Int J Clin Exp Pathol 2015;8(7):8628-8631
www.ijcep.com /ISSN:1936-2625/IJCEP0009909

Case Report

Chronic sclerosing sialadenitis of the submandibular gland: an entity of IgG4-related sclerosing disease

Tzu-Wei Wei[1], Ching-Feng Lien[1], Tun-Yen Hsu[1], Hong-Lin He[2,3]

[1]Department of Otolaryngology, E-DA Hospital, I-Shou University, Kaohsiung, Taiwan; [2]Department of Pathology, E-DA Hospital, I-Shou University, Kaohsiung, Taiwan; [3]Institute of Biomedical Science, National Sun Yat-Sen University, Kaohsiung, Taiwan

Received May 5, 2015; Accepted June 23, 2015; Epub July 1, 2015; Published July 15, 2015

Abstract: Chronic sclerosing sialadenitis typically involves the submandibular gland. It usually occurs in the middle-aged and elderly adults with a slight male predominance. Recent evidences have suggested that it is an entity of IgG4-related sclerosing disease and has distinct histopathological features, such as a dense lymphoplasmacytic infiltrate, sclerosis and obliterative phlebitis. It is important to discriminate this entity from other diseases, trying to give effective treatment to the patients. In this report, we described a patient having chronic sclerosing sialadenitis in the submandibular gland.

Keywords: Chronic sclerosing sialadenitis, IgG4-related sclerosing disease, IgG4

Introduction

Chronic sclerosing sialadenitis (also known as Küttner tumor), originally described by H. Küttner in 1896, is a relatively uncommon and under-recognized cause of salivary gland enlargement, especially in the submandibular gland. To make definite diagnosis before operation is challenging since chronic sclerosing sialadenitis shares similar clinical presentation with other diseases, such as Sjögren syndrome, lymphoma and epithelial malignancies [1]. Mounting evidences have suggested that chronic sclerosing sialadenitis is IgG4-associated, which has the characteristic finding of a dense infiltrate of immunoglobulin (Ig) G4-positive plasma cells [2, 3]. In this report, we described the histopathological features and immunohistochemical results in a patient with chronic sclerosing sialadenitis in the submandibular gland.

Case report

The patient was a 61-year-old man who suffered from an enlarged mass in the right upper neck for several days. Physical examination showed a firm and non-tender mass in the right submandibular area. The laboratory values were within normal limit, including normal leukocyte count (6.22 × 10^9/L), hemoglobin level (15.3 g/dL), and platelet count (283 × 10^9/L). Head and neck computerized tomography (CT) scan disclosed asymmetrical enlargement of right submandibular gland (**Figure 1**). No lithiasis was found. Therefore, he was admitted for surgical extirpation of right submandibular gland. Grossly, the right submandibular gland measured 3.8 × 2.9 × 2.4 cm. It was firm with grayish-white cut surface and nodular formation. The microscopic examination revealed prominent lymphoplasmacytic infiltration with lymphoid follicle formation in the sclerotic stroma, characterized by interlobular cellular fibrosis with lobular formation (**Figure 2A-C**). Foci of atrophic salivary acini are found. There are some lymphoid follicles having irregular, large geographic germinal centers. In the immunohistochemical study, the plasma cells were highlighted by CD138 (**Figure 2D**) with variable expression for IgG (**Figure 2E**) and IgG4 (**Figure 2F**). The number of plasma cells per high power field (HPF) was more than 50 in several areas. The IgG4/IgG ratio was approximately 80%-90%. After one-year follow-up, the patient has been well without evidence of recurrence.

