CASE REPORT

Giant Cell Arteritis with Generalized Granuloma Annulare

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Abstract:
We report the case of an 80-year-old man with generalized granuloma annulare (GGA) who subsequently developed giant cell arteritis (GCA). Steroid treatment was effective for both diseases in this case. Although cases of concomitant GGA and GCA have rarely been reported, previous studies suggest that common histological characteristics underlie the two diseases. It is therefore necessary to recognize that GGA can be complicated by GCA, particularly when typical symptoms, such as headache and visual disturbance, are present.

Key words: giant cell arteritis, generalized granuloma annulare, vasculitis

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Introduction

Giant cell arteritis (GCA), also called temporal arteritis, is a granulomatous arteritis that frequently affects the temporal arteries (1). Generalized granuloma annulare (GGA) is one of four subtypes (limited, generalized, perforating, and subcutaneous) of granuloma annulare (GA), and is characterized by inflammatory dermatosis of unknown origin (2). GCA and GGA reportedly share common histological features (3, 4); this suggests that the two diseases might also share some etiologies. However, GCA associated with GGA appears rare, with only four reported cases (5-8). We herein describe the case of an 80-year-old man with GGA and GCA who was successfully treated with oral prednisolone (PSL).

Case Report

An 80-year-old man was admitted to our hospital with a loss of visual acuity. His medical history included iritis and cataract, which were diagnosed four years and two years prior to admission, respectively. Approximately one year prior to admission, he developed generalized erythema and papules on his trunk and extremities; skin biopsy performed in a neighboring dermatology clinic led to a diagnosis of GGA. Treatment for GGA, including topical glucocorticoid and ultraviolet therapy was initiated; however, the effects were not satisfactory. Approximately two weeks before admission, he noticed deterioration in his left visual acuity, followed by pyrexia, headache, jaw claudication, and general malaise. The day after he lost left visual acuity, he lost right visual acuity. GCA was suspected and the patient was admitted to our department for examination and treatment.

When examined upon admission, his vital statistics were as follows: body temperature, 36.6°C, heart rate, 56 bpm; and blood pressure, 139/62 mmHg. The temporal arteries were found to be tender and distended, but no oral ulcers were found. No extra heart sound or murmur was present. Crepitation in the left lung field was audible. No abdominal distension, rigidity or tenderness was noted. Old and new papules were scattered on his trunk and extremities (Fig. 1A). No musculoskeletal abnormalities were identified.

The results of laboratory tests on admission were as follows: white blood cell count, 6,400/μL; hemoglobin, 9.2 g/dL; platelet count, 291,000/μL; total protein, 7.7 g/dL; albumin, 2.8 g/dL; total bilirubin, 0.4 mg/dL; aspartate aminotransferase 78 IU/L; alanine aminotransferase 78 IU/L; lactate dehydrogenase, 177 IU/L; alkaline phosphatase, 913 IU/L; γ-glutamyl transpeptidase, 102 IU/L; creatine kinase, 20 U/

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blood urea nitrogen, 22.3 mg/dL; serum creatinine, 1.05 mg/dL; Na, 139 mEq/L; K, 4.1 mEq/L; Cl, 104 mEq/L; total cholesterol, 178 mg/dL; C-reactive protein, 15.97 mg/dL; glucose 87 mg/dL; erythrocyte sedimentation rate, 90 mm/h; immunoglobulin (Ig) G, 1,903 mg/dL; IgA, 413 mg/dL; IgM, 62 mg/dL; IgE, 384 IU/mL; IgD, 1.6 mg/dL; IgG4, 278 mg/dL; hemoglobin A1c, 5.8%; C3, 163 mg/dL; C4, 22 mg/dL; prothrombin time, 83.9%; international normalized ratio, 1.13; activated partial thromboplastin time, 26.3 seconds; fibrinogen, 506.2 mg/dL; fibrinogen degradation product, 7.7 μg/mL; D-dimer, 1.4 μg/mL; soluble interleukin-2 receptor, 1,850 U/mL; and angiotensin converting enzyme, 13.7 U/L.

The patient was negative for hepatitis B virus antigen, anti-hepatitis C virus antibody, and syphilis (rapid plasma regain and Treponema pallidum hemagglutination). The results of tests to detect autoantibodies were as follows: rheumatoid factor, positive (79 IU/mL); antinuclear antibody, positive (×40, speckled pattern); anti-cardiolipin antibody IgG, negative (25 U/mL); lupus anticoagulant (dilute Russell’s viper venom time), negative (1.0); myeloperoxidase anti-neutrophil cytoplasmic antibodies (ANCA), negative (<1.0 U/mL); proteinase 3-ANCA, negative (<1.0 U/mL); anti-SS-A-antibody, negative (<1.0 U/mL); anti-SS-B-antibody, negative (<1.0 U/mL); and anti-mitochondrial M2 antibody, negative. A liver biopsy specimen showed centrilobular liver damage suggesting acute-phase autoimmune hepatitis, without granuloma or vasculitis. A human leukocyte antigen typing analysis was positive for the A26, A33, B61 and B58 haplotypes. The patient’s urine was negative for protein, sugar, and occult blood. Ophthalmoscopy revealed vitreous clouding in both eyes, paleness at the left retinal posterior pole and partial opacity at the right retinal posterior pole (Fig. 2). Contrast-enhanced CT indicated irregularities in the wall thickness and lumen of the superficial temporal arteries, whereas the bilateral ophthalmic arteries appeared normal (Fig. 3A and B). Ultrasonography of the temporal arteries revealed concentric wall thickening, hypoechoic halo, and the lumen was compressed bilaterally. However, ultrasound analyses of the shoulder joints were negative for active synovitis, the presence of which is indicative of polymyalgia rheumatica.

