Co-Presentation of Giant Cell Arteritis and Granulomatosis with Polyangiitis: A Case Report and Review of Literature

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Patient: Female, 67
Final Diagnosis: GPA and GCA
Symptoms: Blurry vision • headache • nosebleed • sinus congestion
Medication: —
Clinical Procedure: —
Specialty: Rheumatology

Objective: Rare co-existence of disease or pathology
Background: Systemic vasculitis can present with a multitude of symptoms involving multiple organ systems. Clinicians should avoid anchoring bias and be cognizant that different types of vasculitides can be present in the same patient and that the diagnosis of one should not preclude the subsequent diagnosis of another.

Case Report: A 67-year-old woman was referred for evaluation of episodes of epistaxis and recurrent severe sinusitis. Her physical examination showed nasal congestion and purpuric rash on the lower extremities. CT of the sinuses showed severe mucosal thickening. ANCA serologies were positive with a c-ANCA titer of 1: 5120 and anti-proteinase-3 (anti-PR3) antibodies of 1061 units. Serum creatinine was elevated at 1.32 mg/dL (GFR of 40.62 ml/min). Urine analysis showed proteinuria and hematuria. The patient declined treatment initially, but while awaiting kidney biopsy she developed episodes of headache and blurry vision. She underwent right temporal artery biopsy 4 days later, which confirmed the diagnosis of GCA. The biopsy showed characteristic histopathology findings and she was started on 60 mg of prednisone daily. The kidney biopsy showed pauci-immune crescentic glomerulonephritis (PICGN) consistent with ANCA-associated vasculitis. We identified all the cases of co-presentation of GCA and GPA in the literature and summarized their clinical features in this report.

Conclusions: Astute clinicians should be cognizant of overlapping and atypical presentations of vasculitides to avoid delayed diagnosis and errors in management.

MeSH Keywords: Giant Cell Arteritis • Glomerulonephritis • Wegener Granulomatosis

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Background

There have been several case reports and case series describing patients diagnosed with giant cell arteritis (GCA) who subsequently developed full-blown granulomatosis with polyangiitis (GPA). This presentation could be characterized as “polyangiitis overlap syndrome” [1]. However, rarely has GCA been reported in patients with an established diagnosis of GPA. We report the case of a 67-year-old woman who initially had a clinical diagnosis of GPA based on severe, recurrent sinusitis, renal biopsy findings, and very high titers of antineutrophil cytoplasmic antibodies (ANCA), who subsequently developed classic clinical features of GCA with diagnosis confirmed by temporal artery biopsy. The symptoms of patients with vasculitides should be continuously reevaluated and existence of a previous diagnosis should not preclude the possibility of another diagnosis (anchoring bias).

Case Report

A 67-year-old woman was referred to the rheumatology clinic for evaluation of episodes of epistaxis and recurrent severe sinusitis for the previous 3 years. Her physical examination showed nasal congestion and purpuric rash on the lower extremities. CT of the sinuses showed severe mucosal thickening in multiple sinuses. ANCA serologies were positive with a c-ANCA titer of 1: 5120 and anti-proteinase-3 (anti-PR3) antibodies of 1061 units. Complete blood count was normal, but serum creatinine was elevated at 1.32 mg/dL (GFR of 40.62 ml/min). Her urine analysis showed proteinuria of 30 mg/dL along with hematuria (>30 red blood cells/high-power field). The patient declined treatment but agreed to schedule a kidney biopsy. While awaiting the biopsy, she developed episodes of headache and blurry vision for which she was referred to the ophthalmology clinic. She was found to have an erythrocyte sedimentation rate (ESR) of 78 mm and a C-reactive protein (CRP) of 8.4 mg/dL. A right temporal artery biopsy showed characteristic histopathologic findings of GCA. There were significant foci of histiocytic infiltration of the internal elastic lamina. A Verhoeff-Van Gieson trichrome combination stain demonstrated considerable loss of the internal elastic lamina (IEL), and a CD68 immunostain was positive, demonstrating histiocytic infiltration of the internal elastic lamina. She was started on 60 mg of prednisone daily. The kidney biopsy showed pauci-immune crescentic glomerulonephritis (PICGN), consistent with ANCA-associated vasculitis. She was treated with rituximab and prednisone. The proteinuria and hematuria resolved and her serum creatinine improved.

