Difficulty of diagnosing Granulomatosis with Polyangiitis involving head and neck

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ABSTRACT

Granulomatosis with polyangiitis (GPA) is a rare autoimmune disorder of unknown etiology characterized by necrotizing granulomatous inflammation and vasculitis. Most of the initial symptoms begin in the head and neck region with a wide spectrum of involvement. Diagnosis may be delayed because of the nonspecific symptoms of this rare disease.
We describe a rare case of GPA with confusing initial head and neck manifestations. These manifestations must be recognizes to permit early diagnosis and management of this uncommon condition.
Key words: Granulomatosis with polyangiitis, Wegener's, ENT, Facial palsy, Hearing Loss

INTRODUCTION

Granulomatosis with polyangiitis (Wegener's) (GPA) is a rare autoimmune disorder of unknown etiology that is characterized by granulomatous inflammation and antineutrophil cytoplasmic antibodies (ANCA)-associated small-vessel vasculitis [1].
This primary systemic vasculitis affects the head and neck region in up to 95% of the patients (2). Vasculitis is typically associated with ANCA directed against proteinase 3 [1].
Early recognition of the head and neck manifestations of GPA by first-line physicians is essential to prevent progression and severe complications.
Here, we describe a rare case of GPA associated with confusing initial head and neck manifestations.

CASE REPORT

A 40-year old male, with no particular medical history, who presented a bilateral nasal obstruction associated with a bloody rhinorrhea, a bilateral progressive hearing loss evolving for 4 weeks. His symptoms progressed despite amoxicillinclavulanate treatment with nasal saline irrigations and were associated with a cough and mild dyspnea. Three weeks after the beginning of symptoms, he developed a facial asymmetry and was referred to the Otorhinolaryngology Department.
Physical examination found a left facial nerve palsy categorized as grade III (House-Brackmann) and the otoscopic examination revealed a thickened tympanic membrane. Nasal endoscopy showed a granulomatous mucosa with ulcerated lesions of the nasal septum, the turbinates and nasopharynx (Fig1).

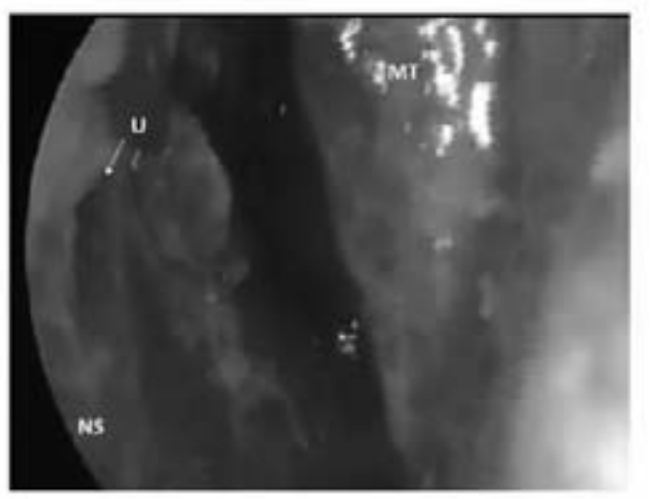

Figure 1 : Endoscopic view of the left nasal cavity showing granulomatous mucosa of the middle turbinate (MT), bloody discharge and an ulcer (u) on the nasal septum (NS)

Lung auscultation revealed bilateral crepitations with rhonchi in all lung fields.
The pure tone audiometry showed a bilateral mixed hearing loss.
Computed tomography (CT) of the sinuses showed a diffuse mucosal thickening, a pansinus disease, a heterogeneous infiltration of the nasopharynx without bone destruction. (Fig2).
CT of the temporal bones showed nonspecific bilateral totally obliterated middle ears including the bony part of the Eustachian tubes (Fig3).

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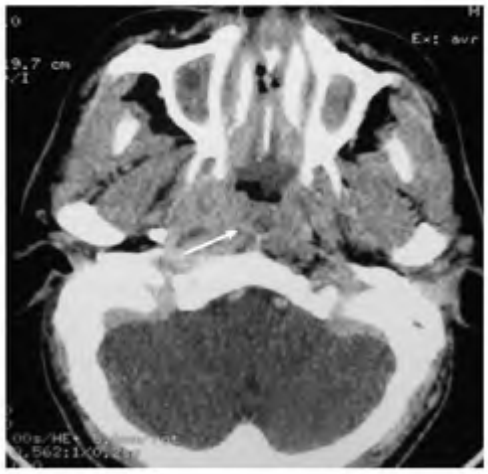

Figure 2 : Computed tomography of the sinuses shows diffuse mucosal thickening with pansinus disease and a heterogeneous infiltration of the nasopharynx (white arrow).

