

A Case of Immunoglobulin (Ig) G4-related Sclerosing Periaortitis Mimicking Mediastinal Malignant Tumor

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ABSTRACT

Sclerosing mediastinitis was first described by Oulmont in 1855. The aggressive fibro-inflammatory process that occurs in the mediastinum is the end result of a number of inflammatory processes. It is thought that hypersensitivity reactions to various antigens, autoimmune reactions, and idiopathic fibro-inflammatory responses play a role in the etiology of the disease. It has been shown in recent years that immunoglobulin (Ig) G4-related autoimmune diseases may lead to sclerosing mediastinitis. In this study, a rare case of Ig G4-related sclerosing periaortitis is presented in a 50-year male patient. The disease responded well to steroid treatment, but soon recurred following stoppage of the treatment. The treatment with deflazacort was started again; and he responded well. The lesion disappeared within six months of re-treatment.

Key Words: IgG4, Sclerosing, Periaortitis.

How to cite this article: Erel F, Kuzucuoglu M, Sarioglu N, Altun E. A case of immunoglobulin (ig) g4-related sclerosing periaortitis mimicking mediastinal malignant tumor. *J Coll Physicians Surg Pak* 2019; **29** (Supplement 2):S144-S147.

INTRODUCTION

The etiology of sclerosing mediastinitis, which occurs in the mediastinum following an aggressive fibroinflammatory process, is still unknown and is believed to be caused by autoimmune and idiopathic fibroinflammatory processes or from extreme hypersensitivity reactions against antigens of various infectious pathogens.¹

IgG4-related diseases, increasingly recognised in the past 10 years, were shown to have caused sclerosing mediastinitis in many cases. IgG4-related diseases are characterised by aggressive fibrosis and progressive inflammatory processes at any part of the body; and these diseases may mimic infectious and inflammatory disorders and malignancy that can turn into mass formation.²

In this study, we present a case which first fully responded, but recurred over a short period of time, showing mass formation around aortic arch. Very few cases have been reported in the literature involving aortic arch and diagnosed as IgG4-related sclerosing periaortitis.

CASE REPORT

A 50-year male was admitted to chest clinic with the complaint of chronic cough for the last seven years. The

patient was non-smoker. Postero-anterior chest radiograph of the patient and routine biochemical investigations were normal. No abnormality was detected on physical examination and his respiratory function tests were within normal limits. He was diagnosed as a case of cough-variant asthma, and treated by formoterol and budesonide. For definitive diagnosis, computed tomography (CT) scan chest was done, which showed multiple nodules in the lung parenchyma; largest one measuring at 3 mm, in both lungs, and multiple mediastinal lymph nodules; largest one with 16 mm diameter, in right upper and lower paratracheal and aorto-pulmonary window.

One year after the follow-up, a thoracic CT scan revealed a new lesion measuring 30x14x12 mm. The new lesion encircled the aorta in the anterior mediastinum. Regression was observed in mediastinal lymph nodes and pulmonary nodules were stable.

In control thorax CT, taken three months later, it was seen that the size of the lesion near the arch of the aorta at the ventral part of brachiocephalic trunk origin increased and reached up to 48x18x16 mm. Meanwhile, no change was detected in the shape, size, and number of pulmonary nodules (Figure 1).

The patient had no clinical complaints during follow-up. Biochemical tests of the patient showed C-reactive protein (CRP) at 9.4 mg/l, erythrocyte sedimentation rate (ESR) of 28 mm/hour, total IgE of 9.72 IU/ml, and no peripheral eosinophilia. We performed a skin prick test with inhalant allergens, and the result was negative. While in positron emission tomography CT (PET/CT), SUVmax was 7. Fluorodeoxyglucose (FDG) uptake was

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Received: January 08, 2019; Revised: May 25, 2019;

