

Correspondence

Chronic spontaneous urticaria associated with vitiligo and thyroiditis (autoimmune polyglandular syndrome IIIC): case series

Autoimmune polyglandular syndromes (APS) are a group of rare disorders defined by autoimmune activity against endocrine and nonendocrine organs. APS type IIIC includes autoimmune thyroiditis (AIT), vitiligo and/or alopecia, and/or other autoimmune disease such as chronic spontaneous urticaria (CSU).^{1–4} CSU is a mast cell-driven disease characterized by recurrent wheals and/or angioedema lasting for at least 6 weeks.⁵ Since 1983, there have been only a few reports of APS-IIIC encompassing CSU, vitiligo, and AIT.^{2–4} Herein, we describe a case series of 6 CSU patients with APS-IIIC, five females and one male, that were seen at our department over 3 years. Urticaria activity score 7 (UAS7) and Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL) results were obtained. Autologous serum skin test (ASST) and antithyroid antibody tests were performed. TSH, T3, and T4 blood levels were measured. The patients were diagnosed with generalized vitiligo based on clinical grounds. They were followed up for a period of 6 to 38 months and treated in accordance with EAACI/GA(2)LEN/EDF/WAO guidelines.⁵

The age of the patients varied from 34 to 67 years (Table 1). The duration of CSU and vitiligo was from 6 months to 13 years (mean: 5 years 3 months) and from 5 to 35 years (mean:

19 years), respectively. All patients experienced several episodes of angioedema monthly; wheals occurred daily. Vitiligo preceded CSU development in all our patients, which was previously shown in other studies.^{2,3,6} The duration of AIT ranged from 6 months to 21 years (mean: 12 years). Hypothyroidism was found in five females, the male being euthyroid. The patients had no signs of other autoimmune disorders.

The quality of life in the group was overall decreased. Most patients had severe CSU. All patients with hypothyroidism were treated with levothyroxine, but no one showed any improvement in urticaria symptoms. We observed the efficacy of cyclosporine A (CsA) at a dose of 2–3 mg/kg/d in three patients with poor response to up-dosed antihistamines. Adding CsA to high doses of antihistamines for 2 months led to improvement in CSU symptoms (Fig. 1a,b) and induction of remission in all three patients. The male patient was in remission for 8 months following discontinuation of treatment. Two other patients are still in remission.

Genetic and autoimmune mechanisms may explain the presence of different components of APS.⁷ Autoimmunity is crucial to CSU pathogenesis in up to 50% of cases.⁸ Such patients usually score positive on ASST, respond well to immunosuppression, and show high rates of comorbidity for other autoimmune disorders^{8,9} including AIT and vitiligo.^{3,6} Genetic predisposition for other autoimmune diseases in CSU patients

Table 1 Characteristic features of autoimmune polyglandular syndromes (APS) type IIIC patients

#	Gender	Age, years	Duration, years			Family history	Thyroid status	CU-Q2oL, %	UAS7	ASST	Elevated laboratory parameters	Treatment efficacy	Follow-up period, years	Remission, years
			CSU	Vitiligo	AIT									
1	F	54	0.7	21	21	No	Hypo	37	40	Pos	ATA, ECP, DD	AHsd (+)	1.2	0.5 ^a
2	M	55	0.5	5	0.5	Vitiligo	Eu	67.4	34	Pos	ATA, ESR, CRP, DD, ANA, Pr, ECP	AHhd (–), CsA (+)	3	0.7 ^b , 1.2 ^a
3	F	34	13	15	8	CSU, AIT	Hypo	33.7	28	Pos	ATA, IL-6, CRP	AHhd (+)	3.2	–
4	F	49	2	20	1	No	Hypo	51.1	35	Pos	ATA, ESR, CRP, ANA, CICs	AHhd (–), CsA (+)	1	0.5 ^b
5	F	61	0.5	19	10	No	Hypo	48.9	37	Pos	ATA, ECP, DD	AHhd (–), CsA (+)	0.5	0.4 ^b
6	F	67	1	35	20	AIT, RA	Hypo	60.9	17	Pos	ATA, ECP, DD, tlgE	AHhd (+)	1	0.9 ^a

