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Squamous cell carcinoma of the soft palate associated with autoantibodies to desmoglein 1 and 3

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Introduction

The desmogleins are a family of cadherins cell-cell adhesion molecules consisting of proteins DSG1, DSG2, DSG3, and DSG4. They play a role in the formation of desmosomes, which form the major types of intercellular adhesive junctions.

DSGs are currently thought to be involved in autoimmune diseases, infectious diseases, and inherited diseases. Patients with pemphigus, an autoimmune blistering disease of the skin and mucous membranes, carry IgG autoantibodies directed against DSG1 and DSG3 [1]. Pemphigus vulgaris antigen is also considered a tissue-specific type of desmoglein [1].

Case presentation

A 67-year-old Japanese woman noted an erosive lesion on the median side of the soft palate four months earlier and was referred to the Department of Oral Surgery for suspected pemphigus vulgaris. Physical examination showed slightly elevated erosive lesion measuring approximately 3 cm in diameter on the central soft palate, with a clear demarcated border (Figure 1). No enanthema were seen in other areas of

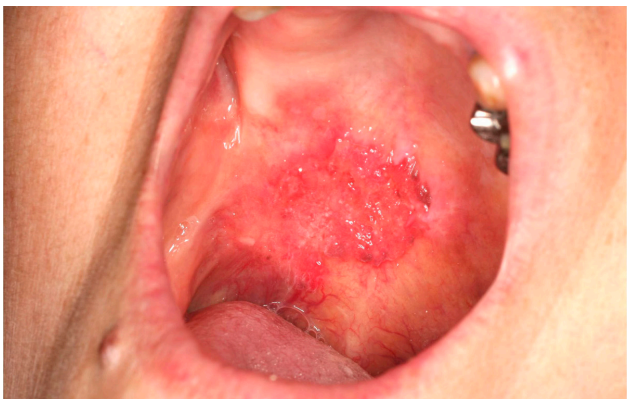

Figure 1. Clinical finding: Erosive lesion measuring approximately 3 cm in diameter on the central part of the soft palate. [Copyright: ©2013 Maumi et al.]

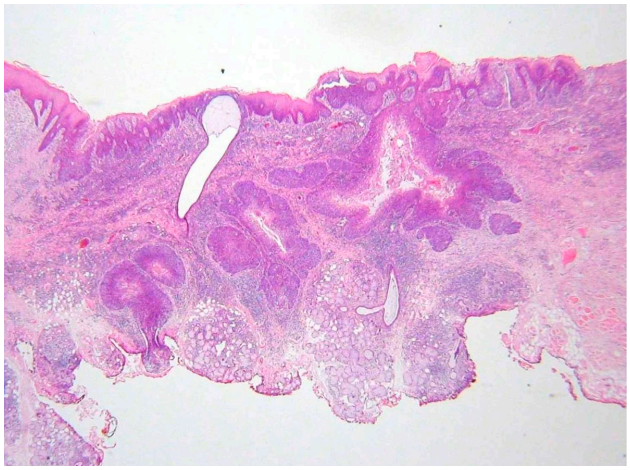

Figure 2. Histopathological examination of hematoxylin-eosin stained tissue biopsy showed invasion of the lamina propria mucosa by tumor cells. Magnification, 20x. [Copyright: ©2013 Maumi et al.]

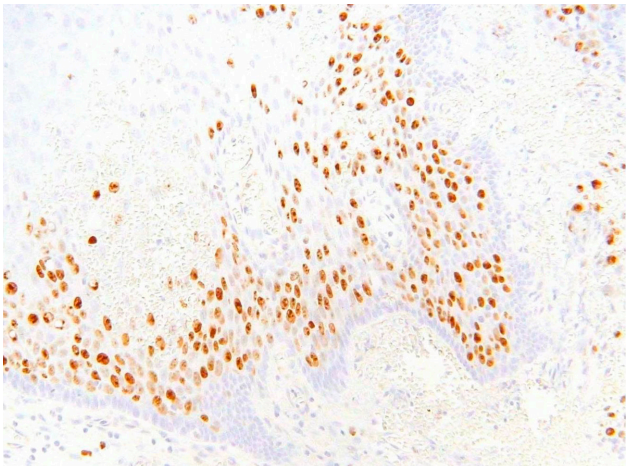

Figure 4. Immunohistochemical staining for MIB1 (Ki67) showed nuclear staining in approximately 80% of tumor cells. Magnification, 200x. [Copyright: ©2013 Maumi et al.]

the oral cavity. Anti-DSG antibodies were positive (DSG1: 42, DSG3: 25) by ELISA, and a biopsy was taken from the soft palate.