Accepted: June 17, 2019

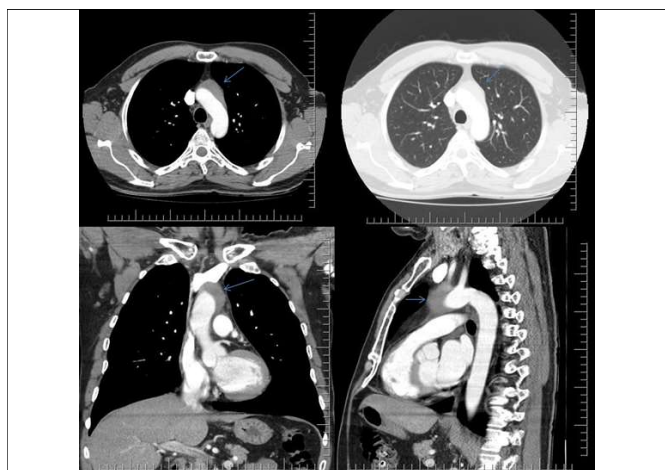


Figure 1: Preoperative computed tomography (CT).

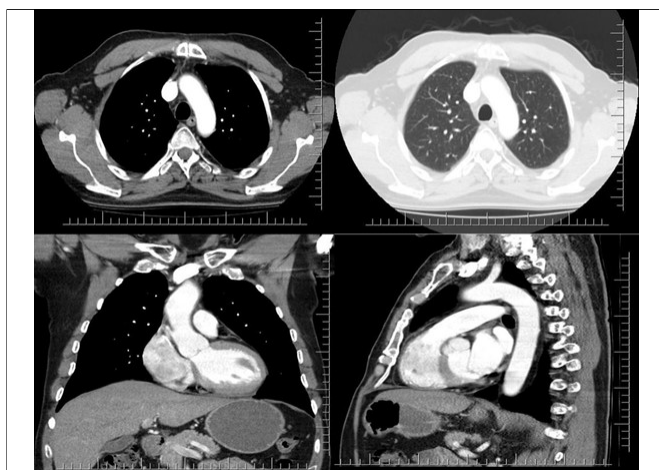


Figure 4: Computed tomography (CT) at the end of third month of treatment.

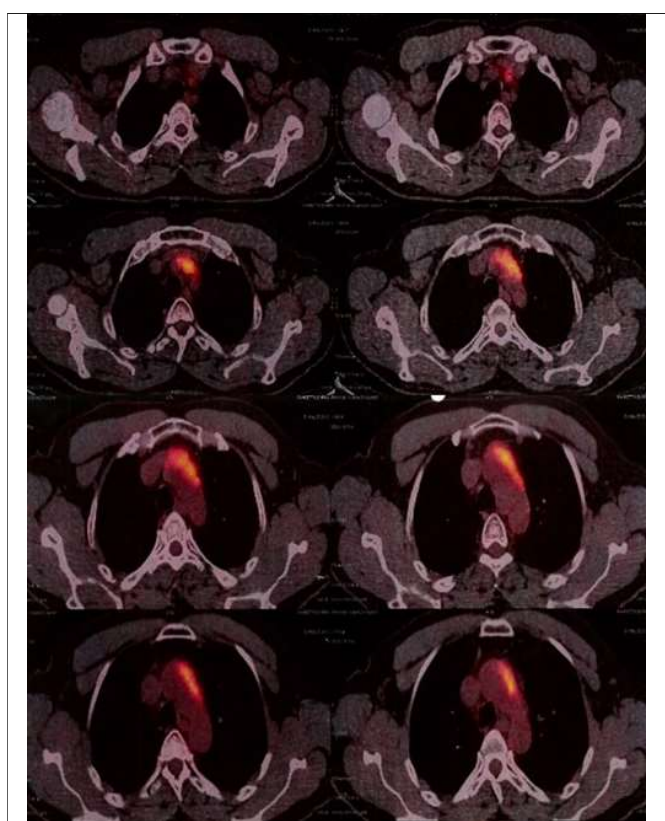


Figure 2: Preoperative positron emission tomography (PET).

