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Case report

Acute paraplegia in a patient with eosinophilic granulomatosis and polyangiitis with 20 years of evolution: case report

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Abstract. Eosinophilic granulomatosis with polyangiitis (EGPA) is a necrotizing vasculitis of small and medium vessels with a heterogeneous presentation, multiorgan involvement, characterized by the presence of chronic rhinosinusitis, asthma, and peripheral eosinophilia. Nervous system involvement is frequent, especially in the peripheral nervous system (PNS). We present the case of a patient with EGPA of more than 20 years' duration who developed bilateral paresthesia of the lower limbs and urinary retention, as well as difficult-to-control asthma for the past two years (despite the use of multiple courses of systemic corticosteroid therapy and the recent introduction of mepolizumab). The neurological exam revealed paraplegia with a sensory level in D4; the MRI showed spinal cord compression in the D2-D7 level, and the patient was emergently submitted to surgical decompression. The histopathology of the surgical specimen demonstrated the presence of epidural adipose tissue with multiple vasculitic lesions. The effects of systemic corticosteroid therapy may contribute to abnormal fat deposition in various body segments, including the neuroaxis, leading to the development of spinal lumbar epidural lipomatosis (SEL). The intralesional vasculitic character is a unique and rare manifestation of myelopathy associated with the disease, leading us to have a more aggressive attitude. (www.actabiomedica.it)

Key word: eosinophilic granulomatosis with polyangiitis, churg-strauss vasculitis, spinal epidural lipomatosisremove spinal epidural lipomatosis, myelopathy, systemic glucocorticoids, anti-neutrophil cytoplasmic antibodies, central nervous system

Introduction

Eosinophilic granulomatosis with polyangiitis (EGPA) is a multisystem disease characterized by chronic rhinosinusitis, asthma, and blood eosinophilia. It affects small and medium-sized arteries; the vasculitis stage comes later in the condition. EGPA is a vasculitis that is linked to the anti-neutrophil cytoplasmic antibody (ANCA), only positive in one-third of the cases and shows a perinuclear staining pattern in the immunofluorescence analysis with specificity against myeloperoxidase (MPO) (1–3). The most involved organ is the lung. EGPA can affect any organ, including the cardiovascular, digestive, renal, and central nervous systems (CNS). Vasculitis of extrapulmonary organs is mainly responsible for the morbidity and mortality associated with EGPA (4-5). Although nervous system involvement can occur in EGPA, its clinical manifestations and pathophysiology are poorly understood. Due to its rarity and unique characteristics, such as granulomatous inflammation rich in eosinophils, there are few studies on this subject. It has been proposed that tissue damage may result from necrotizing vasculitis and eosinophil proliferation and activation, leading to organ deposition and the release of granular cytotoxic proteins (6–8).

Lumbar spinal epidural lipomatosis (SEL) is a syndrome characterized by excess epidural fat deposition in the spinal canal. The pathophysiology of SEL is mainly unknown; still, the illness is caused by an abnormal accumulation of adipose tissue in the spinal canal. Risk factors include the use of exogenous steroids (the leading cause), endogenous steroid overproduction (in Cushing syndrome, carcinoid tumour, hypothyroidism, and pituitary prolactinoma have all been linked to SEL), obesity, spine surgery, and idiopathic disorders. Due to receptor overlap, steroids stimulate glucocorticoid receptors in fat tissue. As a result, persistent steroid use causes hypertrophy of spinal adipose tissue, resulting in neural impingement and compressive spinal cord disease (9-11).

Systemic glucocorticoid (GC) therapy is the mainstay of treatment for EGPA. However, for individuals with end-organ damage or life-threatening disease, treatment usually involves immunomodulatory agents such as cyclophosphamide and rituximab to induce remission and its subsequent maintenance (8). But this type of treatment isn't without risks, and epidural lipomatosis (SEL) is a rare problem that can happen when GC is used.

Case description

We present the case of a 60-year-old man who had been diagnosed at 40 years old with EGPA with pulmonary and neurological involvement in the form of severe and refractory asthma, allergic rhinitis, ground-glass pulmonary infiltrates, and a history of VIII nerve mononeuropathy. He took mepolizumab 100 mg monthly and prednisolone 15 mg daily.

The patient went to the emergency department (ED) due to sudden weakness and bilateral paresis of the lower limbs, and acute urinary retention. He also referred to lumbar pain for the last few weeks. He denied any history of falls, trauma, or recent surgical interventions. Six months before coming to the ED, he had multiple episodes of exacerbated asthma requiring short cycles of intravenous GC therapy at a dose higher than usual. His physician had previously attempted to introduce a steroid-sparing agent like methotrexate and azathioprine; however, the patient developed hepatotoxicity.

