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Granulomatosis Polyangiitis (Wegener's Granulomatosis) Causing Atlantoaxial Instability: A Case Report

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Abstract

Background Context: No previous cases of atlantoaxial instability due to granulomatosis with polyangiitis have been reported.

Purpose: To report a case of granulomatosis polyangiitis causing atlantoaxial instability.

Study Design: Case report.

Patient Sample: A 45-year-old woman.

Outcome Measures: Resolution of the patient's pain and atlantoaxial instability.

Methods: This is a 45-year-old Caucasian woman with a large ulcerative lesion in her oropharynx. She initially presented with chronic sinusitis, pharyngitis, and severe odynophagia. Years after her original symptoms began, she developed neck pain radiating into her upper trapezial region and shoulders.

Results: Atlantoaxial fusion was performed on the patient, resolving her neck, upper trapezial, and shoulder pain. She was diagnosed with granulomatosis with polyangiitis (formerly Wegener's granulomatosis) and treated with cyclophosphamide.

Conclusions: Granulomatosis with polyangiitis should be part of the working differential diagnosis for non-traumatic cervical spine injury. The atlantoaxial instability can be managed with stabilization, and the disease process itself can be treated with cyclophosphamide.

Introduction

Cervical spine degeneration and instability are a common manifestation in many rheumatological disorders, such as rheumatoid arthritis. In rheumatoid arthritis, the most common pathology involving the cervical spine is C1-C2 instability that

often requires surgical treatment. Patients with rheumatoid arthritis are especially prone to injuries at this level because there is no disc between C1 and C2. [1]

Granulomatosis with polyangiitis (GPA, formerly Wegener's granulomatosis) is a vasculitis that classically presents in the kidneys, upper airway, and lower airway. [2] We report a case of a 45-year-old woman with atlantoaxial instability due to GPA, which required an atlantoaxial fusion. We believe this to be the first reported case of GPA threatening the cervical spine.

Case Presentation

A 45-year-old Caucasian woman with a 2½-year history of chronic sinusitis and pharyngitis presented for severe odynophagia. After several months, she developed headaches, bilateral otalgia, and pain inside her nose. She was initially treated with several rounds of antibiotics for presumed bacterial pharyngitis. At an outside academic medical center, a large ulcerative lesion was discovered in her oropharynx, along with smaller ulcers in her nasopharynx, and a nasal septal perforation. Multiple biopsies demonstrated acute and chronic inflammation, necrosis, and bacterial colonization. There was no clear evidence of lymphoma, epithelial malignancy, vasculitis, or granuloma. Results of C-ANCA and other serologic tests were unremarkable (Table 1). Gastroduodenoscopy and colonoscopy revealed no abnormalities. Wound cultures grew normal oral bacteria, along with candida tropicalis; she was treated with antibiotics and antifungals with no improvement. The working diagnosis at this time was

"multifactorial ulcer." She was treated with methotrexate, prednisone, and azathioprine with some initial improvement, though her symptoms recurred after 5 months.

After failure to improve with the above treatments, the patient was referred to our institution for additional evaluation. At this time, she complained of severe throat pain, sinus congestion, non-productive cough, and right ear pain. Repeat laboratory evaluations were non-diagnostic (Table 1). Re-review of all outside pathology slides was conducted to ensure that there were no findings consistent with nasal-type NK / T-cell lymphoma, or any other type of malignancy.

Around the time of admission, she developed new-onset poorly-localized pain in her neck and face. Cervical spine x-rays showed mild C4-C5 and C5-C6 degenerative disc disease. MRI showed edema within the anterior arch of C1 and the body of C2, atlantoaxial joint enhancement, and ulceration of the posterior pharyngeal wall down to the prevertebral fascia. (Figure 1).

Physical exam on admission showed the patient to be awake, alert, and oriented. She appeared to be in mild distress from her pain. Flexible endoscopy showed necrosis down to the prevertebral fascia in an area of the right nasopharynx. Range of motion and strength at the neck and upper extremity were normal, and neurological exam was non-focal.

At this time, the differential diagnosis included infection, pseudogout, lymphoma, autoimmune, and vasculitis. Bacterial and fungal cultures were negative on multiple occasions, ruling out infection. Pseudogout was unlikely since it would have been seen on imaging. A focused biopsy was performed at our institution. Pathological examination with immunohistochemistry stains ruled out lymphoma. There were no histopathologic findings that allowed for definitive diagnosis. Autoimmune diseases, such as rheumatoid arthritis, were unlikely given the lack of response to rituximab. As other possibilities had been excluded, GPA was suspected since the patient had a destructive pharyngeal lesion in the setting of chronic sinusitis. The patient was treated with intravenous (IV) methylprednisolone and IV cyclophosphamide. Her neck and posterior pharyngeal pain improved after this treatment.

