

양측 악하선에 수개월 간격을 두고 발생한 면역글로블린 G4 연관 경화성 타액선염

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IgG4-related chronic sclerosing sialadenitis in both submandibular glands that developed at intervals of months

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= Abstract =

IgG4-related chronic sclerosing sialadenitis commonly occurs in the submandibular glands. The gold standard for diagnosis of IgG4-related chronic sclerosing sialadenitis is a tissue biopsy from the affected organ. Herein, we report the probability of occurrence of IgG4-related chronic sclerosing sialadenitis in both submandibular glands that developed at intervals of months. Therefore, long-term follow-up and whole-body evaluation are essential.

Key Words : IgG, Sialadenitis, Submandibular gland

Introduction

IgG4-related disease is a systemic immune-mediated condition characterized by the enlargement and dense lymphoplasmacytic infiltration of affected organs and elevated serum IgG4 levels.¹⁻⁶⁾ IgG4-related disease has been reported to occur in various body parts in humans, such as pancreas, hepatobiliary system, kidney, lung, retroperitoneum, aorta, salivary gland, lymph nodes, and orbit.¹⁻⁶⁾ The disease can

be confined to a single organ or involve multiple organs.¹⁾ In head and neck region, the submandibular gland is the most frequently affected area.^{1,3,4,6)} Herein, we report a case with IgG4-related chronic sclerosing sialadenitis of both the submandibular glands that developed at intervals of months.

Case report

A 49-year-old woman was presented with a hard, enlarged mass on left submandibular area for a year. The patient did not complain of pain, fever, or postprandial discomfort. The medical history of the patient was unremarkable. On physical examination, about 4 cm sized firm, the non-tender mass was palpated on left submandibular area. Neck computed tomography (CT) showed a 2.2 x 1.5 cm heterogeneously enhancing mass in the left submandibular gland, and normal range of other head and neck structures including right submandibular gland (Fig. 1). Ultrasound-guided

Received : September 4, 2018
Revised : October 2, 2018(1차) / October 18, 2018(2차)
October 19, 2018(3차)
Accepted : October 22, 2018

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fine needle aspiration cytology revealed a chronic sialadenitis. Ultrasound (US) revealed a diffuse, hypoechoic, heterogeneous gland with multiple small hypoechoic foci.

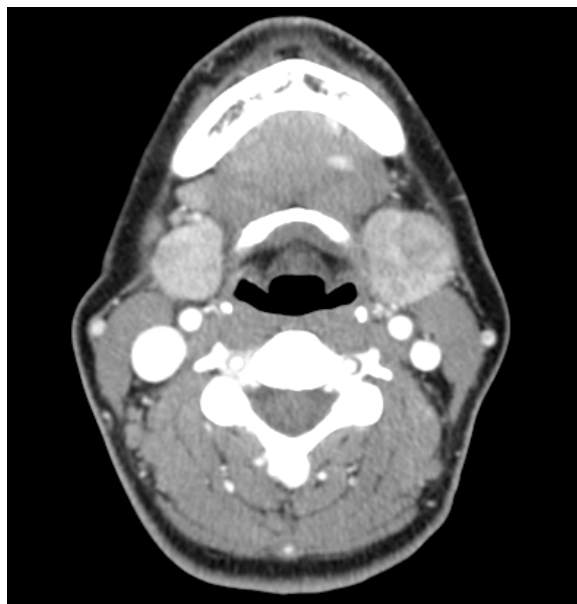


Fig. 1. Neck CT shows a 2.2 x 1.5 cm heterogeneously enhancing mass in the left submandibular gland.

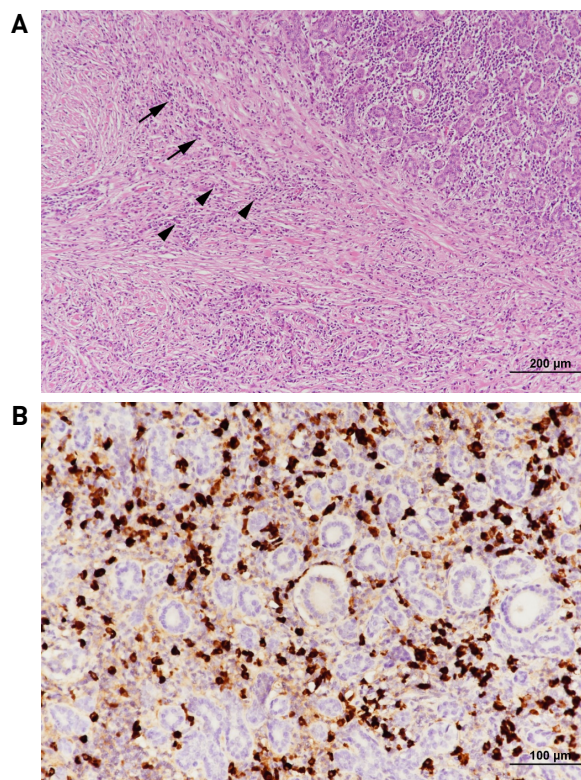


Fig. 2. (A) Histopathologic findings of left submandibular gland shows dense infiltration of lymphocytes (arrow) and plasma cells (arrow head) with marked fibrosis (Hematoxylin and eosin, original magnification $\times 100$). (B) The mass of left submandibular gland is strongly positive for IgG4 on immunohistochemical staining (Immunohistochemistry, original magnification $\times 200$).

