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Case Report / Olgu Sunumu

Wegener granulomatosis presenting as refractory otitis media: A case report

Tedaviye dirençli otitis media ile seyreden Wegener granülomatozu: Olgu sunumu

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Wegener's granulomatosis (WG) is a granulomatous widespread necrotizing vasculitis, sometimes progressing rapidly, characterized by a tendency to involve the upper and lower respiratory tracts, and in most cases, the kidneys. Otologic manifestations may be seen during the course of the disease, however, they are not frequently seen as the first and only presenting feature. The presence of anticytoplasmic antibodies versus neutrophil polymorphonucleate granules (c-ANCA) is highly specific for the diagnosis of WG, being positive in 97% of the cases. The early diagnosis and the timely medical treatment result in high rates of remission of this potentially lethal disease. In this article, we report a case of WG presenting with acute serous otitis media, progressing to suppurative otitis media and granulomas as the first and only symptom, which was refractory to medical therapy during follow-up and which was diagnosed with further examination.

Key Words: c-ANCA; serous otitis media; Wegener's granulomatosis.

Wegener granülomatozu (WG) kimi zaman hızlı ilerleyebilen, üst ve alt solunum yollarını ve çoğu olguda böbrekleri de tutma eğilimi ile karakterize yaygın bir nekrotizan vaskülittir. Hastalığın seyri sırasında otolojik bulgular da görülebilmektedir; ancak ilk ve tek bulgu olarak görülmesi sık değildir. Nötrofil polimorfonükleat granüllerine karşı sitoplazmik antikorların (c-ANCA) bulunması, WG tanısı için yüksek oranda spesifiktir ve hastaların %97'sinde pozitiftir. Erken tanı ve zamanında uygulanan medikal tedavi potansiyel olarak ölümcül olan bu hastalıkta yüksek remisyon oranları sağlamaktadır. Bu yazıda, ilk ve tek bulgu olarak akut seröz otitis media ile seyreden, takip sırasında medikal tedaviye yanıtsız süpüratif otitis media ve granülasyon dokusu gelişen ve ileri incelemelerinde WG saptanan bir olgu sunuldu.

Anahtar Sözcükler: c-ANCA; seröz otitis media; Wegener granülomatozu.

Wegener granulomatosis (WG) is a granulomatous necrotizing vasculitis characterized by a predilection to affect the upper and lower respiratory tracts and, in most cases, the kidneys. The course of illness may be slowly or rapidly progressive. Mild and non-specific symptoms may go unrecognized for months to years, leading to delays in diagnosis and institution of appropriate therapy.[1] Otologic manifestations may be part of the initial presentation in about

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25% of patients with WG and may occur in up to 60% during the course of disease. The most commonly encountered otologic problem is serous otitis media (25% to 44%). It may be complicated by the presence of a suppurative infection in up to 25% of cases.[2] Occasionally otologic signs may be the first symptom of the disease.[3,4]

Cytoplasmic pattern antineutrophil cytoplasmic antibodies (c-ANCA), first reported in 1985 by van der Woude et al.[5] are highly specific for WG in the active phase. Histological examination of biopsy specimens is often not specific in the head and neck region and it is difficult to make a definite histologic diagnosis based on this alone.[6] Biopsy of laryngeal, oral cavity, external ear, and middle ear lesions are infrequently positive. The difficulty of diagnosis in early stages often delays the start of treatment.

A case of WG presenting with acute serous otitis media progressing to suppurative otitis media with perforation and granulation tissue formation is reported to emphasize that an otologic symptom or finding may be the first and only symptom at the initial stage of WG. Testing for centrally accentuated antineutrophil cytoplasmic antibody (c-ANCA) in the differential diagnosis of WG is crucial to aid in good prognosis related to a timely drug therapy.