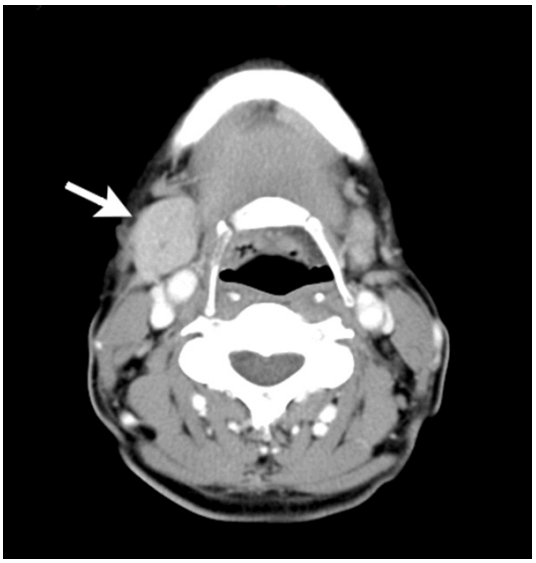

Figure 1. Head and neck CT study image showed asymmetrical enlargement of right submandibular gland measuring 3.5 × 2.5 cm in size.

Discussion

Chronic sclerosing sialadenitis commonly occurs in the submandibular glands. The peak incidence is in the sixth to eighth decades with a slight predilection for male patients. The morphologic features of chronic sclerosing sialadenitis include interlobular cellular fibrosis, periductal inflammation, lobular chronic inflammation with numerous plasma cells, obliterative phlebitis, and florid follicular hyperplasia. More importantly, the plasma cells are usually positive for IgG4 in most cases, given a close correlation with IgG4-related sclerosing disease. In the submandibular gland, more than 90% of cases with chronic sclerosing sialadenitis have been found to be IgG4-related [2, 3]. IgG4 constitutes only 3% to 6% of the total IgG fraction in the serum of healthy subjects and is the least component among the IgG subclasses, namely IgG1, IgG2, IgG3, and IgG4 [4]. In recent years, IgG4-related disease has been an increasingly recognized fibroinflammatory condition composed of a combination of disease that shares similar clinical, serological and pathological features [5]. IgG4-related sclerosing disease has been identified in a wide variety of organs, including pancreas, biliary tree, liver, gallbladder, mesentery, retroperitoneum, orbit, lacrimal gland, salivary gland, kidney, lung, pleura and lymph nodes [6]. However, the biologic function of IgG4 remains uncertain, and some previous studies have suggested that IgG4 may play an important role in allergic reactions [7, 8].

The key histopathological features of chronic sclerosing sialadenitis include a dense lymphoplasmacytic infiltrate, storiform pattern of fibrosis, and obliterative phlebitis. The number of IgG4+ plasma cells per high power field is usually more than 50, accompanied with an increased percentage of IgG4/IgG for more than 40% [6, 9]. Chronic sclerosing sialadenitis (namely IgG4-associated sialadenitis) is discriminated from sialolithiasis-associated sialadenitis by the presence of a cellular fibroinflammatory area composed of plump fibroblasts, lymphocytes and plasma cells. Sialolithiasis-associated sialadenitis is characterized by an interlobular fibrosis with less cellularity. Florid follicular hyperplasia characterized by irregular, large and geographic lymphoid follicles is commonly found in chronic sclerosing sialadenitis. In contrast, the lymphoid follicles in sialolithiasis-associated sialadenitis are usually fewer and smaller if present [2]. Moreover, about one-half of cases with chronic sclerosing sialadenitis have obliterative phlebitis, and an elastin stain is helpful to identify this feature. In terms of lymphoepithelial sialadenitis, it typically involves the parotid gland and may be associated with Sjögren syndrome. It is characterized by the presence of numerous lymphoepithelial lesions and the inflammatory infiltrate is lymphocyte predominant with rare plasma cells and absence of interlobular fibrosis. It is of great importance to discriminate IgG4-associated sialadenitis from other diseases, particularly epithelial malignancies because IgG4-related sclerosing disease has been proven to have a good response to steroid treatment and may have multiple organ involvement, thus potentially eliminating the need for surgical procedures [5, 10].

