Wegener's Granulomatosis: Case Report

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Citation

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Abstract

Wegener's granulomatosis is an inflammatory disease with multi-system involvement that manifests as vasculitis, granulomatosis and necrosis. While its standard form involves the upper and lower respiratory tracts and kidneys, it may essentially involve any organ. In approximately 80-90% of the patients, the nose and the paranasal sinuses are involved. Neurological complications may accompany the disease in 50% of the cases.
Our 65 year-old male patient was investigated at the clinic due to the occurrence of neurological symptoms while he was on treatment for upper respiratory tract and lung lesion. In this report, we wanted to emphasize that Wegener's granulomatosis, although rare, should be considered even if the ANCA values were negative and that treatment should be initiated as soon as possible.

INTRODUCTION

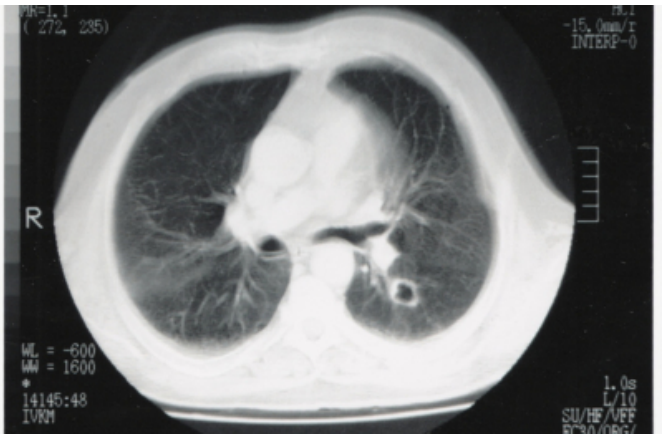
Wegener's Granulomatosis (WG) is a disease of unknown etiology, which has been described for the first time by Wegener in 1936 ([1]). The prevalence of this rare disease is estimated to be 3/100000 in the United States ([2]). WG is characterized by a triad of granulomatous lesions of the upper and lower respiratory tract, focal segmental glomerulonephritis and disseminated necrotizing vasculitis. While involvement of the upper respiratory tract and the lungs is observed in its limited form frequently seen in women, the kidneys are also involved in the common form frequently seen in men ([3]). Direct invasion of the paranasal and paraaural tissues by the granulomatous process, metastasis of the granulomatous process and necrotizing vasculitis cause neurological symptoms. Neurological involvement occurs in one third of the patients. It commonly manifests as peripheral neuropathy or cranial neuropathy (particularly 2,6,7). ANCA is considered to be responsible for the pathogenesis together with the intervening infections. The mortality rate is high among untreated WG cases.

CASE REPORT

A 65 year-old male patient presented with the complaints of pain in the left eye, hyperemia in the conjunctiva, nasal lesion and diplopia on left gaze. His medical history included the complaints of sweating, lack of appetite and debility with an onset in August 2004. Thoracic computed tomography (CT) revealed a cavitary lesion of 1.5 x 2 cm size at the left lung lower lobe superior segment (Figure 1).

Figure 1

Figure 1: A cavitary lesion at the left lung

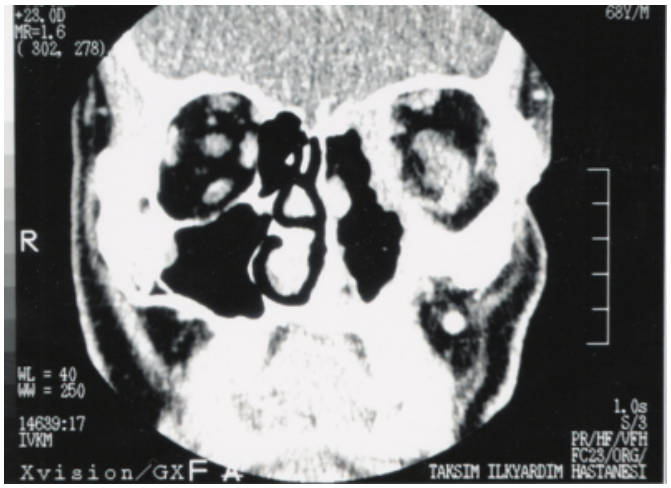


Cytopathological examination by fiberoptic bronchoscopy revealed inflammatory cells; no atypical cells were detected. According to the sputum and culture findings, he was acid-resistant basil- (ARB) and fungus-negative. The other findings were as follows: PPD: 10 mm; CRP (++): positive; sedimentation rate: high (100 mm/h); RF, ANA, c-ANCA, p-ANCA were negative. Treatment with a broad-spectrum antibiotic was initiated in the patient who exhibited normal findings at complete urinalysis. By the CT of the paranasal sinus performed 6 months later due to the emergent complaints of intra-nasal pain and crusting, pain and hyperemia in the left eye, a soft tissue lesion destructing the anterior of the left eyelid, obliterating the borders of the medial and inferior rectus muscles and infiltrating the

ethmoid, sphenoid and maxillary sinus was detected (Figure II).

