

SHORT COMMUNICATION

Reactivation of Herpes Simplex Virus and Cytomegalovirus in a Case of Thymoma-associated Graft-versus-host Disease-like Erythroderma

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Thymoma-associated graft-versus-host disease (GVHD)-like erythroderma is a rare condition that develops in patients with malignant thymoma. We report here a case of thymoma-associated GVHD-like erythroderma that worsened with the recurrence of oral herpes and the aggravation of cytomegalovirus (CMV) antigenemia.

CASE REPORT

A 64-year-old woman with a 4-year history of pruritic erythema was admitted to our hospital because of aggravation of the erythema that did not respond to 20 mg/day oral prednisolone. The patient had had malignant thymoma and myasthenia gravis for 12 years, together with recurrent oral herpes infection for several years. In spite of thymectomy, chemotherapy, and radiation therapy, malignant thymoma was disseminated to the thoracic cavity and no more treatment options could be utilized on admission.

The patient presented with erythema that was scaly, mildly keratotic, and distributed over the face, body trunk, and extremities (Fig. 1a). The patient reported severe pruritus. Biopsy specimen of the erythema revealed superficial perivascular dermatitis with parakeratosis, hypogranulosis, dyskeratosis with satellite cell necrosis, mild acanthosis, and vacuolar change in the epidermis, and moderate infiltration of lymphocytes in the upper dermis (Fig. 1b). Direct immunofluorescence was negative (data not shown). Immunohistochemistry revealed that there were more CD8⁺ T cells than CD4⁺ T cells infiltrated in the epidermis and dermis (Fig. 1c, d).

Differential diagnoses included psoriasis, lichen planus, pityriasis rosea, lichenoid drug eruption, pityriasis lichenoides chronica, and thymoma-associated GVHD-like erythroderma. Psoriasis was ruled out by the presence of dyskeratosis, and parakeratosis is not usually observed in lichen planus. The clinical course was too long for pityriasis rosea, and lichenoid drug eruption could be ruled out because of the absence of eosinophils in the dermis. Furthermore, pityriasis lichenoides chronica is not usually pruritic and the eruptions are more oval than those of our case. Based on the characteristic distribution and clinical features of the erythema and pathological findings, a diagnosis of thymoma-associated GVHD-like erythroderma was made.

Potent topical steroid (clobetasol propionate 0.05%), systemic steroid (prednisolone 2 mg/kg/day), and cyclosporine (5 mg/kg/day) were prescribed for 2 weeks, but did not control the erythema (Fig. S1; available from <http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1577>). Intriguingly, after the initiation of oral acyclovir (15 mg/kg/day) for exacerbated oral herpes infection, the erythema began to subside. Acyclovir was then switched to valacyclovir hydrochloride (15 mg/kg/day). Incidentally, we detected a high level of CMV antigenemia of up to 1,564 cells/slide, although it was only 11 cells/slide 6 months previously. The patient did not report any symptoms of retinitis, pneumonia, or colitis, thus we administered ganciclovir (5 mg/kg/day) and discontinued valacyclovir. The erythema recurred when prednisolone was tapered to 0.75 mg/kg/day; therefore, prednisolone was increased up to 1 mg/kg/day, which was not successful. Next, broadband ultraviolet

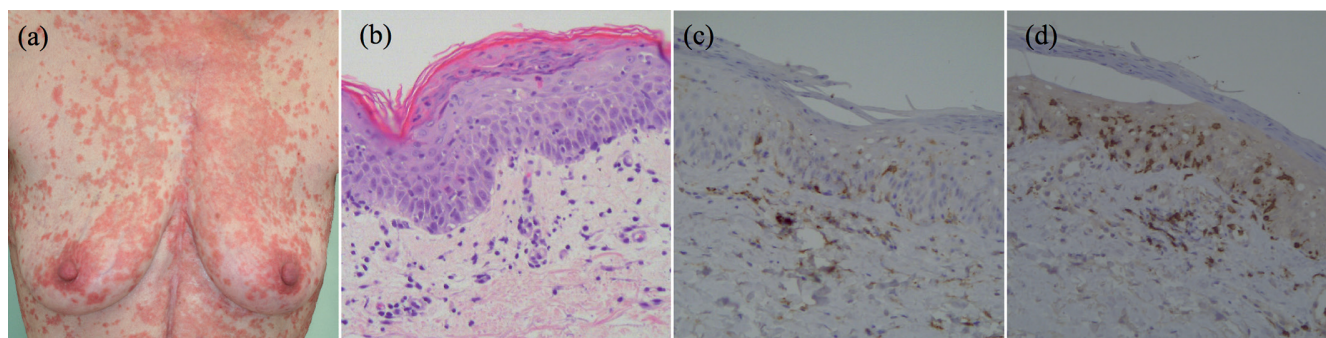


Fig. 1. Clinical and histological findings. (a) Scaly, mildly keratotic erythema was observed on the face, body trunk, and extremities with a symmetrical distribution. (b) Histology of the erythema. Haematoxylin and eosin staining. Immunohistochemistry for (c) CD4⁺ T cells and (d) CD8⁺ T cells (original magnification $\times 200$).

B (UVB) phototherapy was initiated, which cleared the erythema in a week. The phototherapy and oral prednisolone was continued at the same dose. Nevertheless, the erythema recurred after the discontinuation of ganciclovir. Although CMV antigenemia was once resolved to 5 cells/slide, we detected a worsening of CMV antigenemia of 30 cells/slide and prescribed ganciclovir again, which resulted in prompt improvement of the erythema. Thereafter, the erythema was well controlled by low-dose ganciclovir (5 mg/day twice a week); however, the patient died of invasive aspergillosis 5 months after admission to hospital. The human herpesvirus 6-antibody titre was low throughout the clinical course.

DISCUSSION

Thymoma-associated GVHD-like erythroderma is one of the symptoms of thymoma-associated multi-organ autoimmunity (TAMA), as reported by Wadhera et al. (1). It was originally proposed as a GVHD-like disease that is observed in patients with malignant thymoma (1). Because more than half of reported patients died rapidly as a result of serious infections, the development of a GVHD-like eruption in a patient with malignant thymoma portends a progressive course with a fatal outcome (1). Treatments for TAMA include surgical excision of thymoma, systemic corticosteroid, intravenous immunoglobulin, immunosuppressive agents, such

as cyclosporine, plasmapheresis, and psoralen UVA therapies (1). Since corticosteroids or immunosuppressive agents potentiate the complication by secondary infections, the development of an effective treatment is required to improve the prognosis of TAMA.

Recently, it has been demonstrated by Kitamura et al. (2) that human herpesvirus reactivation may be involved in the pathogenesis of GVHD. In our case, the eruption was worsened with the recurrence of oral herpes and the aggravation of CMV antigenemia. In addition, we observed an improvement in the eruption through the administration of the anti-viral agents, valacyclovir and ganciclovir (Fig. S1). Therefore, we presumed that reactivation of the herpes simplex virus and CMV may be involved in the pathogenesis of erythroderma. In conclusion, it is important to be cautious about viral reactivation in the treatment of TAMA because it may be associated with exacerbation of the eruption.

REFERENCES

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2. Kitamura K, Asada H, Iida H, Fukumoto T, Kobayashi N, Niizeki H, et al. Relationship among human herpesvirus 6 reactivation, serum interleukin 10 levels, and rash/graft-versus-host disease after allogeneic stem cell transplantation. *J Am Acad Dermatol* 2008; 58: 802–809.