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Giant Cell Arteritis Overlapping with Rheumatoid Arthritis and Sjögren's Syndrome

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Abstract

Background: Giant cell arteritis (GCA) is an autoimmune vasculitis involving large and medium arteries, but the relationship with other autoimmune diseases is unclear. We reported a case of an 85-year-old woman who was diagnosed with GCA, Sjögren's syndrome (SS) and rheumatoid arthritis (RA) simultaneously, and discussed the potential link between these diseases.

Case presentation: An 85-year-old Chinese woman was admitted to hospital with aggravation of pain in two knees with headache and blurred vision. She had a history of rheumatoid arthritis and rheumatoid heart disease for 30 years and atrial fibrillation for 1 year. On admission, she had bilateral temporal pain accompanied by blurred vision. Physical examination showed dry tongue and decreased coating on the tongue. Initial laboratory results showed that C-reactive protein (CRP) was 24.89 mg/L (normally 0-5), and erythrocyte sedimentation rate (ESR) was 42.4 mm/h (normally 0-20), both of them were significantly elevated.

Results: The anti-nuclear antibody (ANA) and anti-centromere antibody (ACA) was positive in serum. Color Doppler ultrasound of temporal arteries showed thickening and hardening of bilateral temporal artery wall with varying width and narrowness of lumen. She was diagnosed with GCA, SS, and RA. At the same time, she was given anti-inflammatory treatment with methylprednisolone, hydroxychloroquine and tripterygium glycosides. Her condition was controlled; the mental state and inflammatory biomarkers were significantly improved (CRP < 0.5 mg/L, ESR 13.6 mm/h). She was discharged from the hospital and outpatient review regularly.

Conclusion: GCA, SS, and RA can occur simultaneously or continuously, but were rare. The combination of CRP and ESR improved the specificity and positive rate of GCA diagnosis. We speculated that there might be common pathogenic factors involved in GCA, RA and SS through the analysis of this case. Through the analysis of this case, we speculated that there may be a common virulence factor involved in GCA, RA and SS. Further exploration is needed in the future to elucidate their relationship and provide more support for early diagnosis and treatment.

Keywords: Giant cell arteritis; Sjögren's syndrome; Rheumatoid arthritis

Introduction

GCA is an immune-mediated systemic vasculitis that mainly involves the large and middle arteries, especially the temporal arteries. GCA mainly occurs in people over the age of 50 years old [1,2]. GCA tends to occur in western countries such as Europe, but rarely among blacks and Asians [3]. Typical symptoms of GCA include headache, scalp tenderness, jaw claudication, visual impairment and inflammatory biomarkers such as ESR and CRP were significantly increased [4]. Unilateral or bilateral vision loss is the most terrible complication of GCA [5]. RA and SS are systemic autoimmune diseases, although GCA has been reported in patients with RA and SS respectively [6,7], there have been no reports of linking the three diseases.

Case Presentation

An 85-year-old Chinese woman was admitted to the hospital due to aggravated knee pain, bilateral temporal pain and blurred vision for 3 months. She had a history of rheumatoid arthritis and rheumatoid heart disease for 30 years and atrial fibrillation for 1 year. She was admitted to the local hospital for RA 3 months ago due to aggravation of pain in two knees. After discharge, she developed a headache, mainly bilateral temporal, accompanied by occipital scalp pain and neck pain, and blurred vision. For the diagnosis and treatment, she came to our hospital. Physical examination showed blood pressure (BP) was 155/89 mmhg, heart rate (HR) was 78 beats/min, dry tongue, temporal nodules, temporal vascular sclerosis with tenderness. As shown in Table 1, CRP was 24.89 mg/L (normal 0-5), and ESR was 42.4 mm/h (normal 0-20). ACA was strongly positive (+++), ANA was positive, centromere type (titer of 1:1000), and

Laboratory Results	Results	Normal range
WBC	5.47	3.5-9.5
CRP (mg/L)	24.89	0-5
ESR (mm/h)	42.4	0-20
Hemoglobin (g/L)	123	115-150
Serum glucose (mmol/L)	4.39	3.9-6.16
Creatinine (umol/L)	81.3	31-132
Urea (mmol/L)	6.56	3.1-8.8
Magnesium (mmol/L)	0.68	0.75-1.02
B-type natriuretic peptide (BNP, pg/mL)	134.8	0-100
Autoantibody		
ACA	+++	-
ANA		
Centromere type	1:1000	<1:100
Cytoplasmic granular type	1:320	<1:100

Table 1: List of initial laboratory results.

