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Case Report

Orbital neoplasm in a 60-year-old man with a mediastinum mass: a case report of IgG4-related disease

Jia Wei[1*], Hui Li[1,2*], Zhenzhen Cai[1,2*], Lujiang Yi[1,2], Zhongjian Zhao[1,2], Mengyao Yu[1,2], Shuxian Miao[1,2], Li Jiang[1,2], Ruixia Yang[1,2]

[1]*Department of Laboratory Medicine, The First Affiliated Hospital of Nanjing Medical University, Nanjing, P. R. China;* [2]*National Key Clinical Department of Laboratory Medicine, Nanjing, P. R. China.* [*]*Equal contributors.*

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Abstract: Immunoglobulin G4-related disease (IgG4-RD) is a chronic progressive autoimmune disease. Orbits and mediastinum involvement in IgG4-RD is extremely rare. Herein, we report a case of IgG4-RD presenting with bilateral exophthalmos and mediastinum mass. A 60-year-old man was referred for suspected mediastinum mass with a ten-year history of unknown bilateral ophthalmoptosis. A surgical excision of intra-orbital masses and biopsy of the mediastinal mass was proposed. Immunohistochemical examination of intra-orbital masses revealed fibroblastic proliferation with abundant IgG4-positive plasma cells and a diagnosis of IgG4-RD of the mediastinum and ocular region was formulated.

Keywords: IgG4-related disease, orbital neoplasm, mediastinal lymphadenectasis, immunohistochemistry, case report

Introduction

IgG4-related disease (IgG4-RD) is a chronic progressive auto-immune disease characterized by significantly elevated serum IgG4 levels and IgG4-positive plasma cells infiltration in the involved tissue [1-3]. The disease is often typically diagnosed among middle-aged men and the most common sites involves orbital adnexa, salivary glands, pancreas, lymph nodes, and retroperitoneum [1, 4]. However, there are few studies about the multi-organ IgG4-RD. Herein, we report a case of a 60-year-old man with multi-organ IgG4-RD presenting with bilateral exophthalmos and mediastinum mass.

Case presentation

A 60-year-old man was referred to our outpatient clinic for the treatment of suspected mediastinal mass. He complained of an acute attack of chronic bronchitis and an unknown bilateral exophthalmos for ten years. He was a non-smoker and also described a 10-year history of chronic bronchitis. Furthermore, he had been arterial hypertensive for 3 years and accepted antihypertensive medication from that time. No significant alcohol or drug use history was elicited.

Laboratory tests revealed elevated serum IgG4 (1170 mg/dL, normal range: 3-201 mg/dL), and slightly decreased total protein (58.4 g/L, normal range: 65-85 g/L). However, it is worth noting that analytical characteristics of serum IgG4 and total protein assays are different from different laboratories. IgG4-RD was suspected. In addition, thyroid function tests were in the normal range. Antinuclear antibody, anti-SSA, and SSB antibodies and tuberculosis antibody were all negative. Examination of serum tumor markers, including AFP, CEA, CA19-9, CA72-4, CYFRA21-1, as well as NSE indicated no abnormality.

Computed tomography (CT) of the chest in the other primary hospital revealed multiple mediastinum nodular high-density shadow under the tracheal carina and the maximal one was about 32 × 19 mm. The results of endoscopic

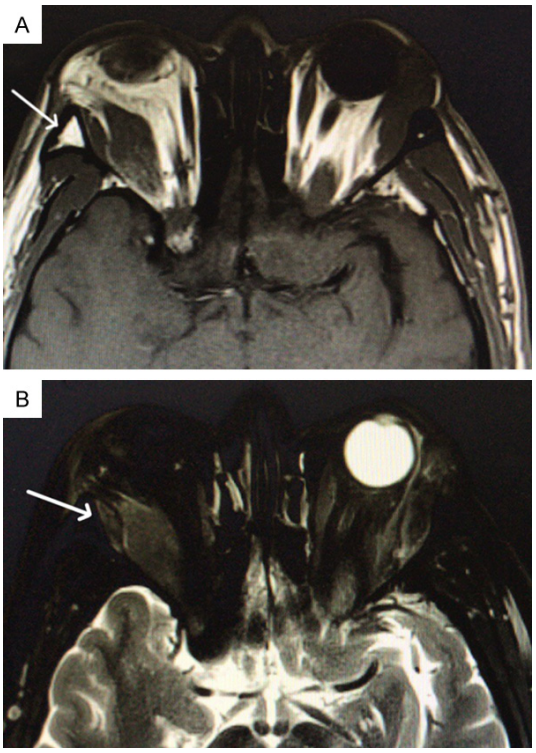

Figure 1. Non-and enhancement ocular MRI reveals bilateral exophthalmos with multiple enlarged bilateral lids, lacrimal glands, extraocular muscles, superior rectus and suborbital ganglions. (A) and (B) indicate a spindle placeholder in the right orbit.

