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Case Report Open Access

IgG4-Related Mastoiditis, Hypertrophic Pachymeningitis and Inflammatory Pseudotumor: A Case Report and Review of the Literature

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Abstract

Background: We present a case of IgG4-related mastoiditis hypertrophic pachymeningitis and intracranial inflammatory pseudotumor.

Case presentation: We report a case of a patient presenting with left ear hearing loss and headaches. Computed tomography (CT) imaging revealed a mass in the left mastoid associated with mastoiditis. She was not responsive to antibiotics and non-systemic steroids. She subsequently underwent mastoidectomy. However, the patient developed central nervous system involvement with frequent headaches. Magnetic resonance imaging (MRI) revealed a mass in the brain associated with hypertrophic pachymeningitis and intracranial inflammatory pseudotumor. Tissue pathology revealed extensive lymphocyte cell infiltration. Immunohistochemistry revealed positive signals for CD38 and IgG4. Importantly, the number of IgG4-positive plasma cells was >50 per high-power field. The patient was diagnosed with IgG4-related disease and responded well to steroid treatment.

Conclusion: This case highlights a unique IgG4-related disease characterized by mastoiditis, hypertrophic pachymeningitis and intracranial inflammatory pseudotumor that was successfully treated with steroids.

Keywords: IgG4-related disease; Mastoiditis; Hypertrophic pachymeningitis; Intracranial inflammatory pseudotumor

Introduction

IgG4-related disease is a systemic disease that mainly involves the pancreas but can affect other organs, such as salivary glands, lacrimal glands, hepatobiliary tract, orbit, lymph node, retroperitoneum, aorta, mediastinum, soft tissue, skin, breast, kidney, prostate, upper aerodigestive tract, and lung [1]. However, IgG4-related disease involving the central nervous system is rarely reported. These cases mainly involve the pituitary [2] and spinal cord [3,4]. Reports of IgG4-related disease involvement of the meninges and intracranial organization have recently been published [5,6]. However, the exact pathogenesis of IgG4-related disease remains unclear.

The diagnosis of IgG4-related disease is mainly based on tissue pathological changes of lymphoplasmacytic infiltration, a storiform pattern of fibrosis, and obliterative phlebitis. Importantly, the disease is associated with increased numbers of IgG4 plasma cells. The diagnostic criteria of IgG4-related disease is based on IgG4 serum concentrations and the number of IgG4-positive plasma cells at high magnification (>50 per high-power field, with an IgG4/IgG ratio>40 %) [1]. IgG4-related disease responds well to steroid therapy. It is important to distinguish IgG4-related disease from malignant tumors and other similar diseases of the affected organ to apply appropriate therapy, which can avoid unnecessary surgery and reduce the pain and economic burden of patients. In this paper, we report a patient with IgG4-related mastoiditis, hypertrophic pachymeningitis and intracranial inflammatory pseudotumor. The symptoms and lesions were significantly alleviated after steroid treatment.

Case Presentation

A 59-year-old woman presented with left ear hearing loss and headaches. Computed tomography (CT) imaging revealed a mass in the left mastoid (Figure 1). She was diagnosed with mastoiditis and treated with a combination of antibiotics and steroids erratically. Three months later, the patient developed central nervous system involvement with frequent headaches. She was evaluated by otolaryngology services. Mastoiditis surgery was performed with biopsy. The specimens were stained with hematoxylin-eosin (HE) and various immunohistochemical stains for immune cells. The results demonstrated that ck-pan was only expressed on residual epithelium (Figure 2A), which eliminated the possibility of cancer. The Kappa:Lambda ratio of 1.5:1 excluded the possibility of a lymphocytic proliferative tumor (Figures 2B and 2C). Pathology revealed considerable lymphocyte infiltration accompanied by fibrosis (Figure 2D) (original magnification 100 ×). Plasma cells (CD38-positive cells) constituted most of the immune cell population (Figure 2E). She received oral steroid treatment daily for a short period of time. However, she also presented with frequent headaches. Brain magnetic resonance imaging (MRI) revealed a hyperintense lesion in the left temporal lobe (Figure 3). The patient was admitted to Shandong Provincial Qianfoshan Hospital. Physical examination revealed mild hearing loss of the left ear. Full blood count and biochemistry tests were within normal limits with the exception of a mild increase in

