The upper thoracic spinal cord compression as the initial manifestation of Wegener's granulomatosis: a case report

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Abstract There are only a few reported cases about spinal cord involvement with Wegener's granulomatosis (WG) in the literature. In these cases, the spinal cord is usually indented or compressed by dural and meningeal masses which are characterized by necrotizing granuloma formation and vasculitis. And, it usually cannot be correctly diagnosed. A 53-year-old woman suffered from Wegener's granulomatosis, in whom the upper thoracic spinal cord compression is the initial manifestation. The surgical biopsy and thoracic laminectomy were performed and the histologic examination was done. This patient was finally diagnosed as WG when the pathologic examination revealed as Wegener's granulomatosis and the serum antineutrophil cytoplasmic antibodies (ANCA) were reported positive; titers of antimyeloperoxidase (MPO) antibodies were markedly elevated. After treatment with cyclophosphamide and corticosteroids this patient partially recovered from neurological involvement. In a case such as this, careful monitoring of clinical parameters is essential for assessing disease activity with repeated MRI if neurologic status changes. Serial measurement of ANCA titers may also be helpful to

establish the diagnosis. Cyclophosphamide and corticosteroids are the agents of choice for induction of remission of WG.

Keywords Spinal cord · Wegener's granulomatosis · Vasculitis

Introduction

Wegener's granulomatosis (WG) is a multisystem disorder characterized by necrotizing granuloma formation and vasculitis in the upper airways, lungs and kidneys [5, 6]. The clinical manifestations and symptoms are nonspecific and include systemic findings such as fever, malaise, weight loss, arthralgia, and myalgia. Although most patients initially present with upper airway illness, ophthalmic and neurologic involvement occur in 22–54% of patients including mononeuritis multiplex, symmetric distal neuropathy, cranial neuropathies, external ophthalmoplegia, cerebral infarction, or seizures [3, 5, 12]. Spinal cord involvement is rare [10, 13]. Pathologic examination in one patient revealed dural vasculitis [13]. We describe a patient with WG who presented with a gradually progressive spastic paraparesis secondary to upper thoracic spinal cord compression by thickened dura anteriorly.

Case report

A 53-year-old woman presented with low fever, night sweat, malaise, and a sensation of tightness in the midthoracic region. She also complained of weakness, dry cough, nasal stuffiness, and epistaxis sometimes.

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General examination revealed a pale face. Neurologic examination revealed a spastic gait in both lower extremities; the knee and ankle reflex were normal. But the Babinski sign was a little positive. Gadolinium-enhanced thoracic MRI revealed an enhancing soft-tissue mass located anteriorly, extending from C7 to T5, with the thecal sac and cord compression (Fig. 1). Laboratory examination revealed C reactive protein 77.7 mg/l; ESR 48 mm/h.

The surgical biopsy was performed through the thoracic posterolateral approach, which revealed no obvious abnormality in T4 and T5 vertebrae posteriorly. Some tissues obtained from these areas were used to do histologic examination which revealed repairable fibroplasias and inflammatory infiltration. Her clinical condition improved in the postoperative period, ceftazidime (6 g/day) and dexamethasone (5 mg/day) were administrated for 3 days, and the patient was discharged from the hospital 10 days postoperatively.

One month later, her condition deteriorated, she also complained of malaise, tightness in the midthoracic region, the right upper and left lower extremity numbness, gradually progressive gait difficulty, urinary retention and lower extremity paresthesia. Neurologic examination revealed a spastic gait, with weakness [Medical Research Council (MRC) grade 4/5] in both

lower extremities; bilateral lower extremity hypertonia; hyperreflexia and extensor plantar responses; and the sensory level below T2 decreased to pinprick testing. The clonus was present and Babinski sign were positive. The thoracic and cervical MRI revealed extensive dural masses located anteriorly with the spinal cord compression (Fig. 2). The exploratory thoracic laminectomy (T1–T4) was performed, revealing no additional soft-tissue infiltration in the upper thoracic thecal sac anteriorly, but the dura became hard. The infiltrated circumferential dural masses resected for histologic examination revealed extensive granulomatous inflammation, with polyclonal lymphocytes, plasma cells, multiple foci of necrosis, and small blood vessel vasculitis (Fig. 3). Subsequent investigations revealed microscopic hematuria and granular and erythrocyte casts on urinalysis, transient elevation of C reactive protein from 0.9 to 1.4 mg/dl, and elevated erythrocyte sedimentation rate (54 mm in the first hour). On postoperative day 7, serum antineutrophil cytoplasmic antibodies (ANCA) were reported positive, with a perinuclear staining pattern (p-ANCA); titers of anti-myeloperoxidase (MPO) antibodies by ELISA were markedly elevated (153 U; normal < 2.8 U). Indirect immunofluorescence for cytoplasmic ANCA (c-ANCA) was negative, serum angiotensin-converting enzyme