Four weeks later, her neck pain returned, now with radiation into the upper trapezial region and shoulders. There were no symptoms of upper cervical radiculopathy or myelopathy. Repeat MRI showed worsening erosion of the odontoid process and anterior ring of C1, as well as progressing atlantoaxial subluxation. Cervical x-rays showed an increase in the atlantoaxial interval on flexion and extension (Figure 2). Evaluation by spine surgery revealed normal sensation C5-T1 bilaterally with 1+ reflexes in her upper and lower extremities. Five out of 5 strength throughout her upper and lower extremities with no focal deficits. She had a normal nonantalgic gait. Because of atlantoaxial instability, a

posterior C1-C2 instrumented fusion was performed that resulted in resolution of her neck, upper trapezial, and shoulder pain.

Over the subsequent 8 months, her throat pain and odynophagia worsened, so monthly IV cyclophosphamide was resumed. The patient continued IV cyclophosphamide for 1 year and has followed-up for 2 years since starting the cyclophosphamide. Her throat pain has improved dramatically. The patient has resumed oral intake of food and stopped losing weight. The lesion is stable in size on repeat MRI and CT studies and appears consistent with a healed ulceration. Furthermore, since her atlantoaxial fusion, the patient has remained neurologically stable with no recurrences in neck, upper trapezial, or shoulder pain.

Discussion

We report the first case of granulomatosis with polyangiitis presenting with involvement of the cervical spine. The patient's disease first began as a pharyngeal ulcer, causing odynophagia and throat pain. As the disease progressed, the lesion eroded into her cervical spine, causing worsening neck pain, radiation of pain into her upper trapezial region and shoulders, and imaging findings of atlantoaxial subluxation. Her cervical spine was stabilized with atlantoaxial fusion, and the disease process itself was treated with cyclophosphamide.

GPA normally manifests as a triad of upper respiratory tract, lower respiratory tract, and kidney issues. [2] Case reports have documented patients with lumbar and thoracic findings. In a case report of a 40 year old man with GPA presenting with thoracic back pain, CT confirmed a prevertebral soft tissue mass. After treatment with cyclophosphamide and glucocorticoids, the mass resolved as seen on follow-up CT. As a result, it has been theorized that back pain in GPA is caused by granulomatous tissue that invades the dural space. Proper treatment of the disease results in resolution of the granuloma. Cervical spine involvement, however, has never been documented as a manifestation of this disease.

We find it important to report this patient, as GPA should be part of the working differential diagnosis for any patient who presents with non-traumatic cervical spine injury. Features consistent with GPA include pulmonary nodules, deteriorating renal function, chronic sinusitis, and nasopharyngeal ulceration. Diagnosis is typically confirmed with histopathologic examination, as the ulceration should show granulomatous in the wall or perivascular area of an artery. [3] After considering a spinal fusion to stabilize the patient neurologically, an individual with GPA should be followed long-term by a rheumatologist and treated with cyclophosphamide and corticosteroids. In patients with GPA, treatment with glucocorticoids and cyclophosphamide results in significant improvement in 91% of affected patients, complete remission in 75%, and an overall survival rate of 80% over 24 years. [4]

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Figure Captions

Figure 1. MRI of the cervical spine performed around the time of admission. As indicated by the arrow, visible is an irregularity of the mucosa along the posterior pharyngeal wall, extending from the roof of the nasopharynx down to the lower border of the oropharynx, which corresponds to the location of her largest ulceration.

Figure 2. Cervical spine radiographs taken preoperatively during flexion (**a**) and extension (**b**), and 6 months after C1-C2 posterior instrumented spinal fusion (**c**). Preoperatively, the atlantoaxial interval widened on flexion (solid line in (**a**)) and reduced on extension (arrow in (**b**)), and postoperatively, it was normal (arrow in (**c**)).

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Table 1. Laboratory Results

Variable	Admission	1 month post-admission	6 months post-admission	15 months post-admission	Normal value
WBC count, x 10^9/liter	20.5	12.5	--	--	3.5-10.5
Differential cell count, %			--		
Neutrophils	73.7	89.8		59.0	62
Lymphocytes	19.7	6.3		29.3	21
Monocytes	6.2	3.9		9.3	16
Hematocrit, %	36.4	36.9	--	38.5	36-45
Platelets, x 10^9/liter	379	279	--	238	150-450
Creatinine, mg/dl	0.61	0.59	--	0.7	0.4-1.2
ESR, mm/hour	--	35	--	--	0-20
CRP level, mg/dl	--	20.4	--	--	0-1.0
HIV	Negative	--	--	--	Negative
EBV PCR		Negative			
ANA	1:160,	1:160,	--	--	Negative

	nucleolar	nucleolar			
ANCA	Negative	Negative	--	--	Negative
Rheumatoid factor		Negative	--	--	Negative
Urine drug screen for cocaine	--	Negative	--	--	--