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CASE REPORT

Thymoma with immunodeficiency with multiple recurrent oral herpetic infections

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Abstract Thymomas with immunodeficiency (formerly Good's syndrome) are a rare acquired disease of combined T- and B-cell immunodeficiency accompanying a thymoma. Recurrent opportunistic infections associated with disorders of both humoral and cell-mediated immunity frequently accompany this rare primary, adult-onset immunodeficiency. This is a report of a case of a thymoma with immunodeficiency in a 65-year-old male patient who developed recurrent oral herpetic infections. He consulted us about recurrent vesiculo-ulcerative lesions on his tongue, lower lip, and buccal mucosa. Results of laboratory examinations indicated hypogammaglobulinemia accompanied by diminished B cells in the peripheral blood, which is consistent with the characteristic features of a thymoma with immunodeficiency. After a diagnosis confirming herpes simplex virus infection, systemic antiviral therapy was administered, which was effective for his vesiculo-ulcerative lesions at follow-up. When an intractable infection accompanied by a thymoma is encountered, increased awareness about the clinical and immunological profiles of this primary immunodeficiency may help in its early diagnosis, thereby preventing mortality.

Introduction

Although thymomas are the most frequently encountered primary neoplasm in the anterior mediastinum in adult patients, they are actually rare malignant neoplasms.[1] Immunodeficiency syndrome associated with a thymoma was first reported by Good and colleagues in 1954 and was

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commonly referred to as Good's syndrome.[2] However, the current classification (2007) of the International Union of Immunological Societies replaced this old eponym with "thymoma with immunodeficiency" and lists it is a primary immunodeficiency.[2]

This syndrome is a rare acquired disease of combined T- and B-cell immunodeficiency accompanying a thymoma and has an incidence rate of approximately 6–11% in thymoma cases.[3] The affected patients are most commonly between 40 and 70 years of age and have a thymoma, fewer or no B cells in the peripheral blood, hypogammaglobulinemia, inversion of the CD4-to-CD8 ratio, and defects in cell-mediated immunity.[1,4] Patients with this primary immunodeficiency are at increased risk of developing severe opportunistic infections including herpes simplex virus (HSV)-related infections.[2]

HSV infections represent one of the most widespread infections of the orofacial region. HSV type 1 and type 2 (HSV-1 and HSV-2) are two strains of the herpes virus family, the Herpesviridae, which infect humans. These two viruses can infect the mouth or genitals; generally, HSV-1 is considered to infect the regions "above the waist", while HSV-2 is considered to infect the region "below the waist". Although most of the primary orofacial HSV infections are caused by HSV-1, infection by HSV-2 is increasingly common.[5] A primary HSV-1 infection in oral and perioral sites usually manifests as gingivostomatitis, whereas reactivation of the virus in the trigeminal sensory ganglion gives rise to mild cutaneous and mucocutaneous disease, which is often termed as recurrent herpes labialis. However, recurrent HSV-1 infection in the mouth is less common than herpes labialis and is unusual in otherwise healthy persons.[6] In immunocompromised patients, recurrent oral HSV infections are described as "atypical" and the lesions are more extensive and aggressive, slow or nonhealing, and extremely painful.[7] Recurrent herpetic infections of the tongue are exceptional and are only encountered in patients with immunodeficiency.[8]

Herein, we report a case of a thymoma with immunodeficiency in a patient who developed excessive recurrent oral herpetic infections.

Case presentation

In October 2009, a 65-year-old man consulted us because he had been suffering from recurrent vesiculo-ulcerative lesions of his tongue, lower lip, and buccal mucosa for approximately 4 years; he had been treated for a clinical diagnosis of lichen planus and fungal infection. He had a history of a thymoma first identified by a computed tomography scan after a traffic accident in 2003 and of an extended thymectomy for the thymoma removal in March 2007. Results of a histopathological analysis revealed "type AB medullary thymoma" (according to the Masaoka system of staging, the tumor was at stage II due to microscopic invasion into the capsule). His medical history also showed that he had received adjuvant (preventive) radiation therapy as a microscopic monitoring of the invasion [5000 cGy in 25 sessions (1 session = 200 cGy administration)] in June 2007 and was treated for a prolonged fever of unknown origin with antibiotics and antipyretics in August and September 2007. In addition, he reported chronic diarrhea, which began about a year ago and is ongoing.

The patient was admitted to our hospital in October 2009. Upon admission, he had a discrete erosive lesion covered by a yellowish-white fibrinous exudate with surrounding mucosal erythema on the lower lip (Fig. 1A) and buccal mucosa (Fig. 1B), and the well-demarcated, indurated, and thickened yellowish-white plaques and nodules on the dorsal tongue (Fig. 1C). Regional lymphadenopathy was present. Written consent was obtained from the patient, and owing to the atypical clinical presentation, a biopsy was performed under local anesthesia. An oral biopsy specimen was taken from the tongue.

A histological analysis revealed the following marked hyperplastic changes in the mucosal epithelium: mainly irregular acanthosis, parakeratosis, edema, and lymphocyte exocytosis (Fig. 2A). In addition, there were ulcerated vesicles. Near the ulcerated areas, characteristic virus-infected keratinocytes were observed along the basal layer of the epithelium. They were large cells with homogenous eosinophilic cytoplasm and mummified chromatin with a thick nuclear membrane. Multinucleation and nuclear molding were frequent (Fig. 2B).

Blood samples were collected on the same day. Results of a laboratory examination revealed the following: white blood cell count, 4600/mm^3; hemoglobin, 12.2 g/dL; platelet count, 152,000/mm^3; C-reactive protein, 10.6 mg/L; total protein, 6.21 g/L; and albumin of 4.48 g/dL. Laboratory data included the following: low immunoglobulin G (IgG), 5.91 g/L (normal: 800–1600 mg/dL); IgA, 0.25 g/L (normal: 80–400 mg/dL); and IgM, 0.17 g/L (normal: 50–180 mg/dL). A lymphocyte subset analysis of

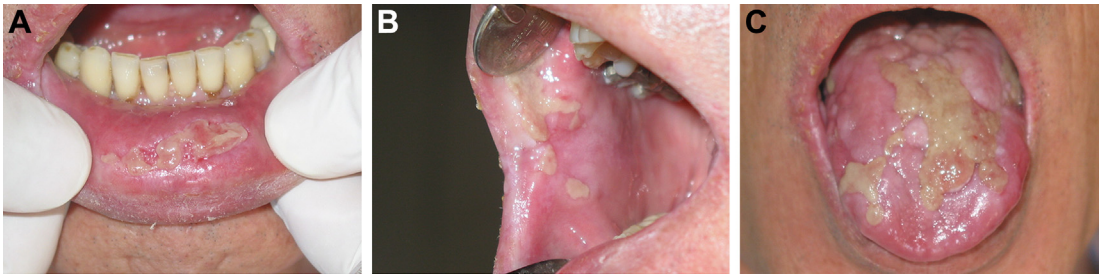

Figure 1 (A) Discrete erosive lesion covered by a yellowish-white fibrinous exudate with surrounding mucosal erythema on the lower lip labial mucosa; (B) appearance of the right buccal mucosa before treatment; and (C) well-demarcated, indurated, and thickened yellowish-white plaques and nodules on the dorsal tongue.