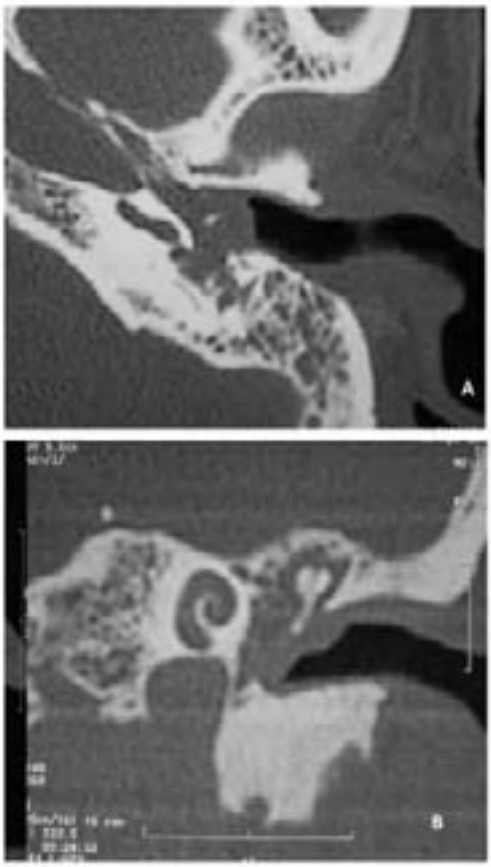

Figure 3 : Axial (A) and coronal (B) CT scan of the left temporal bone showing thickening of the mucosa of the mastoid cavity and middle ear without bone destruction.

The bony canals of the facial nerves were intact throughout its courses, with no associated ossicular or bone destruction. These findings were consistent with acute otomastoiditis. Chest radiography and CT scan revealed not systematized multiple condensations and nodular opacities all over the lung parenchyma (Fig4).

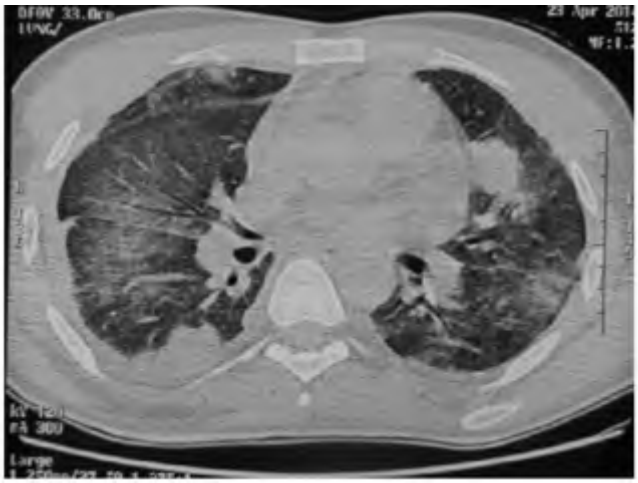

Figure 4 : Axial (A) and coronal (B) CT scan of the left temporal bone showing thickening of the mucosa of the mastoid cavity and middle ear without bone destruction.

The patient was hospitalized and treated with ceftazidime and metronidazole. On admission, investigations revealed microcytic hypochromic anemia with a hemoglobin of 10 g/dL, white blood cell count of 16,500 with neutrophilic leukocytosis and CRP was elevated to 290 mg/L. Viral serology for hepatitis B and C and HIV was negative.
The patient was taken to the operating room for endoscopic nasal evaluation, biopsies and debridement.
Endoscopic nasal examination found diffuse hemorrhage, nasal crusting, friable erythematous mucosa and granulation tissue of the nasal septum, the turbinates and nasopharynx. Biopsy specimens showed a granulomatous inflammation with multinucleated giant cells, small-vessel vasculitis with luminal obliteration (Fig5). Search for alcohol acid resistant bacillus was negative. At this stage, the diagnosis of Wegener's granulomatosis was suspected although immunological analysis were negative.

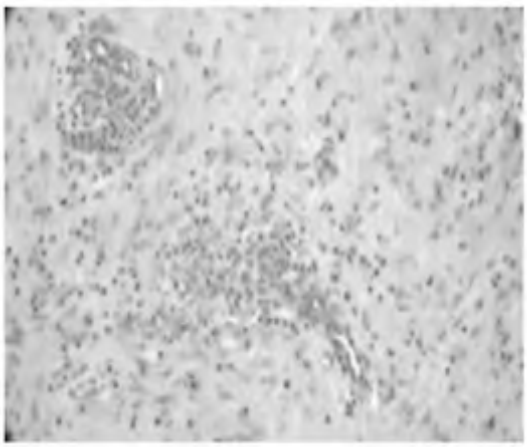

Figure 5 : Histopathology shows granulomatous inflammation with presence of multinucleated giant cells (Hematoxylin and Eosin 200).

