Case report

Early treatment for IgG4-related disease may prevent cognitive impairment caused by cerebral vasculitis: A case report and review of the literature

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ARTICLE INFO

Keywords:
IgG4-related disease
Treatment
Cerebral vasculitis

ABSTRACT

IgG4-related disease (IgG4-RD) is a recently recognized disease entity. A 74-year-old male presented with transient headache. He was diagnosed IgG4-RD by pancreatic biopsy at the age of 72. Magnetic Resonance Imaging (MRI) showed disseminated cerebral microbleeds and microinfarctions in time and space. It suggested cerebral vasculitis, however any causative factor were not confirmed. IgG4-RD rarely causes cerebral vasculitis. This might be a first case of an asymptomatic cerebral vasculitis due to IgG4-RD. Patient was started on oral prednisolone, and no neurological or neuropsychological symptoms was clinically observed. The MRI findings improved after treatment, and revealed no indication of newly lesions at 6-months follow-up. Early treatment for IgG4-RD may be recommended to prevent irreversible cognitive dysfunction.

1. Introduction

IgG4-related disease is recognized as a systemic disease characterized by tumor-like swelling, lymphoplasmacytic infiltrates in IgG4-positive plasma cells, and elevated serum IgG4 concentrations [1]. It causes CNS involvement, i.e., hypertrophic pachymeningitis or hypophysitis [2]. However, there is few case reports about cerebral vasculitis. We are presenting a case of IgG4-RD causing cerebral vasculitis. To our knowledge, there are only 2 cases of IgG4-RD as a cause of cerebral vasculitis reported in the literature.

2. Case report

A 72-year-old male was referred to our hospital with abnormal chest X-ray findings. He did not have any symptom, and physical examination findings were normal. Chest CT revealed a lymphadenopathy of the mediastinum, but a lymph node biopsy showed no evidence of malignancy. During the follow-up, an abdominal CT revealed a thickening of the abdominal aortic wall and diffuse enlargement of the pancreas (Fig. 1). Laboratory examination showed highly elevated serum IgG4 levels (2910 μg/dl), and pancreas biopsy revealed fibrosis with a focal storiform-like pattern, lymphoplasmacytic infiltration, and obliterator phlebitis. Based on the above results, the patient was diagnosed with IgG4-RD. However, he was followed without treatment because clinical symptoms were absent.

At the age of 74, the patient complained of transient headache. His laboratory examination showed an increase in the erythrocyte sedimentation rate (65 mm/h) and IL-6 level (108 pg/ml), despite a normal range of white blood cells (6800/μl) and C-reactive protein (0.17 mg/dl). Diffusion-weighted imaging revealed hyperintense lesions in the right deep white matter. FLAIR imaging showed subtle hyperintense lesions in the right parietal lobe. Neurological and neuropsychological findings were normal. After 2 months, the above lesions enlarged with a leptomeningeal enhancement of gadolinium-contrast. Susceptibility-weighted imaging presented multiple low-intensity spots in the brain parenchyma and laminae on the surface of the right cerebral hemisphere, indicating multiple microbleeds and hemosiderin deposition due to vasculitis (Fig. 1). Serological markers associated with vasculitis, including antinuclear antibody, anti-SS-A/Ro, anti-SS-B/La, anti-neutrophil cytoplasmic antibody, and Mycobacterium tuberculosis-specific interferon-γ release assay, were negative. Coagulation factors, including protein C, protein S, anticardiolipin antibodies, and lupus anticoagulant, were also negative. CSF examination showed an elevated protein level (63 mg/dl) and CSF cell count was normal (5/μl). Polymerase chain reaction on CSF was also negative for herpes simplex virus and varicella-zoster virus. Gadolinium scintigraphy revealed multiple hot spots on cervical lymph nodes and thoracic and abdominal aorta, but none on the brain. Cervical lymph node biopsy showed a reactive...
lymphadenopathy, but not malignant lymphoma.

Although the patient was asymptomatic, prednisolone was administered at 0.6 mg/kg/day as the initial dose to prevent the progression of IgG-related CNS involvement. This initial dose was continued for 4 weeks and was then reduced to a biweekly dose. Serum IgG4 level reached a normal range within 1 month, and hyperintense lesions captured by FLAIR imaging were diminished. A follow-up MRI revealed no indications of newly occurred microbleeds or infarcts.

3. Discussion

In our case, neuroimaging characteristics of the present case presented disseminated cerebral microbleeds and microinfarctions in time and space, suggesting cerebral vasculitis as the pathological etiology. However, any causative factor, such as autoimmune disease, viral infection, and malignant lymphoma, were not serologically confirmed.

In general, IgG4-RD causes systemic vasculitis. In the present case, pathological findings from the pancreas biopsy revealed a vasculitis, and radiological findings from the abdominal CT suggested a periaortitis. There is a potential of cerebral lesions associated with vasculitis from IgG4-RD, although pathological change with an infiltration of IgG4-positive plasma cells is not brain biopsy-proven.

To accomplish literature review, a search of the published literature using the PubMed database was performed. For PubMed (2012 to December 2017) search, the 2 key terms ‘IgG4-related disease’ and ‘brain’ were combined (using the ‘AND’ operator). Results focused on Case reports, English language, and full manuscripts. Then cerebral vasculitis due to IgG4-RD reported with pathological findings is documented in only two previous cases (summarized in Table 1); the first is a case of dolichoectasia of the vertebral basilar artery. An autopsy revealed a marked infiltration of IgG4-containing plasma cells in the adventitia of vertebral and basilar arteries [5]. The second is a case of progressive dementia and spastic hemiparesis; cognitive and motor functions of the patient were completely recovered by prednisolone treatment. In this case, pathological findings of the brain biopsy revealed parenchyma involvement with lymphocyte infiltration, which was the most prominent in perivascular spaces of small brain vessels [6]. Initial radiological findings and the response of the patient to steroid therapy was quite similar to those in our case, although our case presented no clinical symptoms, suggesting an asymptomatic cerebral vasculitis as a manifestation of IgG4-RD.

A delay in the initial treatment or long disease duration has been reported to cause organ damage, such as kidney and pancreatic secretion [7]. Therefore, treatment should be considered in case of multiorgan involvement of IgG4-RD to prevent organ dysfunction. In the present case, we started oral prednisolone administration to prevent symptomatic cerebrovascular disease due to disease progression.

A limitation of cerebral amyloid angiopathy-related inflammation (CAA-rI) is that it causes CNS vasculitis [3]. Usually, CAA-rI patients present clinical symptoms of subacute dementia or a change of mental status [4,5]; however, in our case, no neurological or neuropsychological symptom was clinically observed. Nonetheless, we could not exclude CAA-rI because brain biopsy was not performed.

4. Conclusion

In conclusion, this case may be the first report of IgG4-RD where treatment for unusual cerebral involvement was undergone in an asymptomatic state. Even if the patient is asymptomatic, early treatment for IgG4-RD may be recommended to prevent irreversible cognitive dysfunction and probable cerebral vasculitis presenting with repeated cerebral microbleeds and microinfarctions on diminished small
vessels in time and space.

Source of funding

None declared.

Disclosures

The authors have no financial or other conflicts of interest in relation to this research paper.

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