Figure 2

Figure 2: CT of the paranasal sinuses



The mass extending from the left nasal cavity to the fundus that caused pain in the left eye and the nose was operated. Based on the histopathology results, it was observed to be an abscessing, partially granulomatous inflammation. Treatment with various broad-spectrum antibiotics was continued. 6 months later, he was admitted to our clinic due to the continuity and exacerbation of the pain in the left eye and the emergent complaint of diplopia on left gaze.

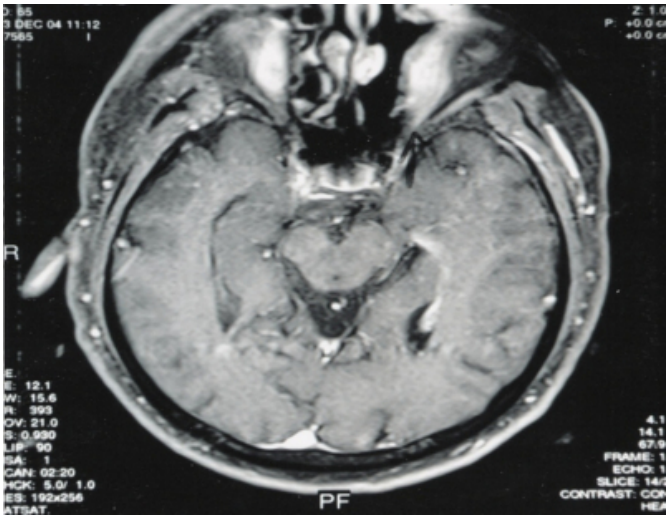
His medical history included HT, DM and Prostate ca operation; there was no particularity in his family history. His conscious was clear and cooperated; TA was measured as 130/90 mmHg and the pulse as 68/minutes. He had pain, episcleritis and proptosis in the left eye. Pupillae were isochoric and light reflex could be elicited bilaterally and the examination of the fundus revealed normal findings. He had diplopia on left and upward gaze due to the limitation in the motion of the left eyeball towards left and upward. The intraocular pressure was normal.

The findings of the biochemical investigations were normal except the high sedimentation rate (140 mm/h) and the positiveness of CRP (++). RF, LE cells, anti-HCV, anti-HBS, anti-HIV, HbsAg, c-ANCA, p-ANCA, MPO-ANCA, PR3-ANCA and ANA were negative. C3 and C4 values were normal. Cryoglobulin was measured as 0.01 mg/dL; VDRL, TPHA and ACE were negative. The value for 24-hour complete urinalysis was normal.

At the contrast cranial MRI, the left conchae and maxillary sinus medial wall had a resected appearance secondary to operation. The left orbital-medial wall didn't reveal integrity. An appearance of postoperative fibrotic tissue was present. There were changes in density showing hypointense, diffused contrast enhancement on T1- and T2-weighted images, which partially surrounded orbital medial rectus, inferior rectus and superior oblique muscles (Figure III). CSF values were normal and no atypical cells were detected. EMG revealed moderate sensorimotor polyneuropathy at the upper and lower extremities. According to the USG of the abdomen, both kidneys were normal except the focal minimal areas of celiectasia. Sarcoidosis, eosinophilic pneumonia, tuberculosis, fungal diseases and syphilis were ruled out at the differential diagnosis.