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cytoplasmic granular type (titer of 1:320) (Table 1). A chest CT scan showed multiple small nodules in both lungs with interstitial changes. Echocardiography showed that she had rheumatic valvular heart disease, cardiac ejection fraction (EF) was 63%, left and right atrium were enlarged, left ventricular diastolic function was reduced and mild pulmonary hypertension (pulmonary artery systolic pressure, PASP, 45 mmHg). The Color Doppler ultrasound of temporal arteries showed that the wall of the bilateral temporal artery was thickened, the width of the lumen was varied, and the blood flow bundle became thinner, and these results suggested temporal arteritis (Figures 1A and 1B). After admission to our hospital, the combination of methylprednisolone (20 mg/qd), hydroxychloroquine (0.2 g/bid) and tripterygium glycoside (20 mg/tid) with anti-inflammatory therapy gradually alleviated the joint pain and headache of the patient, with no obvious improvement in blurred vision. In order to exclude the presence of diseases such as brain tumors, she was examined by the cerebral magnetic resonance imaging (MRI), and the result showed that there was a softening lesion in her right cerebellar hemisphere (Figures 1C and 1D). She said she had been suffering from dry eyes and dry mouth. In order to determine whether she had SS, an ophthalmologist was invited for consultation. By detecting the break-up time (BUT) in both eyes, the doctor found that her right eye was 5.09 s, left eye was 1.61 s (normal > 10 s), and the height of double tears river was 0.1 mm (normal > 0.2 mm). She was diagnosed with SS and suggested to use sodium hyaluronate eye drops and recombinant bovine basic fibroblast growth factor eye-gel to relieve dry eye symptoms. Recombinant bovine basic fibroblast growth factor eye-gel also known as Beifushu eye gel (21000 IU/5g, Zhuhai yisheng bio-pharmaceutical LTD, China), the main ingredient of this product is recombinant bovine basic fibroblast growth factor, and applied to eyes once a day morning and evening. After 12 days of admission, the CRP < 0.5 and the ESR was 9 mm/h. Other general indicators such as renal function, fasting blood glucose test showed no obvious abnormalities. The changes of CRP and ESR in patients during hospitalization were shown in Table 2. The knee pain and headache were significantly relieved, but no significant improvement in blurred vision. The general condition was good, and she was allowed to continue treatment after discharge and return to the hospital regularly.

Discussion

GCA is a chronic autoimmune vasculitis, also known as temporal arteritis, and clinical reports of GCA combined with other autoimmune

Data	CRP (mg/L)	ESR (mm/h)
Admission	24.89	42.4
Day 2	23.88	39.7
Day 6	2.48	23.4
Day 12	<0.5	9

Table 2: The multiple results of inflammatory markers.

