

CPD

Refractory chronic spontaneous urticaria associated with CD4 lymphocytopenia in a patient with thymoma

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Chronic spontaneous urticaria (CSU) is a disease characterized by recurrent itchy weals, with or without angio-oedema, for > 6 weeks. CSU associated with CD4 lymphocytopenia has been rarely reported.¹ We report a case of CSU associated with CD4 lymphocytopenia and thymoma.

A 29-year-old Chinese woman presented at the end of July 2014 with a 2-month history of daily episodes of itchy hives. She had undergone thymectomy for thymoma type B2 in May 2013, followed by mediastinal radiation of 68 Gy and six cycles of docetaxel–cisplatin chemotherapy. She was diagnosed as having acute urticaria and treated with methylprednisolone 40 mg, desloratadine 5 mg daily and cetirizine 10 mg daily for 1 week. The weals resolved but relapsed rapidly after discontinuation of corticosteroid. Ebastine 20 mg, loratadine 10 mg, fexofenadine 180 mg daily and compound glycyrrhizin 3 tablets (25 mg each) thrice daily were administered for 2 weeks with little response. She was admitted to hospital in September 2014, at which time, physical examination showed approximately 40, widespread, solitary, coin-sized weals (Fig. 1a).

Tests with serum-specific IgEs for mugwort and cat were 3+ positive (EUROIMMUN, Germany). CD4+ T-cell count was 235/mm³ (Table 1).

The patient was diagnosed with CSU associated with CD4 lymphocytopenia. Montelukast 10 mg daily was added for a week with no response. Intramuscular thymopentin 20 mg daily was administered at the end of September, and the pruritus and weals

improved significantly after 10 days (< 10 weals daily) (Fig. 1b). One month later, the patient discontinued thymopentin by herself because of the expense, but the weals then worsened. The CSU spontaneously improved in December 2015, and in April 2016, she discontinued all medications. There was no relapse in her CSU up to the most recent follow-up.

To our knowledge, this is only the second case of CSU associated with CD4 lymphocytopenia occurring after thymectomy, radiation and chemotherapy in a patient with malignant thymoma. The first case was reported by Wickemeyer *et al.* in a 59-year-old Asian man with microinvasive thymoma,¹ who developed CSU 2 weeks after thymectomy. He received mediastinal radiation of 62 Gy over 6 weeks following thymectomy, and then completed cisplatin-based chemotherapy. His CD4 lymphocytopenia was severe (75/mm³) and occurred 3 months after radiation. Fexofenadine 180 mg and doxepin 50 mg daily reduced the itch and weals by 40–50%. During a 7-year follow-up, his CSU was partially controlled, with CD4+ T cell count varying from 130 to 164/mm³.

Idiopathic CD4 lymphocytopenia is defined as an absolute CD4+ T-lymphocyte count of < 300 cells/mm³ at two separate time points at least 6 weeks apart without evidence of human immunodeficiency infection and without immunodeficiency or therapy related to the decrease in CD4+ T cells.

Thymectomy results in elimination of CD4+ CD25⁺ regulatory T cells (Tregs), but spares some CD4+ T cells expressing endogenous T cell receptor.² Central tolerance can paradoxically result in systemic autoimmunity through differential susceptibility of Tregs and autoreactive T cells to thymic deletion. Thymectomized patients with myasthenia gravis display increases in serum IgM and IgG and in organ- and nonorgan-specific autoantibodies including anti-

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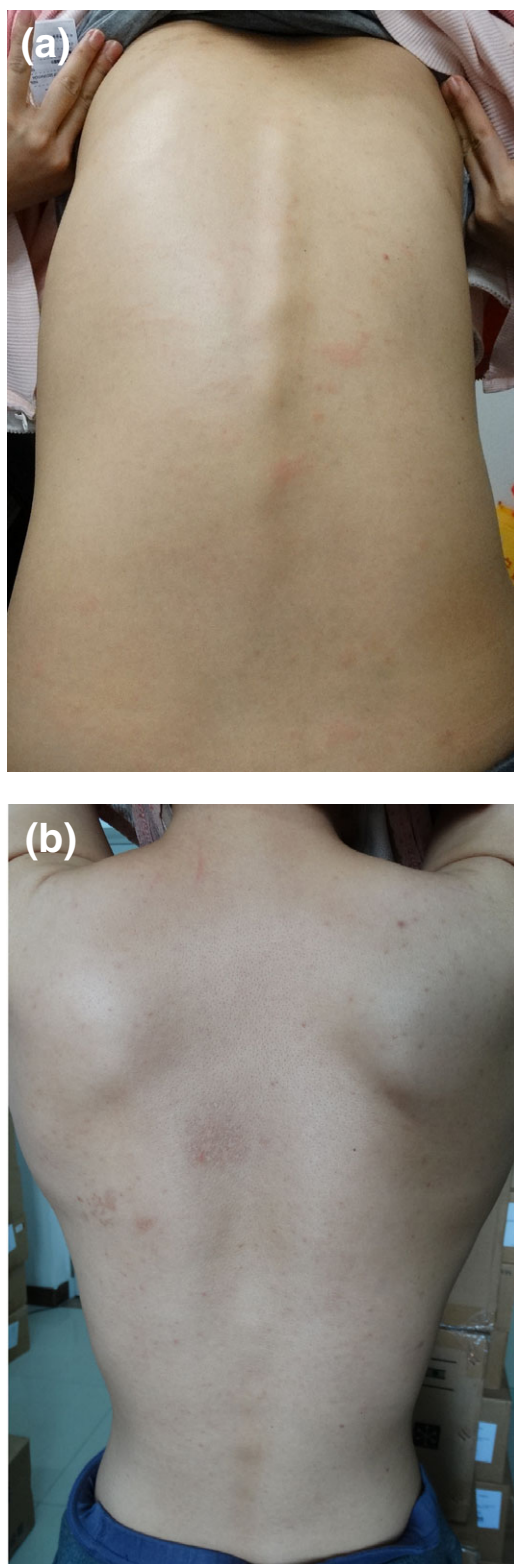


