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Case Report

Delayed diagnose and successful radiation treatment for submandibular gland enlargement dominated IgG4-related sialoadenitis: a case report

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Abstract: Mikulicz's disease, a disorder known for more than 100 years, characterized by dacryoadenitis and enlargement of submandibular glands, is now recognized as a classic IgG4-related condition, called IgG4-related dacryoadenitis (DA) and sialoadenitis (SA). We report a patient with massive submandibular gland enlargement. No properly diagnose had been made after more than 10 times of hospital visits and 3 times of localized tumor resection in various hospitals during the last 3 years. To confirm the diagnosis, an extended biopsy of the submandibular gland was made and the histological findings were consistent with the manifestation of IgG4-related Sialoadenitis (IgG4-SA). Only two sessions of X-ray radiation therapy were applied, then the glandular enlargement was completely subsided in 3 weeks. No corticosteroids nor other immunosuppressive agents was used for the treatment. During 10 years follow-up no recurrence was noticed.

Keywords: IgG4-related sialoadenitis, diagnose, treatment

Introduction

IgG4-DA/SA, one of the most common forms of IgG4-related disease (IgG4-RD), is characterized by symmetrical swelling of the lacrimal and salivary glands and often misdiagnosed as malignant, infectious, inflammatory disorders, or undefined. Furthermore, the therapy is still followed the therapeutic experiences of AIP and "Gold standard" treatment means to be standardized. In 2011, a Japanese research group, under the sponsorship of the Japanese Ministry of Health, Labor and Welfare, directed by Kazuichi Okazaki, established comprehensive diagnostic criteria (CD criteria) for IgG4-RD. Though a unifying diagnostic criterion has not been established, this is the most referenced criteria at present. Here, we report this case to present some problem existing in IgG4-SA criteria, and propose single radiation therapy is effective on IgG4-SA. This case report has been approved by Medical Ethics Committee of Weifang Medical University with the ethics approval number: weiyilunyan 2017306. And the informed consent has been obtained.

Case report

In October 2004, a 39-year-old male presented with quiet massive submandibular gland enlargement for 3 years. Without any other complaints, the patient had made more than 10 times of hospital visits and been given 3 times of mistreating of localized mass resection due to the negative results of histopathological examinations. However, relapses were noticed in 2 to 3 months after each surgery. On physical examination, an 11×16 cm no clear margin mass was palpable at each side of the submandibular gland area and there was no apparent abnormal in the rest examination. In addition, the lab results, including IgG, C3, IgA, IgM, C4, RF, and ASO, were in normal range. We performed a widened biopsy on this patient. In this time, the result (**Figure 1**) revealed remarkable lymphoid infiltration and proliferation, and some of the gland tissues were totally replaced with lymphatic cells, while the residual gland tissue was in irregular line-up and segregated by the proliferation of lymphatic cells. Based on this pathological finding, a diagnosis of sub-

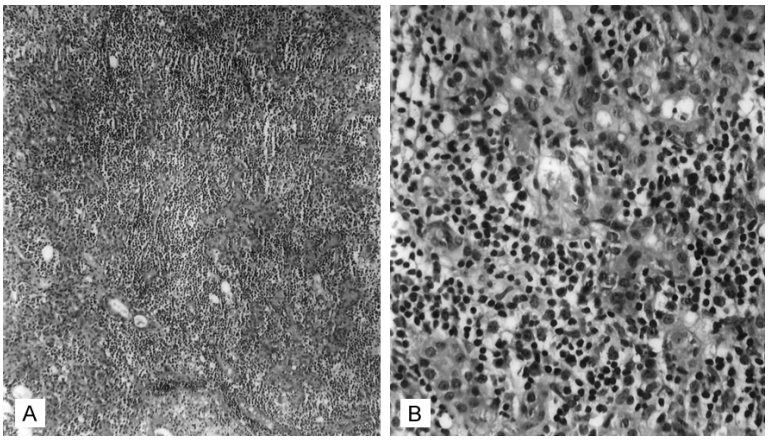

Figure 1. Histological pictures of patient's submandibular gland show remarkable lymphoid infiltration and proliferation. Some of the gland tissue was totally replaced with lymphatic cells, and the residual gland tissue was in irregular line-up and segregated by proliferated lymph cells. A. ×40; B. ×400.

