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Optic Perineuritis as the First Manifestation in a Patient with Microscopic Polyangiitis and Mastoiditis with Elevated Serum IgG4

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Abstract **Case Report**

A 77-year-old woman presented with right visual disturbance. Her past medical history included left hearing loss and body weight loss. On ophthalmic examination, best-corrected visual acuity was counting finger in the right eye and 1.2 in the left eye. Brain magnetic resonance imaging (MRI) demonstrated right optic perineuritis and left mastoiditis. Laboratory examination revealed elevated erythrocyte sedimentation rate, C-reactive protein (CRP), and myeloperoxidase-antineutrophil cytoplasmic antibody (MPO-ANCA). Urinalysis revealed a microscopic hematuria. Therefore, she received a diagnosis of microscopic polyangiitis (MPA) concomitant with IgG4-related disease (IgG4-RD). The patient was treated for oral prednisolone. After treatment, the symptoms showed gradually improved and her visual acuity improved to 0.01 in the right eye. MPO-ANCA and CRP were gradually improved, and the MRI findings of optic perineuritis and mastoiditis were also improved. This case highlights the importance for clinicians to be aware of a concomitant diagnosis of MPA and IgG4-RD.

Key words: Microscopic polyangiitis, Optic perineuritis, Mastoiditis, Immunoglobulin G4–related disease.

INTRODUCTION

Microscopic polyangiitis (MPA) is a member of the family of anti-neutrophil cytoplasmic antibody (ANCA) -associated vasculitis (AAV). Its characteristic histology shows a necrotizing small vessel vasculitis with little or absent immune deposits [1]. Immunoglobulin G4 (IgG4)-related disease (IgG4-RD) is characterized by high serum IgG4 concentration and comprised of a spectrum of systemic disorders [2, 3]. Although AAV and IgG4-RD are distinguishable based on characteristic findings in many cases, the diagnosis can be unclear in rare cases, in which clinicians should consider possible coexistence of AAV and IgG4-RD [4-7].

There are several reports on optic nerve involvement in AAV [8-11] and IgG4-RD [12-16]. Optic perineuritis (OPN) is a very rare form of orbital inflammatory disease involving the optic nerve sheath [17]. Most cases are idiopathic; however, OPN can seldom be the manifestation of AAV [18-21] and IgG4-RD [12-16]. Only a few cases of patients having IgG4-RD and exhibiting mastoiditis have been reported [22-24], however, there is no report with AAV presenting as mastoiditis.

Here, we report the case of a patient with MPA with elevated serum IgG4 who had a history of mastoiditis.

CASE REPORT

A 77-year-old woman presented with right visual disturbance for 2 months. Her past medical history included left hearing loss 10 months before the initial visit and body weight loss. On ophthalmic examination, best-corrected visual acuity was counting finger in the right eye and 1.2 in the left eye. The anterior segment of both eyes was unremarkable. Funduscopy of both eyes was unremarkable. Brain magnetic resonance imaging (MRI) demonstrated OPN in the right eye and left mastoiditis. Laboratory examination revealed white blood cell count at 5700 cells/μL, with 74.0% neutrophils, 18.0% lymphocytes, 7.0% monocytes, and 1.0% eosinophils. Hemoglobin level was 11.2 g/dL, erythrocyte sedimentation rate was 116 mm/h, and C-reactive protein (CRP) level was 5.12 mg/L (reference range 0-0.14). Liver and renal functions were within normal limits. Levels of total IgG, IgA, IgM, and IgG4 were 3178 mg/dL (861-1747), 671 mg/dL (93-393), 141 mg/dL (50-269), and 408 mg/dL (4.5-117), respectively. Myeloperoxidase-antineutrophil cytoplasmic antibody (MPO-ANCA) was

16.0 U/ mL (< 3.5) and proteinase 3 (PR3)-ANCA was < 1.0 U/ mL (< 3.5). Urinalysis revealed a microscopic hematuria of 5-9/HPF, and WBC count at 1-4/HPF. Therefore, she received a diagnosis of MPA concomitant with IgG4-RD. The patient was treated for oral prednisolone (20 mg/day). One month following steroid therapy, the symptoms showed gradually improved and her visual acuity improved to 0.01 in the right eye. The steroid dosage was gradually reduced over several months. MPO-ANCA was gradually improved to 10.4 U/ mL, and CRP level had decreased to 0.03 mg/L. The MRI finding of optic perineuritis and mastoiditis were improved. The patient was doing well and there were no indicative signs of disease recurrence. Histological examination was not available in this case.