Figure 3

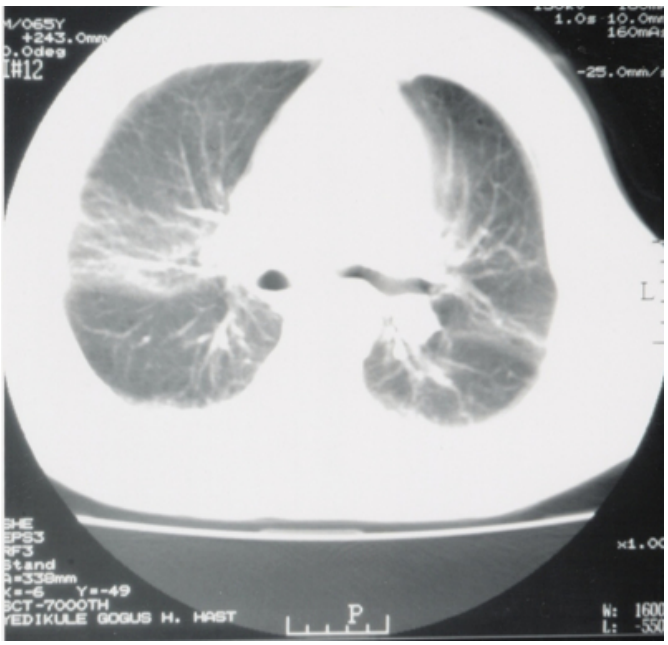
Figure 3: Cranial MRI with contrast



He was diagnosed with WG and steroid treatment was initiated. After a month of treatment, the pain and episcleritis in the left eye were improved. The cavity observed in the left lung lower lobe superior segment at the thoracic CT disappeared (Figure IV). Due to the occurrence of limitation in the downward gaze and microscopic hematuria in addition to the limitation in left and upward gaze of the left eyeball, he was put under follow-up at the rheumatology clinic, administering standard treatment with steroid-cyclophosphamide combination.

Figure 4

Figure 4: The cavitiy observed in the left lung lower lobe superior segment at the thoracic CT disappeared



DISCUSSION

Although WG may occur at any age, the mean age of occurrence is 40 to 55 years old. The M/F ratio is 1/1. The four criteria of diagnosis defined by the American College of Rheumatology (ACR) for WG are as follows: 1) Oral or nasal ulcers, or purulent bloody flux 2) An abnormal lung graphy revealing nodules and cavities 3) An abnormal urinary sediment 4) Granulomatous inflammation in the extravascular region at biopsy. The presence of 2 or more of these criteria has a sensitivity of 88% and a specificity of 99% ([4,5]).

As for the limited WG, the typical pathology is observed but the lungs and the kidneys are not involved. Our patient was diagnosed with WG since he had all the criteria except the kidney involvement when admitted to our clinic. The presence of nasal ulcers, the detection of a result of granulomatous inflammation at the biopsy of the soft tissue infiltrating the mucosa at that region, the lung cavernoma detected at the thoracic CT and the findings of bronchoscopy were consistent with WG. The c-ANCA assay is being used for the diagnosis of the disease and the evaluation of the activity lately. This test with a sensitivity of 99% is 80-90% positive for the standard WG and 55-66% positive for the limited WG ([6]). The measurement of ANCA values repeated two times in our patient revealed negative findings. The presence of normal p-ANCA and c-ANCA values, which are immunological markers doesn't rule out the diagnosis of WG. In addition, they are not included in the criteria of diagnosis. However, a negative ANCA finding may help in ruling out the potential diseases associated with ANCA in cases with a low clinical suspicion ([6]). Although typical clinical findings and a positive c-ANCA result are adequate to suggest the presence of WG, biopsy is required to make a decisive diagnosis. Renal involvement is observed in 20% of the cases as the initial finding ([7]), and identified by focal segmental glomerulonephritis. In our patient, renal USG revealed normal findings except microhematuria detected in repeated complete urinalyses.

The incidence of neurological involvement in WG is 50%. This includes the peripheral neuropathies in the form of polyneuropathy and mononeuropathy multiplex, and multiple cranial neural involvement developing with the nasal and sinus granulomas pervading the upper cranial nerves and the pharyngeal lesions pervading the lower cranial nerves. Narrowing of the carotid siphon due to cerebral arterial involvement, cases of aneurism secondary to this and lateral sinus obstruction due to mastoiditis have been reported ([7]). In untreated patients, seizures, stroke and encephalopathy may develop as the late complications ([8]).

Our patient clinically meets the criteria of diagnosis (ACR) based on the radiology and biopsy findings. The facilitative role of positive ANCA findings in the diagnosis of WG can not be denied ([9]). Peripheral neuropathy, a neurological complication was detected in our patient via EMG diagnostic method. Diplopia due to episcleritis and limitation of ocular motion is another neurological complication. When all these findings were evaluated together, there was no suspicion about our diagnosis of WG. However, we believe that the repeated negative results for the immunological markers (ANCA) render our case rather interesting.

Steroids are recommended for treatment. The monitoring of sedimentation may determine the efficacy of the treatment. While the mean rate of survival was 5 months in the 1960s, now this rate has increased up to 5 years in 75% of the cases with a combination of cyclophosphamide and prednisolon administered at high doses ([10]). In our patient, treatment was initiated with steroid at a dose of 100 mg/day. Response to treatment was achieved in the short-term with respect to pain and episcleritis in the left eye and lung findings. Due to the progression of diplopia and the occurrence of hematuria as another finding, he was put under follow-up at the rheumatology clinic with the addition of cyclophosphamide to steroid treatment.

As a conclusion, WG should be considered in cases with cranial and peripheral neural involvement, and early diagnosis and treatment should be performed. If left untreated, WG is fatal, and the mean survival is 5 months in untreated patients.

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