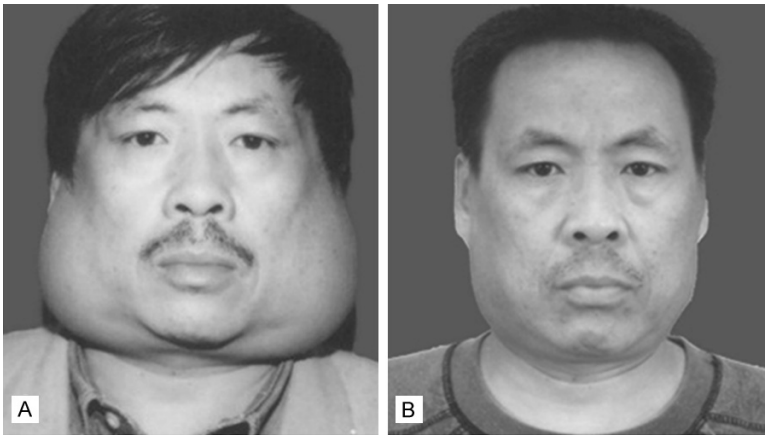

Figure 2. Pictures of the patient shows that swelling of the submandibular glands was dramatically reduced after 2 sessions of radiation therapy. A. Before radiation therapy, B. Two years after radiation therapy.

mandibular gland hypertrophy dominated Mikulicz's disease (now known as IgG4-SA) was made. Without any corticosteroids or immunosuppressive agents, two sessions of X-ray radiation therapies (10 days in each session) under 140-180 KV and HVL6AI-0.5Cu were applied. After a total dosage of 20-25 Gy/2-3W's therapy, the glandular enlargement was completely subsided in 3 weeks (**Figure 2**). The patient was tracked for up to a decade, and no recurrence or side-effect was noticed.

Discussion

Similar cases have been summarized in **Table 1**. In this case, the level of serum IgG4 appears as a non-essential diagnostic figure. As been reported in some literatures [1, 2], the sensitivity of IgG4 concentration in making a diagnosis of IgG4-SA needs further consideration, especially in patient with only a single organ involvement [3]. Reviewing this patient's experiences of treatment, there are some points that may help the clinicians to better identify this disease. Due to the rarity of this disease, atypical clinical presentations, as well as the normal laboratory features, the proper diagnosis for this patient had been repeatedly missed. In the past three attempts of incisional biopsy it seemed that the right submandibular gland tissue which could have revealed the nature of the disease had been missing. This can be explained that the tumor was massive and full of unremarkable hyperplastic fibrous tissue. On top of that the surgeons might be cautious to go deeper to pick the right tissue in only a miner biopsy process in order to avoid nerve damage and bleeding. Therefore, a multiple site expanded incisional biopsy with an experienced surgeon is recommended for the unrecognized mass in this region.

As IgG4-SA may results in irreversible organ damage, it is important to make a definite diagnosis and manage as early as possible. Depending on the recently published guidance statement, glucocorticoids, radioactive therapy and surgery are the first-line therapeutic approaches [4, 5]. We believe as in this case, radiation therapy alone, without any adjuvant treatment such as glucocorticoids or immunosuppressive agents, provide a good option with the advantages of shortening the time of treatment and especially decreasing the chance of disfigure. However, the overall effectiveness of solo radiation therapy for this disease still need more studies. The success management of this case may serve as a reminder for peers.

Table 1. Case material

Case	Gender/Age (years)	Serum IgG4 Level (mg/dL)	Other Involved Organs	Treatments
1 [6]	M/45	normal	None	Surgery and immunological treatment
2 [7]	F/75	759	Lachrymal	Corticosteroids
3 [7]	F/62	488	Lachrymal	Corticosteroids
4 [8]	F/56	1733	Lachrymal and lymph node	Surgery and immunological treatment
5 [9]	M/70	2220	Lachrymal and pituitary gland	Corticosteroids
6 [10]	M/48	3729	Lachrymal and renal	Corticosteroids
7 [11]	M/51	3390	Lachrymal and lymph nodes	Corticosteroids
8 [12]	M/82	1320	Pancreas, nephridium, hypophysis, and thyroid	Corticosteroids
9 [13]	M/76	1500	Lachrymal	Corticosteroids
10 [14]	M/63	1520	Neck lymph node and pancreas	Corticosteroids

Disclosure of conflict of interest

None.

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