Fig. 1 **a** Sagittal T1-weighted MR images indicate anterior dural thickening with the same signal intensity features to spinal cord at the upper thoracic levels. **b** Sagittal T1-weighted contrast-enhanced images reveal prominent enhancement at the upper thoracic vertebrae posteriorly. **c** Axial T1-weighted contrast-enhanced images reveal enhancement of the upper thoracic dura thickening with spinal cord compression

Fig. 2 **a** Sagittal T1-weighted MR images indicate anterior dural masses with almost the same signal intensity features to spinal cord at the upper thoracic levels. **b** Sagittal T2-weighted image reveal prominently hypointense dural masses anteriorly at the upper thoracic level with the spinal cord compression, the cervical and upper thoracic spinal cord are hyperintense, the C5,6 nucleus pulposus prolapse. **c** Axial T2-weighted image reveal hypointense dural masses anteriorly at the upper thoracic level with spinal cord compression. **d** Sagittal T1-weighted contrast-enhanced images reveal prominent enhancement at the upper thoracic vertebrae posteriorly

Fig. 3 Histologic findings revealed dural masses tissue with signs of a granulomatous inflammatory. The vessels show endothelial necrosis, fibrin deposition with an inflammatory infiltration

(ACE) concentration was normal, and stains and cultures of CSF for mycobacteria were negative. The content of total protein and immunoglobulin (IgG, IgA, IgM) of CSF increased prominently; total protein 1,876 mg/l, IgG 392 mg/l, IgA 18.2 mg/l, IgM 52.8 mg/l.

A diagnosis of WG was made, and treatment with corticosteroids (methylprednisolone 7 mg/kg/day, followed by oral prednisone taper) and oral cyclophosphamide (2 mg/kg/day) was started. On follow-up evaluation 1 year later, there were no symptoms of sphincter disturbance, sensory examination of the lower limbs was normal, lower extremity strength was MRC grade 4/5 on the right and 5/5 on the left, and the patient could walk for several hours daily. Serum MPO titers decreased rapidly after immunosuppressant therapy to a titer of 3.8 U 7 months after initiation of treatment.

Discussion

Neurologic complications due to granulomas at sites remote from the paranasal sinuses occur rarely [3]. The peripheral nervous system was primarily involved in cases of WG, usually in the form of multiple peripheral neuropathies (mononeuritis multiplex) [4, 5, 12]. Central neurologic manifestations of WG include cranial neuropathy, external ophthalmoplegia, hearing loss, headache (common manifestations), cerebrovascular accidents, cerebritis, Horner syndrome, and meningitis (rare manifestations) [5, 12, 13]. Cranial neuropathy is the most common CNS manifestation [4].

Contiguous involvement of cranial nerves at the skull base, and basal meninges from spread of nasal or paranasal granulomas is less common. Both the peripheral and cranial neuropathies are thought to be the result of small vessel vasculitis. Although one early article regarding the neurologic complications of any type in patients with WG reported a prevalence of 50%, subsequent articles have reported rates between 22 and 33% [4, 12].

The pathologic mechanism of cranial neuropathy is not very clear, the cranial meningeal involvement with WG was often reported, and both the dura and leptomeningeal structures can also be affected [7, 14–16, 18].