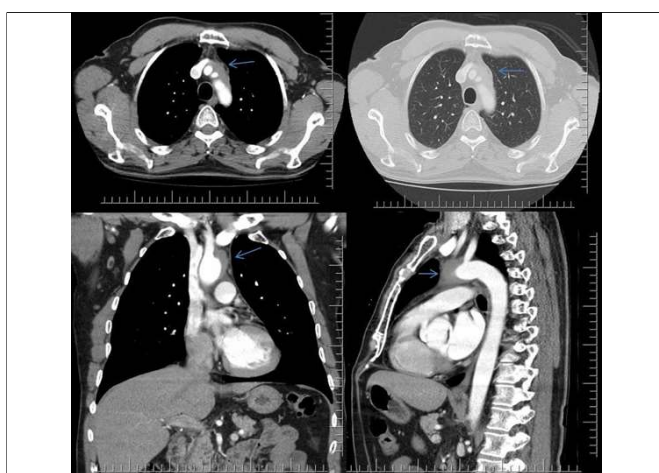


Figure 5: Post-treatment six-month control computed tomography (CT).

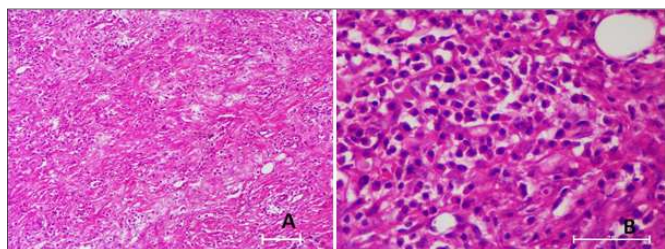


Figure 3: Histopathology of paraaortic mass: (A) Low power view of hematoxylin & eosine fibrous stroma and mononuclear cells (H&E X100). (B) High power view of diffuse plasma cell infiltration (H&E X200).

observed at the soft tissue mass near aorta, and no FDG uptake was detected in other parts of the body (Figure 2).

With suspected aortic invasion, the patient was directed to chest surgery polyclinic for diagnosis. He did not consent to mediastinoscopy, so diagnostic and therapeutic surgery was planned. During surgery, a mass was detected, which began at the level of proximal end of aortic arch and continued along descending aorta, and wrapping aorta around 120°. As determined by exploration, the mass was invading the aorta and incisional biopsies, taken from the mass, were sent to pathology for frozen study. Since benign-malignant distinction could not be made, the procedure was concluded by taking additional biopsies from the mass. Histopathology report confirmed that it was a case of IgG4-related sclerosing periaortitis (Figure 3).

Serum IgG values were: Total IgG of 1343mg/dl (N: 700-1600), IgG1 of 942 mg/dl, IgG2 of 341 mg/dl, IgG3 of 40,90 mg/dl, and IgG4 of 19,60 mg/dl (N: 3-201). These values were normal. Treatment was initiated with a daily dose of 90 mg deflazacort. Partial regression was observed

at the end of the first month, and treatment was continued with 60 mg/day for two more months. At the end of the third postoperative month, significant regression was observed (Figure 4).

Treatment was continued for 6 months with daily dose of 30, 15 and 7.5 mg deflazacort; the dose decreased by 50% each month and the patient was fully recovered. Follow-up CT scan of the patient was done after six months of treatment, which revealed recurrence of the previous disease at same site, which measured 53x34x18 mm (Figure 5). The CRP and ESR were normal.

Treatment with 60 mg/day deflazacort was started again. Long-term and low-dose treatment was decided. One-year treatment was planned with 50% monthly dose decrease, 6 mg starting from 4th month. Six months after the second treatment, no relapse is observed yet.

DISCUSSION

Until 1925, it was thought that syphilis and tuberculosis result in sclerosing mediastinitis, which was first recognised in 1855 by Oulmont. Especially, in cases diagnosed in North America, it was revealed that histoplasma capsulatum resulted in mediastinal fibrosis development.¹ Diseases like fungal infections, tuberculosis or sarcoidosis causing granulomatous reactions, autoimmune diseases and fibro-inflammatory diseases of unknown etiology can be listed as the main causes of sclerosing mediastinitis.³

IgG4-related sclerosing mediastinitis can be classified under diseases presenting with autoimmune fibrosis. It shows similarity to autoimmune fibrous diseases in salivary glands, pancreas, bile ducts, and retroperitoneum. Autoimmune pancreatitis was first defined in 1995, and it was shown in 2003 that it is a disease which can present with autoimmune fibrosis in organs other than pancreas.⁴ Hamano *et al.* detected that the case of sclerosing pancreatitis had high serum IgG4 level; and in immunohistochemical studies, they showed that there were IgG4 positive plasma cells in fibrous tissue.⁵