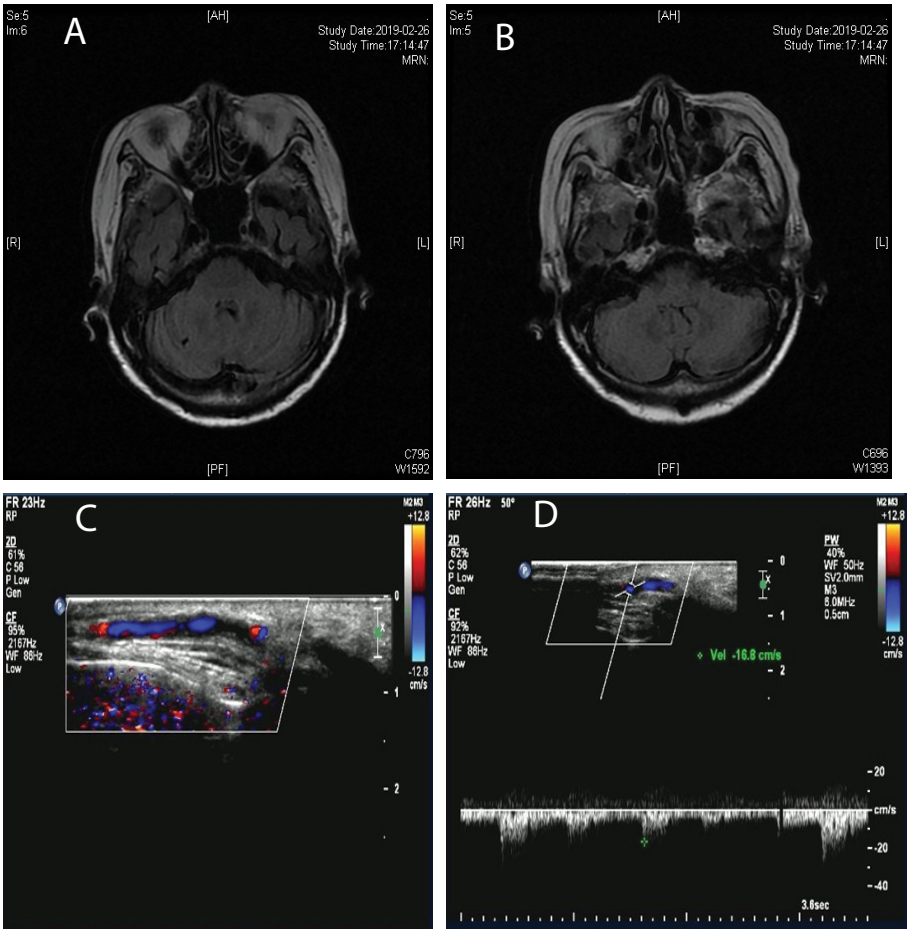

Figure 1: MRI and Color Doppler ultrasound of temporal arteries.

Note: MRI showed right cerebellar hemisphere had a softening lesion (**A** and **B**). Color Doppler ultrasound of temporal arteries showed the wall of the bilateral temporal artery was thickened, the width of the lumen was varied, and the blood flow bundle became thinner (**C** and **D**).

diseases are rare. Semble et al. [6] reported the first case of SS complicated with temporal arteritis in 1985. The combination of the two diseases may be sporadic or may have a common etiology and pathogenesis. GCA may supplement the spectrum of SS and provide new insights into the occurrence of two diseases. Rheumatoid arthritis is the most common form of autoimmune disease, with joint pain as the main symptom. There have been reports of RA overlapped with GCA [8], but the coexistence of the two diseases is still considered to be rare. In our case, she did have the same performance of GCA, RA and SS. This is the first report that these three diseases exist simultaneously, but the relationship between them has not been determined.

The pathogenesis of GCA is still unclear, and experts believe that it may be caused by a combination of genetic and environmental factors [9]. At present, it is generally believed that the pathogenesis of GCA [3,5] is dendritic cells (DCs) which in the middle and endometrium layer of the vascular wall are activated, secrete various inflammatory factors and chemokines such as IL6 and IL8, active and recruit $CD4^+$ T cells and macrophages into the vascular wall. Activated $CD4^+$ T cells can polarize to Th1 and Th17 cells, and participate in vascular inflammation. DCs and $CD4^+$ T cells also play a vital role in the pathogenesis of RA and SS. In this case, GCA and SS appeared on the basis of RA and after the aggravation of RA, which strongly suggested that there may be a common pathogenesis between the three diseases and may promote the occurrence and development of each other.

Previous report showed that multiple autoimmune diseases such as RA and SS can be complicated with vasculitis [10], which may obscure some clinical manifestations of GCA and increase the difficulty of diagnosis and treatment of diseases. In addition, 15% of patients with GCA can develop ischemic optic neuropathy (AION), presenting irreversible visual impairment or even loss [1]. Compared with young patients, elderly patients with GCA have a higher incidence of ischemic complications and risk of early death [11]. Therefore, rapid diagnosis and treatment are crucial for GCA patients, especially for elderly patients. ESR and CRP are the preferred inflammatory indicators for the diagnosis of GCA. Studies had shown that [12,13] combining the results of ESR and CRP can improve the diagnostic value of GCA and achieve 97% specificity. A recent systematic review reported that the Color Doppler ultrasound of temporal arteries is widely used to detect arterial inflammation and obtain reliable results because of its simplicity, non-invasiveness and ease of operation, helping patients to obtain rapid diagnosis and early treatment [14].

Steroids are the primary means of improving the clinical symptoms of GCA patients and reducing the risk of severe ischemic complications (such as loss of vision) [15,16], and are also routinely used for the treatment of RA and SS. This result may be combined with RA and SS for steroid and immunosuppressive therapy. The consensus is good. In this study, knee joint pain and headache were alleviated, inflammatory biomarkers were decreased, and the patient's condition was improved rapidly after treatment with methylprednisolone, hydroxychloroquine and tripterygium glycosides. This result may be consistent with the idea that RA and SS merged with GCA respond well to steroid and immunosuppressive therapy. It was known that patients with GCA may have a tendency of chronic recurrence after steroid reduction or discontinuation. Therefore, long-term steroid application was needed to reduce the risk of recurrence and control the progression of RA and SS, as well as regular outpatient review to monitor changes in the condition.

Conclusion

To sum up, an 85-year-old Chinese woman with GCA, RA and SS is reported in this paper, and had a significant effect on the treatment of methylprednisolone. The coexistence of these three diseases indicates that there may be common pathogenic factors involved in GCA, RA and SS. These diseases need to be investigated on a larger scale to clarify their close relationships and provide more support for early diagnosis and treatment of patients.

Conflicts of Interest

None.

Ethical Standards

This study was agreed by the ethics committee of Qingdao University and all subjects signed informed consent forms.

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