Given the above clinical findings and the criteria proposed by the American College of Rheumatology, the patient was diagnosed with GCA (9), bilateral central retinal artery oc-
Figure 3. A: Contrast-enhanced computed tomography: wall thickening and lumen irregularities of the patient’s superficial temporal arteries (arrows) were identified, which were compatible with giant cell arteritis. B: In contrast, bilateral ophthalmic arteries were depicted.

Figure 4. The clinical course. CRP: C-reactive protein, MZR: mizoribine, t-PA: tissue-plasminogen activator

Discussion

Although cases in which GCA is associated with GGA have rarely been reported, there are indications that GCA and GGA share common immunohistochemical, therapeutic and genetic features. Although we could not show the histological findings of GCA and GGA in the presented case, previous studies reported that histopathologic evidence of vasculitis in temporal artery biopsy specimens is a typical and important diagnostic manifestation of GCA (10). Liang et al. noted that IgG, IgM and C3 were deposited on GCA-damaged arteries, while Dahl et al. found the deposition of
IgM and C3 on GGA-damaged biopsy specimens (3, 4). Furthermore, the latter specimens demonstrated wall necrosis, fibrinoid changes and thickening or occlusion of blood vessels; taken together, these findings show that immunoglobulin-mediated vasculitis plays an important role in both GGA and GCA (3, 4). Corticosteroids, currently the first-line treatment for GCA (11), have been successfully used in the treatment of a patient with GGA complicated by GCA (5). Corticosteroid-sparing agents are considered for preventing the adverse effects arising from long-term exposure to glucocorticoid: for example, methotrexate is frequently used in combination with corticosteroids (11). However, methotrexate might not have been suitable in the present case because the patient had liver dysfunction. In this case, we chose MZR, a purine anti-metabolic immunosuppressant. MZR is reported to show good corticosteroid-sparing effects and safety in the treatment of lupus nephritis (12). MZR, a drug that has a similar mechanism to mycophenolate mofetil with less hepatotoxicity, was also reported to be effective for Takayasu arteritis, another form of large-vessel vasculitis (13). MZR should be considered as a corticosteroid-sparing agent for large-vessel vasculitis with risk factors for drug-related problems.

Gonzalez-Gay et al. reported that human leukocyte antigen-B15, which is reportedly increased in GGA patients (14), was also frequently identified in patients with GCA (15); however, it was not identified in the present case. Thus, GCA and GGA might have common genetic factors. Taken together, these findings support the hypothesis that GCA and GGA share common etiologies. To date, there have only been four case reports of concomitant GCA and GGA (5-8) (Table). Shoimer et al. diagnosed their case as annular elastolytic giant cell granuloma (AEGCG), which they considered to be different from GA (7). However, the differential diagnosis of the two conditions is difficult, and other literature describes AEGCG as a variant of GA (16). Notably, in the case reported by Yáñez et al. (6), GCA was diagnosed three years prior to GGA. However, GGA was followed by GCA in three of the four previously reported cases, as well as ours (5, 7, 8). Since GCA frequently affects the branches of the carotid arteries, 10-20% of patients with GCA develop vision loss due to ischemic optic neuritis (1). Physicians should be aware of the potential for developing GCA during the clinical course of GGA. Further studies are necessary to clarify the pathophysiology underlying the coexistence of GCA and GGA.

In this paper, we reported a case of GCA that emerged one year after the diagnosis of GGA, both of which were effectively treated with oral corticosteroids. Clinicians should be alert for the development of GCA in patients with GGA who develop GCA-diagnostic symptoms such as headache and visual disturbances.

The authors state that they have no Conflict of Interest (COI).

**Table.** Cases of Giant Cell Arteritis (GCA) Complicated with Generalized Granuloma Annulare (GGA).

| Reference | Age | Sex | Preceding symptoms | Complications | Therapy | Outcome |
|-----------|-----|-----|--------------------|---------------|---------|---------|
| (5)       | 79  | M   | GGA 7 months before the onset of GCA | None          | PSL (60 mg/day) | Recovered |
| (6)       | 69  | F   | GCA 3 years before the onset of GGA | None          | PSL (30 mg/day) | Recovered |
| (7)       | 71  | M   | GGA 5 months before the onset of GCA | Episcleritis  | PSL (50 mg/day) | Recovered |
| (8)       | 78  | M   | GGA 1 year before the onset of GCA | Uveitis       | PSL (0.7 mg/kg/day) | Recovered |

Presented case: 80 M GGA 1 year before the onset of GCA Uveitis PSL (50 mg/day) Recovered

F: female, GCA: giant cell arteritis, GGA: generalized granuloma annulare, M: male, PSL: prednisolone

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