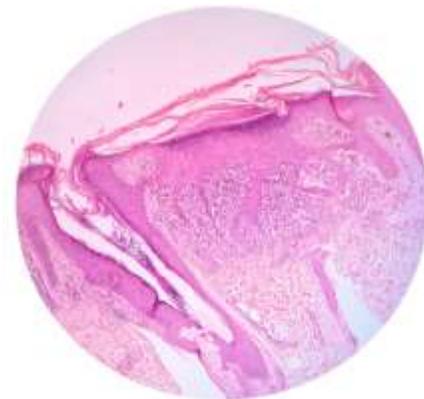
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**Figure 1,** 1a Alopecia areata over scalp; 1b alopecia areata over beard; 1c lichen planus papules with depigmentation and erythema; 1d lichen planus over neck and face.



**Figure 2** Dorsum of left hand showing acral vitiligo on fingertips and depigmented lichen planus papules over dorsum.



**Figure 3** Histopathology specimen, showing hyperkeratosis, wedged hypergranulosis, saw-tooth acanthosis, vacuolar degeneration of basal layer and dense bandlike inflammatory infiltrate in upper dermis, consistent with lichen planus (H & E stained, 20X).

Direct immunofluorescence from another raised papule showed clusters of colloid bodies staining with IgM, IgA and C3 along with a ragged fibrin basement membrane zone band

consistent with lichen planus. Scalp lesions and vitiliginous patches were not biopsied as the diagnosis was clinically evident. Thyroid profile and complement levels were normal. Hepatitis B

surface antigen and antibodies to HCV-IgM were negative. He refused repeat ANA, ASMA and LKM-1 antibody tests indicative of autoimmune hepatitis. He was treated with intralesional triamcinolone 10 mg/ml for alopecia areata, topical fluticasone propionate for face lesions and clobetasol propionate for body lesions and reported improvement on follow-up.

## **Discussion**

Polyautoimmunity is the coexistence of two or more autoimmune diseases in an individual, and if there are three or more autoimmune diseases, it is called Multiple Autoimmune Syndrome (MAS), of which vitiligo is often a component. Etiopathogenesis of MAS is speculative and is explained on the basis of similarity in underlying pathology, sharing of genes common to multiple autoimmune diseases, and molecular mimicry or similar mechanisms. Family history and female gender are strong predictors. Genetic, epigenetic, environmental, immunological, infective and psychological factors also have been implicated. Cytomegalovirus infection is frequently implicated. It is also known that 25% cases of autoimmune disease patients may develop other autoimmune diseases. The term autoimmune tautology is used to describe the common physiopathological mechanisms and genetic factors shared by many autoimmune diseases, and clinically this is evident on encountering cases of polyautoimmunity and familial autoimmunity.<sup>2</sup>

*Dermatology and MAS* Humbert *et al.*<sup>3</sup> in 1989 reported cutaneous autoimmune disorders like alopecia areata, vitiligo, pemphigus and bullous pemphigoid as a part of MAS.

Based on their occurrence and prevalence, MAS can be classified into three groups: types 1, 2, and 3.

Type 1 MAS does not have any skin features. Scleroderma is seen in type 2 MAS, whereas vitiligo, SLE and dermatitis herpetiformis are components of type 3.<sup>1</sup> Bullous pemphigoid, psoriasis, alopecia areata, pemphigus are the other skin specific autoimmune diseases reported in MAS. Vitiligo as a part of MAS has been well studied. It is usually associated with autoimmune thyroid disease and acrofacial vitiligo in females is the predominant type encountered.<sup>4</sup>

The following combinations of MAS with skin manifestations have been so far reported in literature<sup>5-7</sup>: [i] alopecia universalis, pemphigus vulgaris and insulin-dependent diabetes mellitus; [ii] pemphigus along with autoimmune thrombocytopenia, hemolytic anemia and hepatitis as a part of type II MAS<sup>6</sup>; [iii] psoriasis, primary biliary cirrhosis and SLE/scleroderma/Sjogren's syndrome overlap; [iv] vitiligo, bullous pemphigoid and rheumatoid arthritis<sup>8</sup>; [v] bullous pemphigoid, primary biliary cirrhosis and vitiligo; [vi] vitiligo, alopecia areata and ulcerative colitis.

Isotopic response described in 1955 by Wyburn-Mason, later characterized by Wolf and Wolf, is the occurrence of a new dermatological disease at the site of a healed or pre-existing previous dermatological disease, and is well reported with a second disease occurring in herpes zoster scars.<sup>8</sup> The proposed pathomechanisms are viral, neurologic, immunologic, vascular, and the concept of 'locus minoris resistentiae' (a locus of least resistance, meaning the skin already damaged by a preexisting disease).<sup>9</sup>

Alopecia areata, as well as, lichen planus have predominant CD8+ T cell population, which mount immune response against keratinocytes and can lead to epidermal damage, as well as, lichenoid reaction. Vitiligo too exhibits CD8+ T cell driven destruction of melanocytes.<sup>10</sup> Further

studies are needed to see if these three diseases have a common CD8+ T lymphocyte-mediated pathogenic mechanism.

Our case is unique in that in addition to developing MAS consisting of three dermatological autoimmune diseases along with possible autoimmune hepatitis, there was demonstration of isotopic phenomenon in the form of depigmentation occurring over certain lichen planus lesions, especially on the dorsa of the hands. This case reconfirms the fact that a person with an autoimmune disease should be closely monitored for future development of related diseases, and screening of family members may be done wherever deemed necessary.

### Conclusion

Multiple autoimmune syndrome (MAS) is being increasingly recognized and dermatological conditions form an important part of MAS. Family members of MAS patients need to be scrutinized for development of autoimmune diseases

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