In summary, we described a case with chronic sclerosing sialadenitis in the submandibular gland. Chronic sclerosing sialadenitis is an entity of IgG4-related sclerosing disease with distinct histopathological features. It is important to identify such cases preoperatively since this disease is steroid-sensitive.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Hong-Lin He, Department of Pathology, E-Da Hospital, 1 Yida Rd., Yanchao Dist., Kaohsiung City, Taiwan. Tel: 886-7-

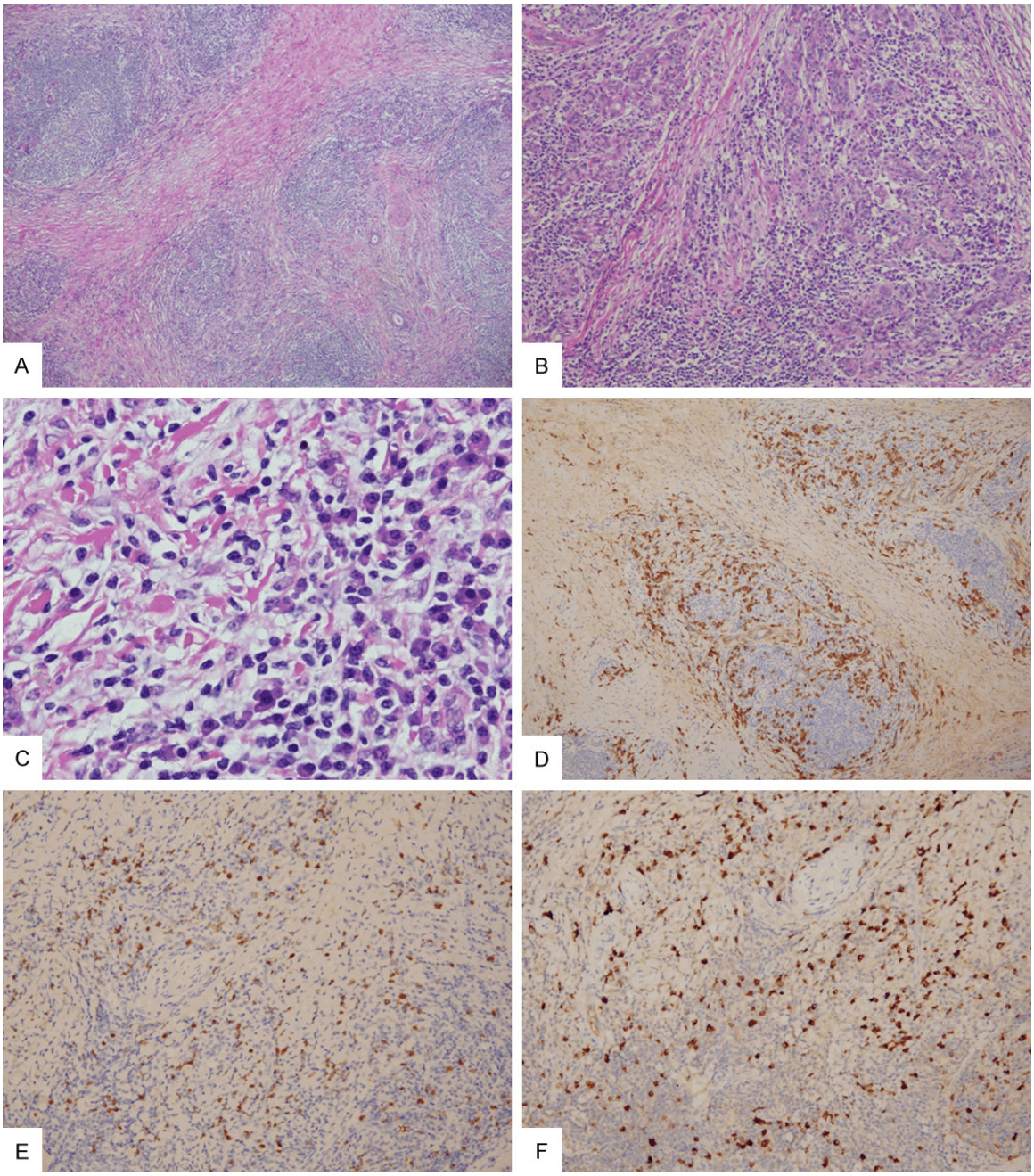

Figure 2. On hematoxylin and eosin-stained sections, the submandibular glandular tissue showed heavy inflammatory cell infiltrates with lymphoid follicle formation, separated by fibrous bands with lobular formation (A: × 40). The salivary acini were atrophic (B: × 100) and diffusely infiltrated by lymphocytes and plasma cells (C: × 400). The plasma cells were highlighted with CD138 positivity (D: × 100). Of note, the plasma cells had variable expression for IgG (E: × 200) and IgG4 (F: × 200), accompanied with an increased IgG4/IgG ratio.

6150011 Ext. 2903; Fax: 886-7-6150974; E-mail: ed107348@edah.org.tw

References

[1] Chan JK. Kuttner tumor (chronic sclerosing sialadenitis) of the submandibular gland: an underrecognized entity. Adv Anat Pathol 1998; 5: 239-251.

[2] Geyer JT, Ferry JA, Harris NL, Stone JH, Zukerberg LR, Lauwers GY, Pilch BZ and Deshpande V. Chronic sclerosing sialadenitis (Kuttner tumor) is an IgG4-associated disease. Am J Surg Pathol 2010; 34: 202-210.

