

LETTER TO THE EDITOR

Case of angioedema and urticaria induced by lenalidomide

Dear Editor,

A 76-year-old Japanese woman was diagnosed as having multiple myeloma in 2010. She had been treated with melphalan plus prednisolone (PSL) therapy for 6 months, and thalidomide plus dexamethasone therapy for 5 months. Because the disease activity was not controlled, lenalidomide and dexamethasone combination therapy (lenalidomide 25 mg daily with dexamethasone 40 mg weekly) was started in January 2013. One week later, she noticed hemifacial swelling and eruption of the abdomen. Physical examination revealed edematous swelling of both upper and lower right eyelids and right cheek without erythema and local heat (Fig. 1a). Pale-reddish wheals were also observed on her abdomen (Fig. 1b). Abnormal laboratory results included only decreased serum red blood cells ($2.42 \times 10^6/\text{mL}$; normal, $4.2\text{--}5.7 \times 10^6/\text{mL}$) and platelet count ($9.4 \times 10^4/\text{mL}$; normal, $16\text{--}35 \times 10^4/\text{mL}$), and increased serum

immunoglobulin (Ig)E (457.6 IU/mL; normal, <170 IU/mL). Histopathological examination of the abdominal eruption demonstrated perivascular infiltration of lymphocytes, neutrophils and eosinophils in the upper dermis (Fig. 1c). Other causes of urticaria such as infections and non-steroidal anti-inflammatory drugs were excluded. Based on clinical and histopathological findings, the diagnosis of angioedema and urticaria induced by lenalidomide was established. Lenalidomide and dexamethasone were stopped and treatment with PSL 20 mg/day was started. Seven days after discontinuation of lenalidomide, swelling of the right face and abdominal eruptions completely disappeared, and serum IgE was returned to within normal range in parallel with clinical improvement. There has been no recurrence during a 4-month follow-up period.

Lenalidomide is an analog of thalidomide approved to treat multiple myeloma.¹ Lenalidomide suppresses the production of