Neurological examination revealed paraplegia with a sensory level on D4 and bilateral extensor plantar reflexes. The laboratory study identified hypocomplementemia, VS elevation (56 mms), and ANCA-MPO positivity. Multiple ground-glass infiltrates were found bilaterally on a chest X-ray that were absent on earlier scans.

A magnetic resonance imaging (MRI) of the thoracic spine was performed, which revealed the presence of a solid formation extending longitudinally from D3 to D7 with circumferential involvement of the medullary cord with a characteristic signal of fat (hyper signal on T1 and T2, suppressing fatsat sequences on T1 and T2), exercising spinal cord compression (Figures 1 and 2).

The excessive fat deposition was also visible in the suitable paravertebral space at the thoracic and lumbar transition (Figure 3). He also had pachymeningeal enhancement, which could be extramedullary granulomatosis in a clinical setting (Figure 4).

Before this episode, the patient had never undergone an MRI of the spine, so it is impossible to compare the changes identified with previous examinations. His most recent CT of the lumbar spine revealed osteoporosis and depression of the upper bone platform of L1, but no significant misalignment of the vertebral body.

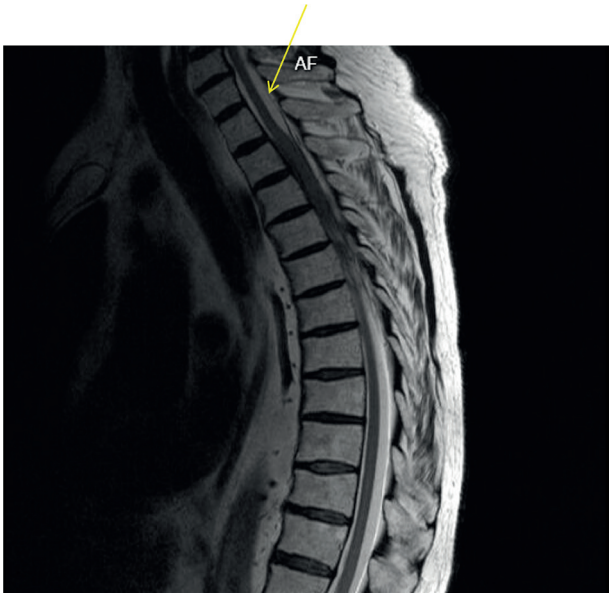

Figure 1. Sagittal T2-weighted MRI scan showing a solid mass (yellow arrow) in the posterior dorsal epidural space extending longitudinally between D2 and D7.

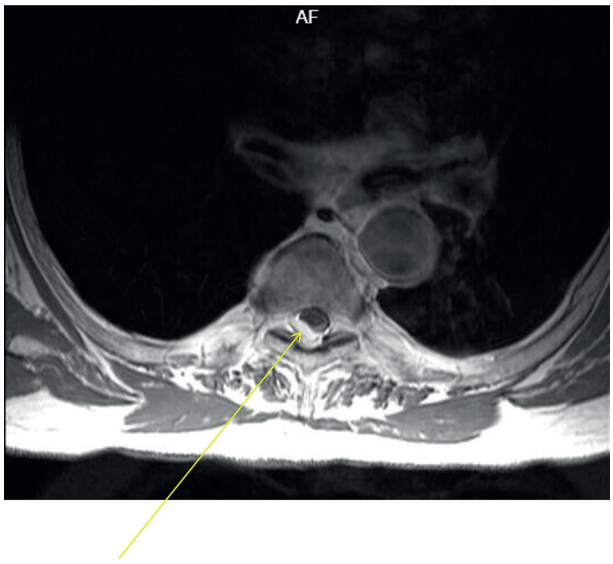

Figure 2. Axial T1-weighted MRI scan showing a solid mass (yellow arrow) within the epidural space compressing the spinal cord.

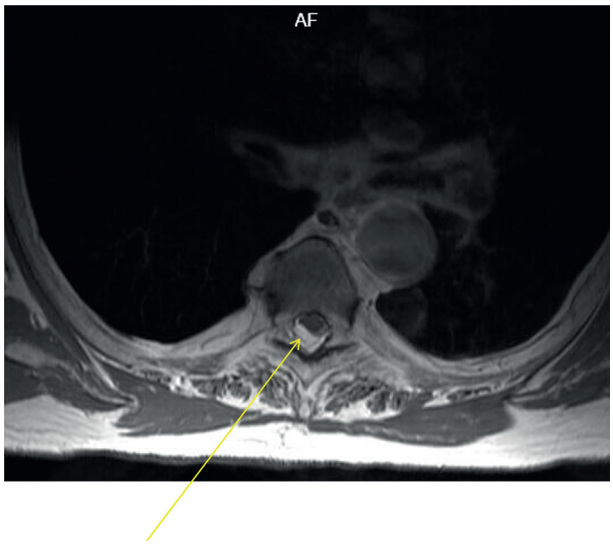

Figure 3. Axial section of gadolinium-weighted T1-weighted MRI showing lesional enhancement (yellow arrow), sign of greater compression on the right.