[3] Kitagawa S, Zen Y, Harada K, Sasaki M, Sato Y, Minato H, Watanabe K, Kurumaya H, Katayanagi K, Masuda S, Niwa H, Tsuneyama K, Saito K, Haratake J, Takagawa K and Nakanuma Y. Abundant IgG4-positive plasma cell infiltration characterizes chronic sclerosing sialadenitis (Kuttner's tumor). Am J Surg Pathol 2005; 29: 783-791.

[4] Spiegelberg HL. Biological activities of immunoglobulins of different classes and subclasses. Adv Immunol 1974; 19: 259-294.

[5] Stone JH, Zen Y and Deshpande V. IgG4-related disease. N Engl J Med 2012; 366: 539-551.

[6] Cheuk W and Chan JK. IgG4-related sclerosing disease: a critical appraisal of an evolving clinicopathologic entity. Adv Anat Pathol 2010; 17: 303-332.

[7] Futei Y, Amagai M, Ishii K, Kuroda-Kinoshita K, Ohya K and Nishikawa T. Predominant IgG4 subclass in autoantibodies of pemphigus vulgaris and foliaceus. J Dermatol Sci 2001; 26: 55-61.

[8] Hawrylowicz CM and O'Garra A. Potential role of interleukin-10-secreting regulatory T cells in allergy and asthma. Nat Rev Immunol 2005; 5: 271-283.

[9] Deshpande V, Zen Y, Chan JK, Yi EE, Sato Y, Yoshino T, Kloppel G, Heathcote JG, Khosroshahi A, Ferry JA, Aalberse RC, Bloch DB, Brugge WR, Bateman AC, Carruthers MN, Chari ST, Cheuk W, Cornell LD, Fernandez-Del Castillo C, Forcione DG, Hamilos DL, Kamisawa T, Kasashima S, Kawa S, Kawano M, Lauwers GY, Masaki Y, Nakanuma Y, Notohara K, Okazaki K, Ryu JK, Saeki T, Sahani DV, Smyrk TC, Stone JR, Takahira M, Webster GJ, Yamamoto M, Zamboni G, Umehara H and Stone JH. Consensus statement on the pathology of IgG4-related disease. Mod Pathol 2012; 25: 1181-1192.

[10] Kamisawa T, Okazaki K, Kawa S, Shimosegawa T and Tanaka M. Japanese consensus guidelines for management of autoimmune pancreatitis: III. Treatment and prognosis of AIP. J Gastroenterol 2010; 45: 471-477.