Discussion

There have been several case reports of patients concomitantly presenting with clinical features of different types of vasculitides. Here, we described a patient who presented with GCA and GPA, identified similar patients in the literature [1–10], and abstracted data on the clinical features of such co-presentations. Some authors use the term polyangiitis overlap syndrome to describe systemic vasculitides that does not fit into a single diagnostic category but has aspects from several categories of vasculitides [11]. In some cases, as in ours, it can involve features of GCA and GPA. A review of the literature revealed that the most common presentation for GCA was headache, while in GPA, epistaxis was the most common. The duration between the presentations of these 2 entities ranged from 1 week to 8 years. A few cases were diagnosed simultaneously. Not all of the reported cases had biopsy confirmation; some diagnoses were made based on clinical features. In this report, we have summarized all the cases of co-presentation of GCA and GPA reported in the literature (Table 1).

Most patients received corticosteroids and/or cyclophosphamide, historically the most widely used medications. Our case is unusual in that GPA preceding GCA is quite rare and this is the third such reported case.

Unlike in the past, it is more important now to differentiate these 2 entities since we have more targeted, effective treatments. Additional diagnosis of GCA in patients with established diagnosis of other systemic vasculitides may also be important since GCA is associated with rapidly-progressive visual loss and cerebrovascular accidents [12,13]. The pathogenesis of GCA has been shown to be mainly cell-mediated [14]. The inflammatory infiltrate is chiefly composed of lymphocytes, macrophages, and multinucleated Langerhans cells [15,16]. The formation of cytokines, particularly interleukin-6, has been shown to be correlated with the severity of systemic symptoms [17]. On the other hand, the pathogenesis of GPA is mainly humoral-mediated through the ANCA-PR3 complex [18]. Hence, pathogenesis-based therapy is often used. For example, tocilizumab, an IL-6 antagonist, has shown efficacy in GCA, while rituximab has been effective in GPA. Although the pathogenesis of GCA and GPA are quite different, there is evidence of a common pathway: B cell activation. Authors have described patients with GCA who were successfully treated with rituximab [19,20].

Conclusions

In summary, systemic vasculitis can present with a multitude of symptoms involving multiple organs. Clinicians should be cognizant that different types of vasculitides can be present in the same patient and that the diagnosis of one should not preclude the subsequent diagnosis of another.
Table 1. Co-presentation of GCA and GPA.

| Patient # | Author             | Age/sex | Cranial manifestations                                                                 | Extracranial manifestations                           | Time between presentations | ANCA       | Histology (via biopsy)                  | Treatment        |
|-----------|--------------------|---------|----------------------------------------------------------------------------------------|-------------------------------------------------------|---------------------------|------------|----------------------------------------|-----------------|
| 1         | Bradley et al. [1] | 59/F    | Temporal headache                                                                      | Shoulder pain, pulmonary nodules                      | 6 months                  | N/A        | TA: GCA Lung: giant cells in granulomas | CS, CYC         |
| 2         | Tone et al. [2]    | 61/F    | Frontal and occipital headache, binocular vertical diplopia, jaw claudication, otitis media, rhinosinusitis, epistaxis | Shoulder and arm pain                                  | None                      | PR3        | TA: GCA. Kidney: PICGN                | CS, CYC         |
| 3         | McCarthy et al. [3]| 65/M    | Headache, scalp tenderness, visual loss, fronto-temporal dura enhancement              | Weight loss                                            | 3 months                  | Negative ANCA | TA: GCA                        | CS, CYC         |
| 4         | Palaic et al. [4]  | 74/M    | Right-sided headache, frontal scalp burning, diplopia, loss of vision, recurrent sinus congestion | PMR, pulmonary opacities with cavitation              | None                      | N/A        | Sphenoid sinus: CS vasculitis       |                 |
| 5         | Small et al. [5]   | 69/F    | Unilateral hearing loss, cough, bitemporal headaches, and tenderness of the scalp      | Fever, rash, anemia                                    | 1 month                   | N/A        | TA: GCA Kidney: necrotizing vasculitis, with giant cells, focal and segmental GN, with crescents | CS, CYC         |
| 6         | Vermeulen et al. [6]| 62/F   | Jaw claudication, nasal discharge, frontal headache                                    | Fatigue, night sweats, weight loss, basal infiltrates | None                      | N/A        | TA: focal intimal fibrosis. Lung biopsy: necrotizing granulomatous vasculitis | CS, CYC         |
| 7         | Astudillo et al. [7]| 51/F   | Sinusitis, rhinitis, temporal headaches                                                | Fever, weight loss, arthralgias, hematuria            | None                      | PR3        | TA: discretely thickened intima with normal media (clinical diagnosis of GCA & GPA) | CS              |
| 8         | Nishino et al. [8] | 61/F    | Jaw claudication                                                                       | Fever, myalgia, nasal pain, lung nodules              | 14 months                 | N/A        | TA: GCA Lung.: GPA                  | CS, CYC         |
### Table 1 continued. Co-presentation of GCA and GPA.