Figure 1 (a) Multiple weals on the patient's back at admission; (b) resolution of weals after 10 days of thymopentin treatment.

Table 1 Lymphocyte counts in 2 years following thymectomy.

Months after thymectomy	Completed therapies	Cell counts, per mm ³			CD4+/CD8+ ratio
		CD3+	CD4+	CD8+	
1		2151	758	1186	0.64
2	Radiation: 9 times (18 Gy)	1027	431	535	0.84
3	Chemotherapy:* 3 cycles	1360	365	912	0.4
7	Chemotherapy:* 3 cycles	1789	561	1100	0.51
12	Radiation: 25 times (50 Gy)	780	235	443	0.53
14		928	285	545	0.52
15		740	262	427	0.61
16		820	260	483	0.54
17		815	253	482	0.52
18		603	190	358	0.53
23		825	216	499	0.43
24		1127	308	711	0.43

Normal ranges: CD3+ T lymphocyte, 690–2540/mm³; CD4+ T lymphocyte, 410–1590/mm³; CD8+ T lymphocyte, 190–1140/mm³. *Chemotherapy regimen: docetaxel 120 mg on day 1, cisplatin 30 mg on days 1–3, and cisplatin 30 mg thoracic perfusion only in the first cycle.

double-stranded DNA and anticardiolipin, and later develop systemic lupus erythematosus and undifferentiated connective tissue disease.³

Radiation can result in persistent lymphocytopenia mediated by galectin-1.^{4,5} Docetaxel has a reversible nonspecific lymphopenic effect.⁶ We consider both our and the previously reported case to be secondary CD4 lymphocytopenia. In our case, CD4 lymphocytopenia occurred 12 months after thymectomy and 5 months after chemotherapy, immediately after radiation, while the CSU developed 2 months after the occurrence of CD4 lymphocytopenia. However, the CSU in the previously reported patient occurred 2 weeks after thymectomy, and his CD4 lymphocytopenia developed 8 months after thymectomy and 3 months after radiation.¹ It seems likely that his CSU was induced by thymectomy, whereas our patient's CSU was induced by radiation-induced CD4 lymphocytopenia.

In conclusion, we report a case of CSU associated with CD4 lymphocytopenia occurring after thymectomy, which is only the second such case to our knowledge.

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CPD questions

Learning objective

To demonstrate up-to-date knowledge in the management of chronic idiopathic/spontaneous urticaria.

Question 1

What treatment is first-line therapy licensed for chronic idiopathic/spontaneous urticaria?

- (a) H1 antihistamines.
- (b) H2 antihistamines.
- (c) Corticosteroids.
- (d) Leucotriene antagonists.
- (e) Ciclosporin.

Question 2

What treatment is licensed for chronic idiopathic urticaria/chronic spontaneous urticaria (CIU/CSU) refractory to antihistamines?

- (a) Corticosteroids.
- (b) Leucotriene antagonists.
- (c) Ciclosporin.
- (d) Intravenous immunoglobulin.
- (e) Omalizumab.

Instructions for answering questions

This learning activity is freely available online at <http://www.wileyhealthlearning.com/ced>

Users are encouraged to

- Read the article in print or online, paying particular attention to the learning points and any author conflict of interest disclosures
- Reflect on the article
- Register or login online at <http://www.wileyhealthlearning.com/ced> and answer the CPD questions
- Complete the required evaluation component of the activity

Once the test is passed, you will receive a certificate and the learning activity can be added to your RCP CPD diary as a self-certified entry.

This activity will be available for CPD credit for 2 years following its publication date. At that time, it will be reviewed and potentially updated and extended for an additional period.