The diagnosis of granulomatosis with polyangiitis (Wegners's) was made and the patient was referred to the Department of Internal Medicine where a treatment using a combination of glucocorticoids and cyclophosphamide was initiated. The further immunological analysis confirmed positivity for ANCA with a titer of 1/64.
After treatment, the patient recovered completely from the facial nerve palsy and other lesions. After one-year of follow-up, the patient developed a recurrence of nasal symptoms and was readmitted in the Internal Medicine department.

DISCUSSION

GPA, historically known as Wegener's granulomatosis, is a relatively rare autoimmune disorder of unknown etiology that is characterized by systemic vasculitis that affects small and medium vessels predominately in the kidneys, lungs, and the mucosa of the upper respiratory tract [3]. In up to 95% of the patients initial GPA symptoms are observed in the head and neck region [2].
The case we presented illustrates the florid manifestations of GPA in a patient presenting with ear, nose, and throat (ENT) and lower respiratory tract involvement.
Rhinosinusitis is the typical manifestation of GPA leading to nasal bloody discharge, crusting, and epistaxis [1]. Granulomatous inflammation in the nasal cavity and sinuses may lead to bone erosion and cartilage destruction causing nose deformity [1]. The most common site of active nasal disease is the anterior portion of the nasal septum, where the perforation generally begins and may progress to involve the entire cartilage [4].
Otological involvement (35% of cases) may be in the form of serous otitis media, chronic otitis media, sensorineural hearing loss, vertigo and facial palsy [5, 6]. Serous otitis media is the most common type of otological involvement resulting from granulation tissue in the middle ear cleft or from nasopharyngeal ulceration and obstruction of the Eustachian tube [5].
In the present case, the conductive hearing loss was attributable to a direct involvement of the middle ear mucosa and dysfunction of the Eustachian tube (obliteration of the bony part of the Eustachian tubes and mucosal involvement of the nasopharynx). The etiology of the sensorineural hearing loss is unknown but theories were proposed for this disorder, such as vasculitis of the cochlear vessels, deposition of the immune complex in the cochlea, granulomatous compression of the cochlea or nerve damage from polyneuritis [4, 5]. Facial nerve involvement may occur during the course of the disease, although it is very rare for it to be the presenting feature [6]. Facial nerve palsy, present in 8% to 10% of cases, is secondary to compression of the nerve in the middle ear when it is dehiscent or due to the existence of vasculitis affecting the microcirculation [5].
Once GPA is suspected, antineutrophilic cytoplasmic antibody (ANCA) levels should be done: the c-ANCA (cytoplasmic –ANCA) is highly specific for active GPA and its titer is directly related to the disease activity [2, 5]. Testing for c-ANCA yields a pooled sensitivity of 91% and specificity of 99%. Sensitivity falls significantly (63%) when the disease is in nonacute stages, while the specificity remains high [7]. Thus, the initial immunological analysis were negative in our patient.
Tissue biopsy is important to confirm the diagnosis before treatment showing concomitant vasculitis, necrosis and granulomatous inflammation. Unfortunately, biopsies are inconclusive in over 50% of the times and serial repeat biopsies should be considered [2]. In our case, clinical presentation, the findings of biopsy samples and the further serologic tests led to make the definite diagnosis of GPA.
For nearly four decades, Cyclophosphamide and glucocorticoids have been the standard therapy and transformed the usual treatment outcome of severe GPA [8]. Cyclophosphamide is recommended for induction of remission and glucocorticoid therapy is a mainstay of therapy for remission induction and maintenance [1].
Recently, Stone et al revealed that rituximab was noninferior to cyclophosphamide in inducing remission in patients with GPA, with the primary end point being disease flares [8]. Induction therapy with rituximab allow patients with GPA to taper off glucocorticoids [9].
Surgery is reserved for complications and exceptional cases whose emergency nature do not permit to wait for a response to medical treatment [2]. Long-term remission is achieved in up to 90% of the cases, especially in the absence of kidney injury [5].
We present a patient showing florid otorhinolaryngological manifestations of GPA. Knowing the atypical presentations of this rare disease is important to avoid delay in diagnosis and treatment to prevent the generalized progression and irreversible complications.

Conflicts of interest: Authors have declared that no competing interests exist.

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