| Patient # | Author          | Age/sex | Cranial manifestations                                      | Extracranial manifestations                   | Time between presentations | ANCA            | Histology (via biopsy)               | Treatment   |
|-----------|-----------------|---------|-------------------------------------------------------------|-----------------------------------------------|-----------------------------|-----------------|--------------------------------------|-------------|
| 9         | Nishino et al. [8] | 65/F    | Visual loss, hemoptysis                                     | Malaise, exertional dyspnea, proteinuria, hematuria, lung nodules | 6 months                   | N/A             | TA: non-granulomatous arteritis. Lung: necrotizing vasculitis. Kidney: crescentic GN. | CS, CYC     |
| 10        | Nishino et al. [8] | 75/F    | Productive cough, otalgia                                   | Myalgia, anemia, proteinuria, hematuria, elevated creatinine | 23 months                  | c-ANCA         | TA: arteritis, fibrinoid necrosis     | CS, CYC     |
| 11        | Nishino et al. [8] | 61/F    | Headache, oral sores, hemoptysis                             | Dyspnea, alveolar infiltrates, hematuria, proteinuria, purpura, arthralgia | 8 years                    | N/A             | TA: non-giant cell arteritis. Lung: diffuse organizing he, bronchiolitis obliterans | CS, CYC     |
| 12        | Hamidou et al. [9] | 63/F    | Jaw claudication, rhinitis, sinusitis                       | Fever, arthritis, myalgia, proteinuria, hematuria | N/A                        | PR3             | TA: GCA                              | CS, CYC     |

**GPA preceding GCA**

| Patient # | Author          | Age/sex | Cranial manifestations                                      | Extracranial manifestations                   | Time between presentations | ANCA            | Histology (via biopsy)               | Treatment   |
|-----------|-----------------|---------|-------------------------------------------------------------|-----------------------------------------------|-----------------------------|-----------------|--------------------------------------|-------------|
| 13        | Zenone et al. [10] | 75/F    | Temporal and frontal headaches, bilateral conjunctivitis, otitis, hearing loss | Fatigue, fever, muscle weakness, myalgia, dyspnea, chest pain | 18 months                  | N/A             | TA: GCA                              | CS          |
| 14        | Nishino et al. [8] | 71/M    | Epistaxis, periorbital headache, diplopia, otitis media     | Calcified nodules, hilar lymph nodes, arthralgias, proteinuria, hematuria | 9 months                   | c-ANCA         | TA: GCA                              | CS, CYC     |
| 15        | Hassane et al. | 67/F    | Epistaxis, sinusitis, headaches, blurred vision             | Purpura, hematuria, proteinuria                | 1 week                     | c-ANCA; PR3   | TA: GCA, Kidney: PICGN.              | CS, RTX     |

N/A – not available; GCA – giant cell arteritis; GPA – granulomatosis with polyangiitis; PICGN – pauci-immune crescentic glomerulonephritis; PMR – polymyalgia rheumatica; c-ANCA – cytoplasmic pattern of anti-neutrophil cytoplasmic antibody; PR3 – proteinase-3 antibody; TA – temporal artery; GN – glomerulonephritis; CS – corticosteroids; CYC – cyclophosphamide; RTX – rituximab.

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