IgG4-related sclerosing diseases are characterised by prominent IgG4-rich lymphoplasmacytic infiltrates, storiform fibrosis and obliterative phlebitis; and high serum IgG4 level is detected in 60-70% of cases.^{2,4} Pathological diagnosis is the golden standard.²

Umehara *et al.* determined the diagnostic criteria for IgG4-related sclerosing diseases.⁶ According to these criteria, organ dysfunction or nodular lesions and serum IgG4 level ≥ 135 mg/dl and histopathologically > 10 IgG4-positive cells or IgG4-positive/IgG-positive cell ratio $\geq 40\%$ in cross-sectional area, is accepted as a definite IgG4-related sclerosing disease. While organ dysfunction or nodular lesions and histopathologically > 10 IgG4-positive cell or IgG4-positive/IgG-positive cell ratio $\geq 40\%$ in cross-sectional area is accepted as probable

diagnosis, and organ dysfunction or nodular lesions and serum IgG4 level ≥ 135 mg/dl as possible diagnosis. According to these criteria, our case was diagnosed as probable IgG4-related sclerosing aortitis with mass appearance around aortic arch at upper mediastinum and detection of IgG4-positive cells in tissue.

Obtaining tissue diagnosis can be difficult due to location of the lesion and may require advanced surgical intervention. Fine needle aspiration biopsies are insufficient, but core biopsies may be beneficial. While Liu *et al.*⁴ made diagnosis of mediastinal fibrosis with transthoracic core needle biopsy taken from mass lesion located at posterior mediastinum, Cha *et al.*⁷ presented the first case of sclerosing periaortitis in the literature that was diagnosed with mediastinoscopy, Oka *et al.*¹ could not obtain diagnosis in a female case aged 61 through minimal invasive procedures but could achieve diagnosis by an invasive procedure where the left brachiocephalic vein was taken out through sternotomy.

No standard treatment is available for IgG4-related cases; therefore, the cases should be treated individually. In addition, only symptomatic cases need to be treated.²

In some cases, spontaneous remission has been seen. As such, in our case, lymphadenopathies seen in the first tomography can be related to existing disease (with no histopathologic diagnosis), and were cured without any treatment. Since significant tissue damage and fibrosis could develop in some cases, it should be diagnosed at early stages and treated urgently.

Generally, complete response to steroids is seen in the early course of the disease (prednisone 40 mg/day).^{2,6} The affected organs and the extent of fibrosis are considered to have significant roles in determining the response to immunosuppressive treatments.^{7,8}

Inoue *et al.* showed that there was a distinct decline in symptoms and compression of vascular structures with 40 mg/day prednisolone for 4 weeks, and no fibrous tissue development observed throughout the 2-year follow-up.³

If treatment by steroids becomes ineffective or appearance of adverse effects precludes its use, rituximab (B cell depletion therapy) can be utilised.²

Inoue *et al.*³ suggested that serum IgG4, Ebbo *et al.*⁹ PET and Wallace *et al.*¹⁰ suggested that plasmablast follow-up is a good indicator for evaluating diagnosis and response to treatment.

In our case, since partial response was achieved in the first month, the treatment was terminated by tapering off the dosage. Serum IgG4 levels were normal at the time of the diagnosis of the disease. Thoracic CT was used to follow-up the treatment response at regular intervals. We observed relapse in thoracic CT, taken at the sixth postoperative month. This indicates that even if the patient does not have complaints, CT follow-up at short intervals is beneficial in early follow-up.

IgG4-related sclerosing aortitis is an important disease because of its rarity, mimicry of malignancy on imaging, difficulty in differential diagnosis, and difficult to treat.

Since full response can be achieved in IgG4-related sclerosing-aortitis cases by medical treatment, radical surgical approaches with higher mortality and morbidity risks should be avoided, whenever possible.

PATIENT'S CONSENT:

Informed consent was obtained from the patient to use the descriptive information, radiological images and treatment process.

CONFLICT OF INTEREST:

Authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

FE, MK, NS, EA: Diagnosis, treatment and follow-up of the patient. Written and finally checked the manuscript.

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