the percentage of neutrophils (77.3 %). Serum autoimmune markers, including erythrocyte sedimentation rate, C3, C4, antineutrophilic cytoplasmic antibody, and antiextractable nuclear antigen, were all within the normal range with the exception of an increased C-reactive protein level (6.80 mg/L; normal range 0–3.48 mg/L), elevated rheumatoid factor (339.00 IU/ml; normal range 0–15 IU/ml), antinuclear antibodies (1:100; types of antinuclear antibodies: homogeneous + particle type) and weak positivity for anti-SSA antibody. In addition, the results of the liver and kidney enzyme levels and the tumor marker test results were negative. Cerebral spinal fluid (CSF) markers, including cell count, protein, and glucose, were within normal limits except for increased IgG levels of 48.70 mg/L. CSF cytology did not reveal malignant cells. Her serum IgG4 levels were 0.35 g/L (range 0.03–2.01 g/L). MRI of the brain revealed hyperintense lesions in the left temporal lobe in the T2 image and a homogenously enhanced mass in the left temporal lobe and near the dura mater. Furthermore, histologic examination of mastoiditis tissues revealed a large amount of IgG4-positive plasma cells (>50 per high-power field) (Figure 2F). IgG4-related mastoiditis, hypertrophic pachymeningitis and intracranial inflammatory pseudotumor of the central nervous system were diagnosed.

For treatment, 40 mg prednisone per day was started for 10 days with a gradual reduction to 5 mg for 10 weeks followed by maintenance of 2.5 mg to date. After 4 months and at the 2 y follow-up visit, her headaches had disappeared, and the lesion was significantly reduced on MRI (Figure 4). Full blood count and biochemistry tests were within normal limits. C-reactive protein was normal. Rheumatoid factor levels were reduced to 77.2 IU/ml and 74 IU/ml at the 4 mon and 2 y follow-up visits, respectively. Following successful induction, the patient responded to the steady maintenance dose of prednisone without any side effects.

Discussion and Conclusions

IgG4-related disease is a recently recognized inflammatory and fibrosing disease that can affect almost any organ, including the central nervous system. The clinical symptoms of IgG4-related disease depend on the pattern of organ involvement and the severity of disease activity. The diagnostic criteria of IgG4-related disease are roughly based on the following features: typical radiological findings; increased serum IgG4 levels; abundant infiltration of IgG4-positive plasma cells and lymphocytes, fibrosis, and obliterative phlebitis; association with other IgG4-related diseases; and response to steroids [7]. In general, systemic glucocorticoids are the first-line approach for IgG4-related disease.

Figure 1: CT reveals confluent areas of the left mastoid.

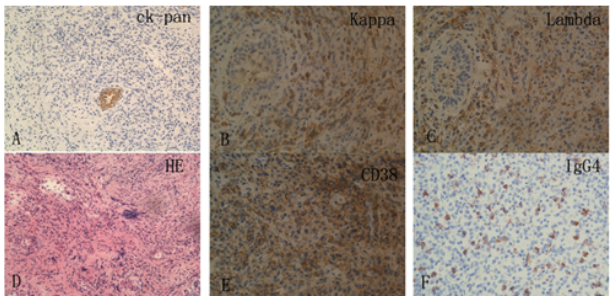

Figure 2: (A) Ck-pan is only expressed on residual epithelium (original magnification 100 ×). (B, C) Lymphocytic proliferative tumor was excluded based on a Kappa:Lambda ratio of 1.5:1. (D) Histological examination of the mastoid tissues revealed that the interstitial infiltration is composed of a large number of lymphoplasmacytic cells and a few eosinophils infiltrated with fibrosis (original magnification 100 ×). (E) An immunohistochemical study revealed a large number of plasma cells (CD38+) in the infiltrate, which constituted most of the immune cell population (original magnification 200 ×). (F) Immunohistochemistry of mastoid tissues revealed markedly increased numbers of IgG4-positive plasma cells (>50 per high-power field) (original magnification 200 ×).

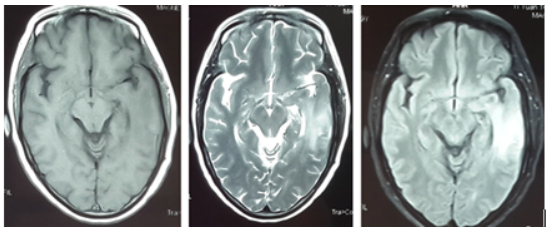

Figure 3: MRI of the brain revealed a hyperintense lesion in the left temporal lobe.

In this paper, we present a patient experiencing left ear hearing loss and headache for 1 year. She received mastoiditis surgery to control the symptoms. However, the symptoms were not obviously relieved after the operation. In addition, the scope of pachymeningitis and intracranial lesion was not altered. The disease was also not cleared. Therefore, we further performed a corresponding pathological examination. Histologic examination revealed a large amount of lymphoplasmacytic infiltration. Plasma cells constituted greater than 10 % of the immune cells. According to the test results of other indicators, tissue pathology eliminated the possibility of cancer and a lymphocytic proliferative tumor. Importantly, a large proportion of plasma cells were stained with IgG4 (>50 per high-power field). The number of IgG4-positive plasma cells per high-power field is regarded as a sufficient criterion. The number of IgG4-positive plasma cells for establishing the diagnosis for most tissues ranges from 30 to 50 cells per high-power field [8]. Even in the kidney, 10 IgG4-positive plasma cells per high-power field may be sufficient [8]. Our mastoid tissue exhibited the required histologic features and an increased number of IgG4-positive plasma cells, thus establishing the diagnosis. According to the criteria of IgG4-related disease, the patient was diagnosed with

IgG4-related mastoiditis, hypertrophic pachymeningitis and intracranial inflammatory pseudotumor.