Considering the imaging characteristics highlighted in the MRI in the context of the underlying disease, the hypothesis of abnormal accumulation of fat in the posterior epidural space of the dorsal column (epidural lipomatosis) with consequent spinal cord compression was considered. The patient underwent emergent surgical decompression and was transferred to the Intensive Care Unit. After reducing the sedation, the patient-maintained paraplegia and sphincter incontinence.

The histopathology of the intraoperative piece showed adipose tissue with fibrovascular septa of variable thickness, an abundant inflammatory infiltrate, some dense transmural and perivascular polymorphic infiltrate, cell debris, and aspects suggestive of endothelial destruction. The inflammatory infiltrates of the lymphoplasmohistiocytic type were abundant in neutrophil nuclear polymorphs with rare eosinophils. No granulomas were identified (Figure 5).

There was no neurological recovery after the intervention. With the positivity for MPO, hypocomplementemia, increased sedimentation velocity, new bilateral pulmonary infiltrates, and the neurologic involvement of the disease, we started rituximab after excluding infections and other contraindications. He also started rehabilitation and was discharged after 58 days of hospitalization with a Modified ranking scale of 4 and a permanent urinary catheter. He completed three cycles of rituximab, which were stopped multiple times due to infections, but despite all the measures taken, the patient died six months after this episode due to pneumonia.

Discussion

EGPA is the least common of the 3 vasculitis linked to neutrophil cytoplasmic antibody (ANCA) (12). Prevalence in Europe ranges from 10.7 to 14 per million (13). Only 40 to 60% of patients have positivity for ANCA-MPO. The exact pathogenesis of EGPA is unknown.

The clinical features typically manifest in several successive phases, though these are rarely easily distinguishable. The prodromal phase is first characterized by atopic disease, allergic rhinitis, and asthma in people in their second and third decades. The patient's condition was initially identified during this phase. The patient quickly advanced to the second phase, the eosinophilic phase, which includes peripheral eosinophilia and eosinophilic infiltration in many organs, particularly the lung and the gastrointestinal tract, despite initial treatment with low-dose corticosteroids (14). Both vascular

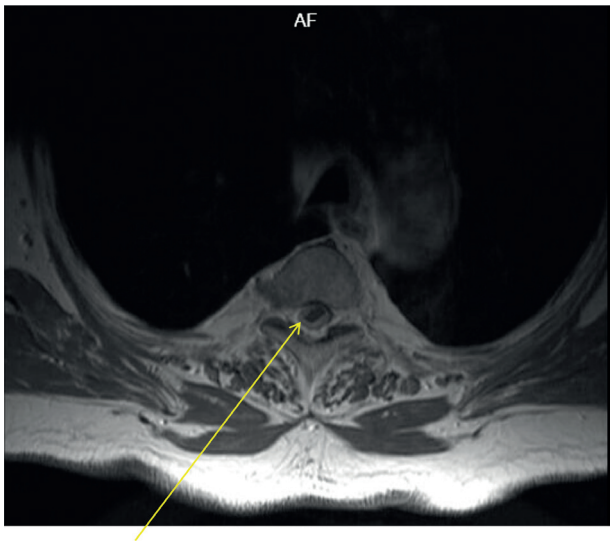

Figure 4. Axial section of gadolinium T1-weighted NMR in which pachymeningeal enhancement is evident (yellow arrow).