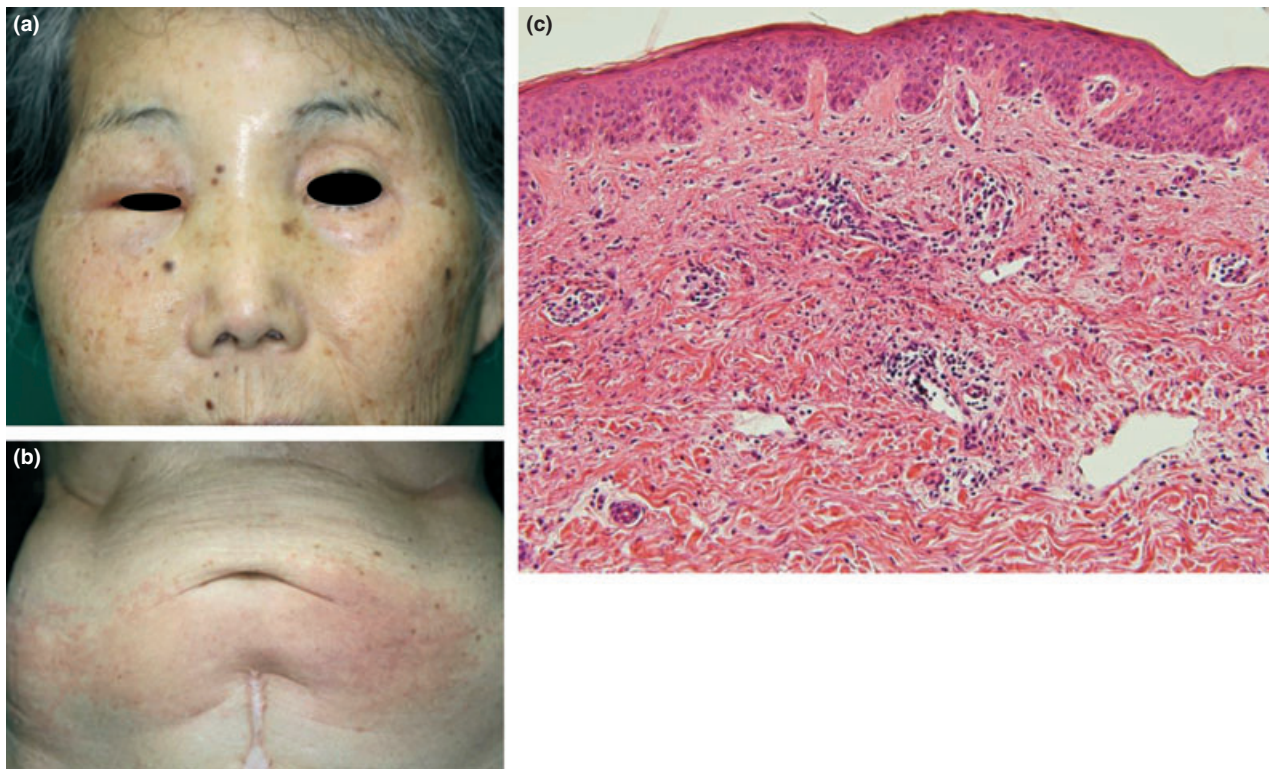


Figure 1. (a) Edematous swelling of both upper and lower right eyelids and right cheek without erythema and local heat. (b) Pale-reddish edematous erythema on her abdomen. (c) Histopathological examination of abdominal eruption. Perivascular infiltration of lymphocytes, neutrophils and eosinophils in the upper dermis (hematoxylin–eosin, original magnification $\times 200$).

tumor necrosis factor- α by T cells as well as the ligand-induced responses including angiogenesis, inflammation, cell adhesion and immune responses.¹

The primary adverse reactions associated with lenalidomide in multiple myeloma patients were myelosuppression (neutropenia, thrombocytopenia and anemia) and venous thromboembolism.² The frequency of mucocutaneous adverse eruptions of lenalidomide was 12–43%.³ Sviggum *et al.*³ reported that the most frequent skin reaction was morbilliform eruption (20%) in 51 patients with multiple myeloma. Other mucocutaneous adverse reactions include urticarial eruption, acneiform eruption, purpuric eruption, targetoid annular plaques and paronychia.³ Most reactions were mild, however, there have been reported a few cases of Stevens–Johnson syndrome or toxic epidermal necrolysis.³ To the best of our knowledge, this is the first case with angioedema induced by lenalidomide.

There are two reports that lenalidomide-induced urticaria was successfully treated with the desensitization to lenalidomide, suggesting that lenalidomide-induced urticaria was thought to be an IgE-mediated reaction.^{4,5} In our case, serum IgE was elevated and returned to within normal range in parallel with clinical improvement, suggesting that lenalidomide-induced skin lesions may be mediated via an IgE-dependent reaction.

Although angioedema induced by lenalidomide may be rare, the condition can be life-threatening risk when the pharynx and larynx are involved. Therefore, awareness of angioedema

induced by lenalidomide is important for dermatologists and hematologists to establish an early diagnosis and start an appropriate treatment.

CONFLICT OF INTEREST: The authors declare that there are no conflicts of interest.

Akihiko UCHIYAMA, Sei-ichiro MOTEGI, Kazuya YAMADA, Akihito UEHARA, Osamu ISHIKAWA

Department of Dermatology, Gunma University Graduate School of Medicine, Maebashi, Gunma, Japan

REFERENCES

- 1 List A, Kurtin S, Roe DJ *et al.* Efficacy of lenalidomide in myelodysplastic syndromes. *N Engl J Med* 2005; **352**: 549–557.
- 2 Mateos MV. Management of treatment-related adverse events in patients with multiple myeloma. *Cancer Treat Rev* 2010; **36**: S24–S32.
- 3 Sviggum HP, Davis MD, Rajkumar SV *et al.* Dermatologic adverse effects of lenalidomide therapy for amyloidosis and multiple myeloma. *Arch Dermatol* 2006; **142**: 1298–1302.
- 4 Phillips J, Kujawa J, Davis-Lorton M, Hindenburg A. Successful desensitization in a patient with lenalidomide hypersensitivity. *Am J Hematol* 2007; **82**: 1030.
- 5 Seki JT, Banglawala S, Lentz EM, Reece DE. Desensitization to lenalidomide in a patient with relapsed multiple myeloma. *Clin Lymphoma Myeloma Leuk* 2013; **13**: 162–165.