Based on these observations, preliminary differential diagnosis revealed submandibular gland tumor or chronic sialadenitis. We performed the left submandibular gland extirpation under general anesthesia, as we could not rule out the possibility of a submandibular tumor. Histological examination of left submandibular gland revealed IgG4-related chronic sclerosing sialadenitis (Fig. 2). The postoperative course was uneventful. The laboratory tests including IgG were within the normal limits. Chest X-ray, abdominal US were performed and there were no other lesions of IgG4 related disease in the patient.

After surgery, the patient was regularly follow-up without any medications. After 10 months of surgery, the patient presented with a hard, enlarged mass of right submandibular area. Patients were treated intermittently for 5 months with conservative therapy including steroids. However, the mass of right submandibular gland had grown compared to the previous CT scans (Fig. 3), and we performed the right submandibular gland extirpation. Histologic examination of right submandibular gland revealed IgG4-related chronic sclerosing sialadenitis. At the last follow-up, the patient has been well without recurrence of the IgG4-related disease.

Discussion

IgG4-related chronic sclerosing sialadenitis commonly



Fig. 3. Neck CT shows an enlarged right submandibular gland with heterogeneous enhancement without focal mass and no recurrence of IgG4-related chronic sclerosing sialadenitis in the left submandibular area.

occurs in the submandibular glands, but the involvement of parotid and minor salivary glands has been reported.^{1,3,4,6)} IgG4-related chronic sclerosing sialadenitis has been suggested to belong to the spectrum of IgG4-related disease, and the disease can occur in a single organ or involve multiple organs of patient's body.^{1,4)} In this study, the patient exhibited lesions in both the submandibular gland that developed at intervals of months.

The pathogenesis of IgG4-related chronic sclerosing sialadenitis is not yet established, and some previous studies suggested that IgG4 may play an important role in the allergic reaction.³⁾ Among the patients with the IgG4-related disease, more than 40% of patients have a history of allergic disease.²⁾ However, our patient had no history of allergic disease.

The criteria for diagnosis of IgG4-related chronic sclerosing sialadenitis has been suggested as follows; first, enlarged masses in single or multiple organs, second, a serum IgG4 concentrations $\geq 135\text{mg/dL}$, third, marked lymphocyte and plasma infiltration and fibrosis, along with a ratio of IgG4-positive cells to IgG-positive cells $> 40\%$ and more than 10 IgG4-positive cells per high-power field.¹⁻⁶⁾

Imaging studies, such as US, CT or magnetic resonance imaging (MRI), play an important role in the differential diagnosis from mimicking diseases, however, there are no specific findings for the diagnosis of IgG4-related chronic sclerosing sialadenitis.^{1,4,6)} It may be difficult to differentiate the lesion from a malignant tumor. In this study, preoperative CT scan suggested a submandibular tumor. FDG-PET CT can be useful modality for determining biopsy site, assessment of treatment response, and monitor the activity of whole-body.⁶⁾ However, the cost of FDG-PET CT is very expensive and difficult to perform easily

Most of the patients with the IgG4-related disease have elevated serum IgG4 levels, however, the levels vary widely.^{2,4,6)} Some patients have normal serum level especially in a single organ involvement, and same was the case with our patient. In addition, elevated serum IgG4 levels have also been associated with other diseases, such as atopic dermatitis, pemphigus, or asthma.⁶⁾ Therefore, serum IgG4 level cannot be used as the sole diagnostic marker.⁶⁾

The gold standard for diagnosis of IgG4-related chronic sclerosing sialadenitis is a tissue biopsy from the affected organ.¹⁻⁶⁾ In addition, most important differential diagnosis

of IgG4-related chronic sclerosing sialadenitis is malignant disease, especially malignant lymphoma, therefore tissue biopsy is mandatory.^{1,2,4,6)} The characteristics of histopathological examination for diagnosis of IgG4-related chronic sclerosing sialadenitis includes lymphoplasmacytic tissue infiltration with dominant IgG4-positive plasma cells accompanied with fibrosis and obliterative phlebitis.¹⁻⁶⁾

The first-line treatment for IgG4-related chronic sclerosing sialadenitis is corticosteroids.¹⁻⁶⁾ Most of the patients respond to steroid therapy within several days, however in approximately 50% of patients with IgG4-related disease relapse in other organ system has been noted.^{1,6)} In addition, long-term outcomes, dosage, and duration of steroids treatments remain unclear.⁴⁾ The second-line treatment is the administration of azathioprine that has been used as a steroid-sparing agent or in a recurrent and refractory disease.^{1,2,5)} Surgical treatment can be indicated for patients who fail to respond to conservative treatment or there exist difficulty in differentiating the lesion from a malignant tumor, similar to our patient.⁴⁾ Malignant transformation of the IgG4-related disease has been reported, and new lesions can develop in other organs over time. The incidence of bilateral involvement of IgG4-related chronic sclerosing sialadenitis in the submandibular glands was high at initial presentation and during the follow-up period.⁴⁾ Therefore, long-term follow-up is mandatory.^{1,2,4)} The patient is being monitored at a local hospital every six months due to thyroid nodules, so we recommend that the abdomen and thorax be examined through US, X-ray, and blood test at the same time.

In conclusion, clinicians should consider IgG4-related chronic sclerosing sialadenitis in the differential diagnosis of enlargement of salivary glands. Herein, we report the probability of occurrence of IgG4-related chronic sclerosing sialadenitis in both the submandibular glands that developed at intervals of months. Therefore, long-term follow-up and whole body evaluation are essential.

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