F, female; M, male; RA, rheumatoid arthritis; CSU, chronic spontaneous urticaria; AIT, autoimmune thyroiditis; ATA, antithyroid antibodies; ANA, antinuclear antibodies; DD, D-dimer; tlgE, total IgE; ECP, eosinophil cationic protein; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; Pr, prolactin; IL-6, interleukin-6; CICs, circulating immune complexes; CU-Q2oL, Chronic Urticaria Quality of Life Questionnaire; UAS7, urticaria activity score 7; ASST, autologous serum skin test; AHsd, standard doses of non-sedative antihistamines; AHhd, high doses of non-sedative antihistamines; CsA, cyclosporine A; Eu, euthyroid; Hypo, hypothyroidism; Pos, positive; +, treatment was effective; –, treatment was not effective; –, still symptomatic.

^aspontaneous remission of CSU.

^bcyclosporine-induced remission.

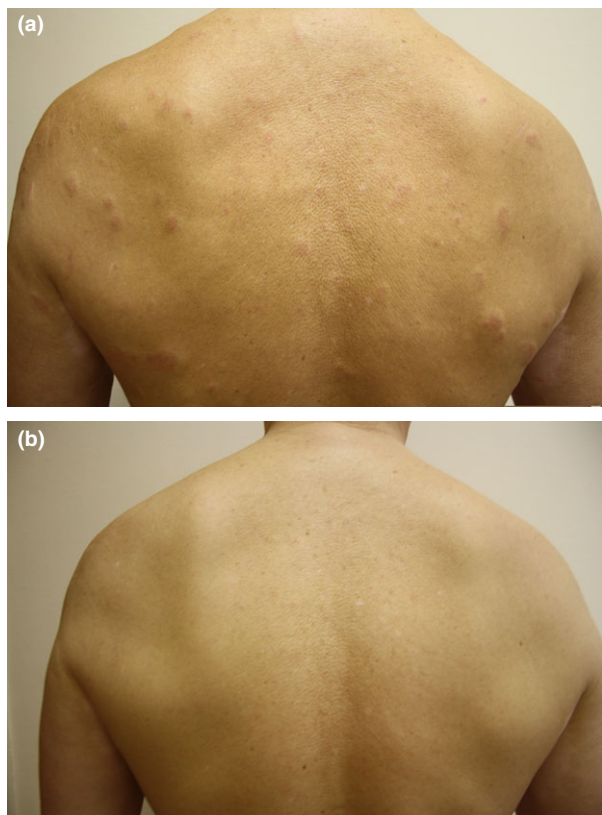


Figure 1 Urticarial rash and vitiligo patches on the back of the patient before (a) and after (b) treatment with cyclosporine A

is associated with an increased frequency of HLA alleles DRB1*04 and DQB1*0302 as compared with a control population.¹⁰ Autoimmune CSU results from synthesis of IgG antibodies against IgE and/or FcεRIα on mast cells and basophils and is assessed by ASST, basophil histamine release assay, and immunoassays.⁸ All our patients were ASST positive, and half of them had a family history of AIT, vitiligo, and/or other autoimmune disorders such as rheumatoid arthritis. In another study, the prevalence of CSU was significantly elevated in generalized vitiligo probands and their first-degree relatives.⁶

In summary, we found that vitiligo preceded CSU development in all cases and may be viewed as a prognostic factor for APS-IIIC in CSU patients. While in previous reports CSU as a component of APS-IIIC was successfully treated with PUVA⁴ and azathioprine,³ we observed rapid response to CsA and subsequent induction of remission in 3 patients in whom antihistamines

proved ineffective. The obvious limitation of our study is the fact that we did not perform HLA genotyping and tests for IgG autoantibodies to IgE and/or FcεRIα in our patients. That may be a potential area for future research.

Pavel Kolkhir, MD, PhD

Dmitry Pogorelov, MD

Nikolay Kochergin, MD, PhD

Department of Dermatology and Venereology

I.M. Sechenov First Moscow State Medical University

Moscow

Russia

E-mail: pavel.kolkhir@yandex.ru

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