Histopathological examination of the biopsy showed proliferation of atypical epithelial cells and invasion into the lamina propria mucosa by tumor cells (Figure 2). These cells showed wide variation in size and mitoses of the nucleus in the mucous membrane. The lamina propria mucosa showed prominent cell infiltration mainly composed of lymphocytes and plasma cells (Figure 3). Immunostaining for MIB1 (Ki67) showed positive staining in approximately 80% of tumor cells (Figure 4). There were no features of acantholysis, suggesting the histopathological diagnosis of pemphigus. Direct immunofluorescence staining demonstrated no deposition of IgG or C3 on the epithelial cell surface or basement membrane zone. The final diagnosis of squamous cell carcinoma was established.

Treatment included complete excision of the tumor on June 6, 2007, followed by chemotherapy [cisplatin (CDDP)/5-fluorouracil (5-FU)] combined with tegafur, gimeracil, and oteracil potassium (TGO). The treatment resulted in a significant fall in anti-DSG antibody titer (DSG1: 10, DSG3: 5) by ELISA.

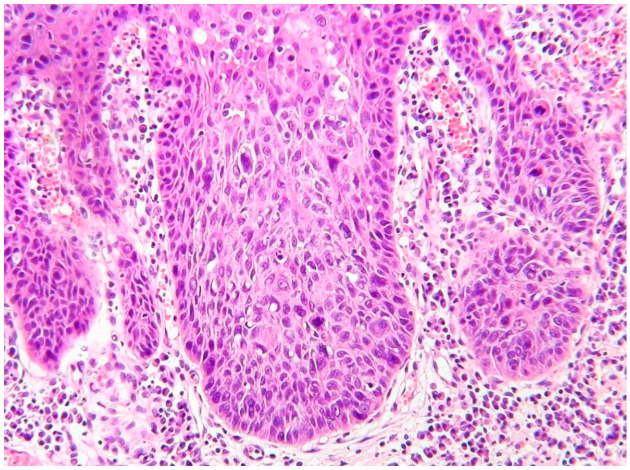

Figure 3. Histopathological examination of hematoxylin-eosin stained tissue biopsy under high magnification confirmed the diagnosis of undifferentiated squamous cell carcinoma. The subepithelial tissue shows marked inflammatory reaction with a mixture of lymphocytes and plasma cells. Magnification, 200x. [Copyright: ©2013 Maumi et al.]

Discussion

To our knowledge, there are no reports of primary squamous cell carcinoma associated with anti-DSG antibody, although there is a case of pemphigus foliaceus developing after metastasis of cutaneous squamous cell carcinoma to regional lymph nodes [2]. Recently, a possible role of DSG3 in the process of squamous cell carcinogenesis has been hypothesized [3]. There are several recent studies reporting the overexpression of DSG3 in head and neck squamous cell carcinoma [4] or conversely decrease in expression of desmocollin 3 and DSG3 in oral squamous cell carcinoma [5] especially when the tumor is poorly differentiated. There is also a study describing decrease of desmoplakin, plakophillin and DSG1 in dysplasia and oral squamous cell carcinoma [6]. Furthermore, DSG3 is reported as a biomarker for occult lymph node metastasis in oral cancer [7].

It was assumed in the present case that the increase in anti-DSG antibody titer was secondary in response to tumor cells, which might be overexpressing DSG1 and DSG3, although no evidence of autoimmune disease was available. Interestingly, surgical treatment followed by CDDP/5-FU and TGO resulted in normalization of autoantibody titer by ELISA.

The findings suggest that anti-DSG antibodies could be potentially used to screen for tumor relapse or metastasis in this patient.

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