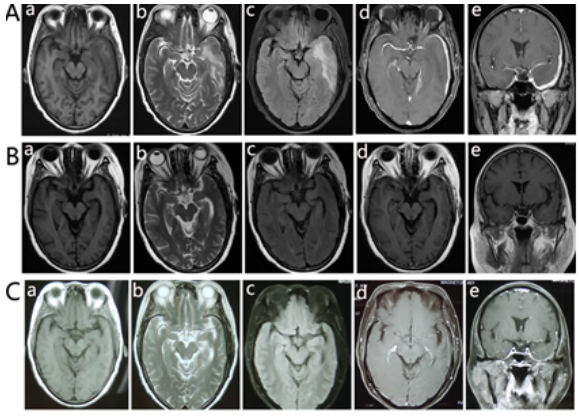

Figure 4: (A) T1, T2, T2-Flair, and gadolinium-enhanced T1-weighed imaging reveal the presence of diffuse meningeal thickening and an intracranial inflammatory pseudotumor. The lesions were significantly reduced after treatment for 4 months (B) and 2 year (C), respectively.

Most patients with IgG4-related disease exhibit an increased serum IgG4 concentration. However, elevated serum IgG4 levels are not restricted to IgG4-related disease. Increased levels are also observed in autoimmune disease, allergic conditions, carcinoma, and other conditions. Elevated serum IgG4 levels were reported in 84 % of patients with IgG4-related disease [9]. Importantly, a study reported that elevated serum IgG4 levels exhibits a low specificity (60 %) and a low positive predictive value (34 %) for the diagnosis of IgG4-related disease [10]. In our patient, IgG4 serum levels were not elevated, which may be associated with the early administration of steroids. Furthermore, increased rheumatoid factor was observed in our patient. Approximately 20 % of patients with IgG4-related disease exhibit increased rheumatoid factor [9]. In addition, several auto-antibodies, including antinuclear antibodies (ANAs) and antibodies against lactoferrin, carbonic anhydrase II and IV, trypsinogens, and pancreatic secretary trypsin inhibitor, have also been observed in patients with IgG4-related disease [11-14]. Della-Torre E et al. reported that rheumatoid factor from the IgG4 subclass is noted in at least some patients with IgG4-related disease [15]. IgG4 can act as a pathogen, anti-inflammatory agent, or rheumatoid factor [16]. In conclusion, these findings suggest an immune-mediated pathogenesis for IgG4-related disease.

In IgG4-related disease, steroids are the main treatment method. Most patients respond to steroid treatment, prompting reductions in lesion size and IgG4 serum levels within several weeks. In this patient, the steroid was tapered to 2.5 mg per day over a 2 y period, which led to marked clinical improvement. The MRI findings also revealed a significantly reduced brain lesion. The case is uniquely characterized by mastoiditis, hypertrophic pachymeningitis and intracranial inflammatory pseudotumor. One case report described a patient who initially presented with an ear effusion and otorrhea, which revealed mastoiditis [17]. This patient underwent a mastoidectomy with similar pathologic findings to our case and developed left cerebritis. Consistent with our case, this patient also improved clinically with prednisone. Another report described a patient who presented with mastoiditis, central nervous system involvement with headaches and right-sided facial paresthesias [18]. Examination of mastoid tissue revealed a significantly increased number of IgG4-positive cells, suggesting a diagnosis of IgG4-related disease. However, the patient improved clinically and radiographically with rituximab and tapered off azathioprine and prednisone. In addition, mycophenolate mofetil, rituximab, cyclophosphamide and methotrexate are also advised for patients who are resistant to glucocorticoids or who are unable to have their glucocorticoid dose sufficiently reduced [19-22].

In summary, we describe a case of IgG4-related disease presenting as mastoiditis that progressed to central nervous system involvement with significant symptoms. In particular, hypertrophic pachymeningitis and intracranial inflammatory pseudotumor are rare manifestations in IgG4-related diseases. This disorder should be considered in the differential diagnosis of central nervous system tumors as a potentially treatable condition with glucocorticoids and other immunosuppressive agents. An accurate diagnosis of IgG4-related disease is conducive to initiate proper treatment and avoid unnecessary surgery.

Acknowledgments

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Competing Interests

The authors declare that they have no competing interests.

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