Spinal Cord Involvement in Granulomatosis With Polyangiitis: An Unusual Presentation

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Abstract

A 40-year-old lady presented with rhinosinusitis, left-sided nodular scleritis and dyspnoea on exertion of 4-month duration. Computed tomography (CT) of the chest showed a cavitary granuloma whose biopsy revealed necrotising vasculitis. Indirect immunofluorescence assay showed anti-neutrophil cytoplasmic antibodies with a cytoplasmic pattern. She was diagnosed as a case of granulomatosis with polyangiitis (GPA) with otorhinological, ocular and pulmonary involvement. A month later, she developed dorsolumbar pain and lower limb paraesthesia. Evaluation for the same revealed MRI evidence of granulation tissue at the lower dorsal levels. She was initially managed with injection of cyclophosphamide (CYC) and high-dose steroids, but with an inadequate response. Her treatment protocol was then modified to pulse injection of rituximab (RTX), and she gradually attained an adequate clinical and radiological recovery.

Keywords: Granulomatosis with polyangiitis; Spine; Cyclophosphamide; Rituximab

Introduction

Heinz Klinger was first to describe the disease process of Wegener’s granulomatosis in 1932 [1]. Subsequently, Frederick Wegener published his two papers in 1936 [2] and 1939 [3] describing post-mortem studies of two patients who died of disseminated vasculitis. In January 2011, the Boards of Directors of the American College of Rheumatology (ACR), the American Society of Nephrology and the European League Against Rheumatism recommended that the name Wegener’s granulomatosis be changed to granulomatosis with polyangiitis, abbreviated as GPA [1-3]. GPA is a distinct clinicopathological entity characterized by granulomatous vasculitis of the upper and lower respiratory tracts together with glomerulonephritis. In addition, variable degrees of disseminated vasculitis involving both small arteries and veins may occur. GPA is not so common disease with a prevalence of 3/100,000. The male-to-female ratio is 1:1 and the mean age of onset is around 40 years. There is a strong and specific association with autoantibodies directed against proteinase 3, a constituent of neutrophil azurophilic granules [4]. The presence of such antibodies is a strong indicator for a diagnosis of GPA. However, it should not be used in place of a tissue diagnosis. The presence of anti-neutrophil cytoplasmic antibody (ANCA) is not mandatory to make a diagnosis of Wegener’s granulomatosis by either the ACR or the Chapel Hill Consensus Conference (CHCC) definitions [5, 6]. Spinal cord involvement in GPA is very rare and it is generally either by local compression with inflamed tissues or spread of inflammation to adjacent cord and leptomeninges. It warrants an early detection and aggressive management to avoid neurological complications like compressive myelopathy. We hereby present a case of GPA with rhinosinusitis, pulmonary cavitating granuloma and nodular scleritis who subsequently developed spinal cord involvement.

Case Report

A 40-year-old lady presented to the rheumatology clinic with rhinosinusitis, left-sided nodular scleritis (Fig. 1a) and dyspnoea on exertion of 4-month duration. Laboratory parameters showed normal haematological and biochemical values. Urine analysis and chest radiography were within normal limits. A non-contrast computed tomography (CT) of the paranasal sinuses revealed mucosal thickening bilateral nasal mucosa and inferior turbinates. Her audiometry confirmed bilateral sensorineural hearing loss. Contrast-enhanced CT of the chest showed a 20 × 28 mm sized thick walled cavitatory granuloma in lateral basal segment in right lower lobe subpleural location (Fig. 1b). A biopsy of this lesion revealed transmural destructive of the vessel wall with infiltration by dense mixed inflammatory infiltrate and areas of necrosis suggestive of necrotising vasculitis (Fig. 1c). Indirect immunofluorescence assay showed ANCA with a cytoplasmic pattern. These findings suggested a diagnosis of GPA with otorhinological, ocular and pulmonary involvement. A month later, she developed repeated episodes of acute-onset excruciating upper abdominal pain with radiation to the dorsolumbar spine. She underwent...
upper gastrointestinal endoscopy which revealed severe antral gastritis and was managed for the same with anti-ulcer therapy, but with no response. A contrast MRI done showed altered signal intensity with enhancement of the epidural fat over D11 and D12 levels extending to the neural foramina with blurred margins of accompanying nerve roots, representing granulation tissue (Fig. 2a, b). This indicated a spinal involvement in this patient of GPA. She was then managed with pulse injection cyclophosphamide (CYC) and high-dose steroids to induce remission. After 20 weeks of induction treatment, she responded well, but later relapsed with recurrence of spinal pain warranting frequent visits to the emergency department. Her treatment protocol was then modified to pulse injection of rituximab (RTX) 500 mg weekly for four doses, and she gradually attained an excellent clinical response. A repeat contrast MRI (Fig. 2c) also showed a significant resolution of the spinal lesions. She is at present off oral steroids and stable on maintenance therapy.

Discussion

The spinal cord involvement in GPA is much rare. In literature, there are only a few cases of spinal cord compression. Kelly et al [7] reported a case of GPA with the granulomatous compressive thoracic myelopathy as the initial manifestation and illustrated that the underlying pathologic mechanism in GPA was extramedullary compression due to extradural and subdural granulomatous involvement of spinal meninges rather than vasculitic meningeal inflammation or cord infarction. Al-
bayram et al [8] had also reported a report of a 52-year-old man with GPA involving the cervical and thoracic spine. Our case also had extensive spinal involvement with granulation tissue at multiple levels of the dorsal spine causing indentation of the spinal cord.

CYC and high-dose corticosteroids are the agents of choice for induction of remission of GPA with severe pulmonary, renal or neurological involvement [9]. However, not all patients respond to CYC, and more than 50% of responders suffer a relapse within 3 - 5 years [10], as we had in our case who was then managed with B-cell depletion therapy (RTX) to induce remission. RTX has been shown to induce remission rates of approximately 90% in open-label clinical trials and case series [11-13]. However, these studies were neither randomized nor controlled, and criteria for remission were not rigidly applied. Two randomized controlled trials (RAVE and RITUXVAS) have investigated the efficacy and safety of RTX in GPA. The US Food and Drug Administration (FDA) approval of RTX was based on data from the RAVE study [14]. Similarly, our case who failed with initial pulse CYC therapy responded well to RTX and at present, she is in complete clinical remission.

Conflict of Interest

None.

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References