DISCUSSION

AAV include granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA, Churg-Strauss syndrome) and MPA [1]. Recently, there have been an increasing number of reports focusing on the relationship of AAV and IgG4-RD [4-10]. IgG4 research teams in Japan proposed comprehensive diagnostic criteria for IgG4-RD [2, 3]. This diagnostic criteria is as follows: clinical examination showing characteristic diffuse/localized swelling or masses in single or multiple organs; hematological examination showing elevated serum IgG4 concentrations (>135 mg/dL); and histopathologic examination revealing marked lymphocyte and plasmacyte infiltration and fibrosis, and infiltration of IgG4+ plasma cells. Thus, a diagnosis of IgG4-RD is definitive in patients who fulfill all of the above criteria. A diagnosis of IgG4-RD is also possible in patients who fulfill the first 2 criteria but not the last. A diagnosis of IgG4-RD is probable in patients with organ involvement who also fulfill the histopathologic criteria but who do not exhibit increased serum IgG4 concentration. The patient in the present case fulfilled the first 2 criteria. Thus, her condition represented a "possible" case of IgG4-RD. In this patient, clinical findings that indicate MPA include hematuria, body weight loss, inflammatory laboratory findings, and positive MPO-ANCA. On the other hand, clinical findings that indicate IgG4-RD include optic perineuritis, mastoiditis, and elevated serum IgG4. Regrettably, however, histological examination was not available in this case. According to these results, we diagnosed the disease as coexistence MPA and IgG4-RD.

Danlos *et al*. [4] stated that AAV and IgG4-RD could overlap. According to their report, AAV and IgG4-RD were diagnosed concomitantly in 13/18 (72%) patients; AAV preceded IgG4-RD in 3/18 (17%) while IgG4-RD preceded AAV in 2/18 (11%). AAV diagnoses included GPA in 14 (78%), MPA in 3 (17%), and EGPA in one case. IgG4-RD diagnosis included definite IgG4-RD in 5 (28%) cases, probable IgG4-RD in 5 (28%) and possible IgG4-RD in 8 (44%). Kawashima *et al*. [5] also suggested that AAV and IgG4-RD might overlap.

In contrast, Yoo *et al.* [7] investigated 46 MPA and GPA patients with results on serum IgG4 and histology whether elevated serum IgG4 at the time of diagnosis of MPA and GPA may be associated with concurrent IgG4-RD. According to their report, twenty-eight patients (60.9%) were classified as MPA and 18 patients (39.1%) as GPA. The serum IgG4 at diagnosis was 1202.7 mg/dL and 37 patients (80.4%) had elevated serum IgG4 at diagnosis. They found no patients, who could be classified as IgG4-RD according to comprehensive diagnostic criteria for IgG4-RD among 46 patients. The mean serum IgG at diagnosis was not different between the two groups. Serum IgG4 was significantly correlated with inflammation-related variables at diagnosis. Elevated serum IgG4 is not associated with concurrent IgG4-RD, and it may reflect activity and inflammatory burden of vasculitis in patients with MPA and GPA at diagnosis. Vaglio *et al*. [6] investigated 46 patients with EPGA, 26 with GPA, 25 with atopic asthma and 20 healthy controls and determined serum IgG subclass levels. According to their report, IgG4 levels were markedly higher in active EPGA patients than in controls. Longitudinal analysis in 12 EPGA cases showed that both the IgG4 level and IgG4/IgG ratio dropped during disease remission. Serum IgG4 levels are markedly elevated in active EPGA and correlate with the number of organ manifestations and disease activity.

Interestingly, OPN was the predominant early clinical sign and a history of mastoiditis was existed in this present case.

CONCLUSIONS

This case highlights the importance for clinicians to be aware of a diagnosis of concomitant MPA and IgG4-RD.

Disclosure

The authors have no conflicts of interest to disclose for this paper.

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