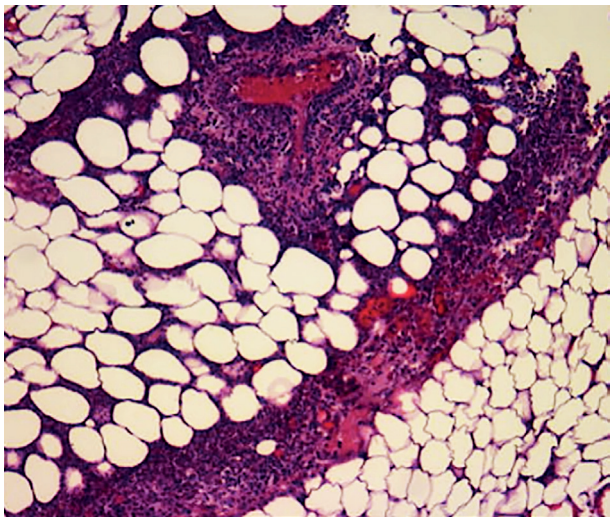

Figure 5. Transmural infiltrate of inflammatory (polymorphonuclear) cells from blood vessels and adipose tissue as seen by hematoxylin and eosin staining at 100 times magnification.

and extravascular granulomatosis frequently accompany the vasculitic stage (15). Systemic vasculitis of the medium and small vessels characterizes this phase.

According to the American College of Rheumatology/Vasculitis Foundation (ACR/VF), cyclophosphamide or rituximab should be used in remission induction rather than GC alone or GC plus mepolizumab for patients with severe EGPA and manifestations of life-threatening or organ disease (8).

Due to the way EGPA was presented, we assumed it was in a vasculitic phase with profound gravity and life-threatening symptoms, so immunosuppressants were the best course of treatment. The choice of rituximab was due to the patient's positive ANCA-MPO.

Nervous system involvement is frequent in EGPA and mainly affects the peripheral nerve. The ACR/VF EGPA classification criteria include polyneuropathy or multiple mononeuropathies. Cerebral infarcts and subarachnoid haemorrhages are the main manifestations of the CNS described in the literature (7). Rarely this vasculitis affects the spinal cord. Most of the time, this happens with granulomatosis with polyangiitis. In general, spinal cord manifestations are related to three possible mechanisms: necrotizing inflammation of the vasculature, compression by inflamed thickened meninges, and granuloma formation (16). Even though there were no granulomas, there was fatty tissue in the pachymeninges due to epidural lipomatosis and inflammatory infiltrates.

SEL is a rare disease defined as the pathological growth of normal epidural fatty tissue. The main risk factors are the chronic and exogenous use of GC, obesity, and Cushing's syndrome (9–11). SEL has been found in conditions often treated with exogenous steroids, such as organ transplantation, Crohn's disease, nephritic syndrome, prostatic neoplasia, pineoblastoma, lichen planus, cerebral lymphoma, multiple sclerosis, chronic obstructive pulmonary disease, and ulcerative colitis (17). This is the first time that this entity has been linked to EGPA.

The pathogenesis of SEL remains unknown, but different hypotheses have been suggested that may point to a metabolic disorder as the underlying cause. The pathogenesis of GC related to SEL potentially involves the adipogenic effect of GC that stimulates the differentiation of mesenchymal stem cells into adipocytes. This contributes to an increased accumulation of fat within the epidural space. Additionally, hormonal imbalances caused by GC can alter the distribution of fatty tissue, potentially favoring fat deposition in the epidural area. Furthermore, corticoids can influence appetite and weight gain and impair lipid metabolism, impacting fat deposition in various tissues, including the epidural space (10).

MRI, computed tomography and myelography can all be used to diagnose. The preferred imaging

technique for determining the degree of lipomatosis is MRI. The thoracic region tends to be more affected, as is evident in the case presented, and the treatment depends on the severity of the neurological signs. The most common treatment involves surgical decompression.

In this case, the patient had respiratory involvement and refractory asthma history. Despite receiving maintenance treatment with GC and mepolizumab, the development of new transient ground-glass pulmonary infiltrates and exacerbated asthma in recent months suggests that the disease may have relapsed. These episodes led to an intensification of GC therapy, making it necessary several times to resort to GC pulses to treat respiratory symptoms. This therapy led to the development of SEL.

During the vasculitic phase of the disease, inflammatory infiltrates formed in the spinal cord, which caused myelopathy.

In conclusion, EGPA rarely affects the CNS. Only a few cases have been written about in the myelopathy literature. Additionally, the metabolism of adipocytes may be affected by systemic corticosteroid therapy, which may result in abnormal fat deposition in a variety of organs.

Affecting the neuraxis by this type of mechanism is also rare. The study of the operative specimen also confirmed that the lesion was vasculitic, which led to a more aggressive approach to treatment. So, the case presented aims to show a unique and rare way of presenting this entity and is the first report in the literature on the development of SEL concerning EGPA.

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Informed consent: Written informed consent was obtained from the patient for the publication of this case report.

Authors Contribution: All authors were responsible for the medical conduct in this patient. MG: corresponding author; responsible for the writing of the manuscript. JC and JF: revising it critically for important intellectual content and the final approval of the version to be published.

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