The spinal cord involvement with WG was much rare. Paraparesis seldom happened as the initial manifestation, not at all occurring in two large case series [3, 5] and in only 3 of 324 patients in another series [12]. Of these three, pathologic data were available in only one patient, identifying dural vasculitis but not granuloma formation, with spinal cord involvement presumably related to either local compression by inflamed tissues or spread of inflammation to adjacent cord and leptomeninges [13]. One other report describes a patient with WG and cauda equina syndrome, with normal CSF and without neuroimaging or pathologic details [10]. Another report describes a patient with a spinal subarachnoid hemorrhage in the context of a preterminal generalized coagulopathy but no pathologic data were available [13]. Kelly et al. [8] reported a case of WG with the granulomatous compressive thoracic myelopathy as the initial manifestation and illustrated that the underlying pathologic mechanism in WG was extramedullary compression due to extradural and subdural granulomatous involvement of spinal meninges rather than vasculitic meningeal inflammation or cord infarction. Albayram et al. [1] reported a report of a 52-year-old man with Wegener granulomatosis involving the cervical and thoracic (C1–C2 and T1–T4, respectively) levels. The dural soft tissue masses caused indentation of the spinal cord without prominent cord compression. These lesions are minimally hyperintense to spinal cord on T1-weighted MR images and prominently hypointense on T2-weighted images. Contrast-enhanced MR images reveal no prominent enhancement in these lesions except minimal peripheral enhancement. Mentzel et al. [11] described the MR imaging findings of WG in the cervical spine and correlate them with the histopathologic features. MR imaging showed epidural liquid masses surrounded by granulomatous masses that compressed the cervical myelin from behind. The case we reported in this paper showed that the upper thoracic spinal cord was involved. MR images showed that anterior dural thickening caused the spinal cord

indentation and slight compression. These lesions are minimally hyperintense to spinal cord on T1-weighted MR images and prominently hypointense on T2-weighted images. High signal intensity was present in the spinal cord on the T2-weighted images at the cervical and upper thoracic levels. Contrast-enhanced MR images revealed prominent enhancement at the level of the lesion. The MR images in our case was similar to the case Mentzel reported, but differed to MR images in the case Albayram described which the contrast-enhanced MR images revealed no prominent enhancement. The different MR images in these cases may be associated with the patients who were in the different pathologic stages. In addition, the lesion in this case was located anteriorly at the upper thoracic level. It is a little difficult to get the pathologic dura tissue anteriorly in the operation.

In this case, we also found that the content of total protein and immunoglobulin (IgG, IgA, IgM) in the cerebrospinal fluid examination increased prominently. This is the first report about abnormality of CSF in cases of WG. Whether the biochemical and immunochemical examination of CSF can be used as the methods of WG diagnosis need further clinical confirmation.

Previously, the diagnosis of WG requires the presence of a histologically proved granulomatous inflammatory process, focal necrosis, and giant cells. The nasal mucosa is an easily accessible biopsy site. But some authors insisted recently that once the clinical manifestation of patient indicating vasculitis in the upper airways, lungs and kidneys combines with elevated c-ANCA titers, the diagnosis of WG can be made. So, the circulating c-ANCA is a diagnostic marker in WG [17]. ANCAs are directed at proteinase three (PR 3), a serine proteinase [9]. In the follow-up of patients in remission, the c-ANCA titer should be determined because an increase in the antibody titer is usually associated with clinical exacerbation [2]. Antiproteinase-3 antibodies more commonly occur in patients who meet the definition of WG, and anti-MPO(p-ANCA) antibodies are more commonly associated with microscopic polyangiitis, Churg–Strauss syndrome and other syndromes.

The patient was finally diagnosed as WG by MR images finding and pathologic examination although the presence of anti-MPO antibodies is somewhat atypical. This is similar to the report of Kelly in which the antiproteinase-3 antibodies were negative and the anti-MPO antibodies were positive. The presence of anti-MPO antibodies in the patient, although somewhat atypical, is not inconsistent with WG [8].

Immunosuppressant therapy likely reduced local residual meningeal inflammation and prevented

systemic progression of disease. Cyclophosphamide and corticosteroids are the agents of choice for induction of remission of WG with severe pulmonary, renal, or neurologic involvement such as the one occurred in this case [5]. After remission, steroids are frequently discontinued after 3–6 months and cyclophosphamide after 6–12 months.

In a case such as this, careful monitoring of clinical parameters is essential for assessing disease activity, with repeat MRI if neurologic status changes. Serial measurement of ANCA titers may also be helpful to establish the diagnosis. In addition, the erythrocyte sedimentation rate and C reactive protein can also be explored as progressive parameters of WG. After treatment with cyclophosphamide and corticosteroids this patient continues to recover lower limb strength and function.

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