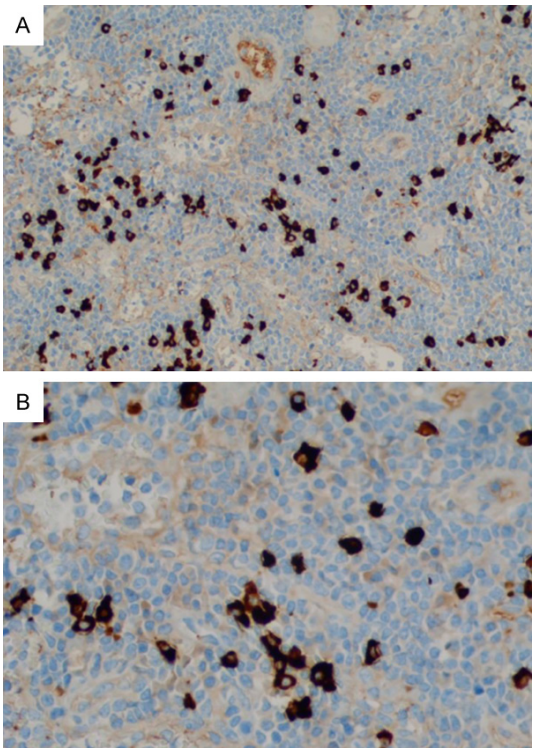

Figure 2. Immunohistochemical stains showing diffuse and intense distribution of IgG4-positive plasma cells under original magnification of 100 times (A) and 400 times (B).

ultrasound-guided fine-needle aspiration showed no malignant tumor cells in the 7th group of lymph nodes. Additionally, bilateral orbital neoplasm was noted by MRI (magnetic resonance imaging, MRI) of ocular region with non-enhancement (see **Figure 1**). A surgical excision of the intra-orbital masses was performed. Immunohistochemical examination of the right eye specimen revealed areas of storiform fibrosis with abundant IgG4-positive plasma cells (see **Figure 2**).

The patient had no additional thoracic manifestations of IgG4-RD. Increased serum level of IgG4 raised suspicion for underlying IgG4-RD. According to the infiltration of IgG4-positive plasma cells in the immunohistochemistry, he was diagnosed as IgG4-RD based on the 2011 comprehensive diagnostic criteria [5]. The efficiency of glucocorticoids were being followed. This study was approved by the Ethics Committee at the First Affiliated Hospital of Nanjing Medical University.

Discussion

We present a rare case of IgG4-RD, which involved both orbits and mediastinum. The study indicates that increased serum level of IgG4 concentrations and significant elevations in IgG4-positive plasma cells infiltration could be one of the options for the diagnosis of multi-organ IgG4-RD.

IgG4-RD is a recently recognized clinical entity caused by an immune mediated-systemic condition that can involve various organs [6]. The major histopathological features associated with IgG4-RD are dense lymphoplasmacytic infiltrate, storiform fibrosis, and obliterative phlebitis [7]. However, the last 2 features are often absent in some sites. Two parallel processes could underlie the observed pathological features in IgG4-RD. The first is the induction of a polarized CD4-positive T-cell population. The second is a feedback negative regulatory process, which might involve the generation of IgG4-secreting plasmablasts, plasma cells, and IgG4 antibodies [8].

This disease is often typically diagnosed among middle-aged men and involves various organs, including orbital adnexa, salivary glands, pancreas, lymph nodes, and retroperitoneum [1, 4]. In our case, orbits and mediastinal lymph nodes were both involved. IgG4-RD of eyes can usually be detected by swollen eyelid, dacryoadenitis and involvement of extraocular muscles [9]. The external eye muscle involvement pattern on MRI is distinct from Graves' orbitopathy, where the inferior and medial rectuses are the most frequently involved muscles [10]. However, intrathoracic IgG4-RD can present as an asymptomatic lesion which is found incidentally by abnormal findings on imaging in most cases [11, 12]. Some patients can manifest with non-specific clinical symptoms like cough, dyspnea, fever, chest pain, and hemoptysis a fact that can delay the diagnosis [13, 14]. Therefore, it's difficult to demonstrate the existence of a mediastinal IgG4-RD lesion extending to eyes.

As in our case, histopathological confirmation of right-eye tissue is crucial to diagnose IgG4-RD. Meanwhile, combining with negative serum tumor markers, biopsy of an involved lymph node ruled out the possibility of neoplasm. Elevated serum IgG4 > 135 mg/dL was included in the diagnostic criteria for IgG4-RD [15, 16]. Furthermore, the mean concentration of serum IgG4 level, among patients with multi-organ disease, was higher compared with those with single-organ disease [17]. In addition, IgG4 positive cells > 30 per HPF and IgG4 positive cells/IgG positive cells ratio > 50% strongly supported diagnosis of IgG4-RD [5]. According to our case, the elevated serum IgG4 level and IgG4-positive plasma cells infiltration may function as a simple suggestive role in early diagnosis. IgG4-RD is sensitive to hormonal therapy.

In summary, this is a case of IgG4-RD affecting mediastinal lymph nodes and orbits. With lymph node biopsy and immunohistochemistry of eye tissues, we could distinguish with malignancies and make a diagnosis of IgG4-RD. The data emphasize the importance of increased serum IgG4 concentrations and elevated IgG4-positive plasma cells for the diagnosis of IgG4-RD. Early diagnosis and treatment of IgG4-RD is clinically significant because the better effectiveness of glucocorticoids in the majority of patients, could prevent irreversible organ damage.

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Disclosure of conflict of interest

None.

Address correspondence to: Li Jiang and Ruixia Yang, Department of Laboratory Medicine, The First Affiliated Hospital of Nanjing Medical University, 300 Guangzhou Road, Nanjing 210029, P. R. China. E-mail: joy232295@163.com (LJ); welcomeyrx@163.com (RXY)

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