CASE REPORT

A 50-year-old female presented with a two-week history of fullness and tinnitus in her right ear. Physical examination revealed serous otitis media on the right. Fiberoptic nasopharyngoscopy and rhinoscopy showed no abnormalities, neither did fiberoptic laryngoscopy. A pure-tone audiogram revealed mixed bilateral hearing loss: a conductive loss in middle and low frequencies with an air-bone gap of 35 dB on the right and 25 dB on the left, and a neurosensorial loss up to 90 dB on high tones on the right and 45 dB on the left. Tympanometry was type B on the right and type C on the left. She failed to respond to medical treatment modalities (Figure 1). After six weeks, a right tympanotomy with a Shepard Grommmet tube (Summit Medical, Inc. St.Paul, MN, USA) insertion was performed, providing minor relief for the patient. On the next visit, it was observed that the ventilation tube had been extruded to the ear canal and there was dense granulation tissue on the tympanic membrane. In addition, otorrhea and two new small perforations were observed in her left ear which was normal on otoscopy at the initial examination. A computed tomography (CT) scan of the temporal bone showed a thickening of mucosa in the mastoid cavities, without bone erosion (Figure 2). In the meantime, patient reported an onset of slight cough.

Based on presence of granulomatous lesions on the tympanic membrane refractory to medical treatment, a specific infection like tuberculosis or some form of granulomatous disease was suspected. A detailed investigation with laboratory tests and chest examination was conducted. Serology using enzyme-linked immunosorbent assay (ELISA) for c-ANCA tested 1/80 positive, perinuclear (p)-ANCA was negative, but PR3 was strongly positive. Rheumatoid factor (RF) was slightly positive. Blood creatinine was 217 mg/dl and urine protein was 43.5 mg/dl on spot urine specimen and 200 mg on 24-hour urine collection. All other diagnostic tests for differential diagnosis were negative or nonspecific. Chest X-ray showed diffuse accentuation of parenchymatous structures and fibrotic sequelae on basal segments. The patient's revised history still revealed no cough or other pulmonary symptoms before her presentation to otolaryngologist. Thoracic CT revealed adenopathy in the left hilus and multiple nodules of 1 cm

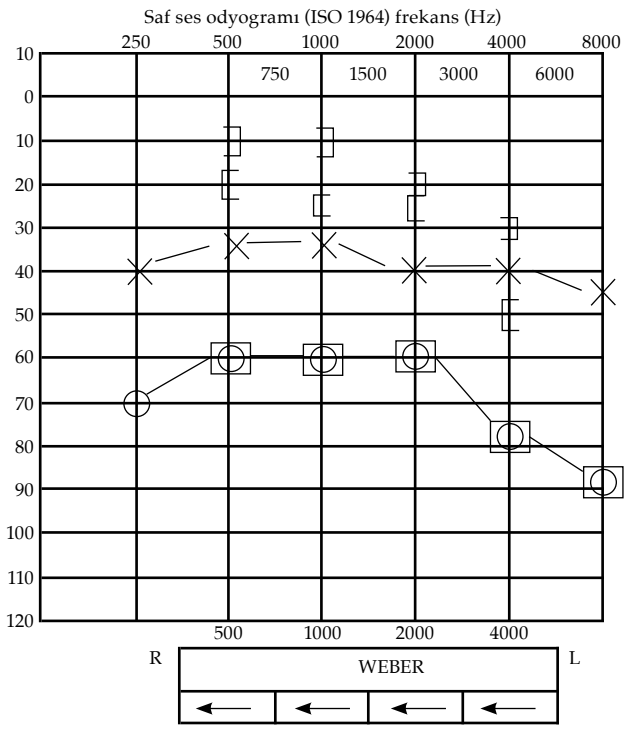

Figure 1. *Bilateral mixed hearing loss in pre-treatment audiogram.*

with central necrosis in the left fourth and tenth segments (Figure 3). The patient was referred to pulmonologist and a biopsy was taken from granulomatous lesions observed by bronchoscopic intervention. Histopathological examination revealed fibrinoid necrosis in vessel walls of submucosal area, granulomatous inflammation with giant cells and eosinophils suggesting WG but recommending serologic tests for differential diagnosis. Periodic acid schiff (PAS) and digested (d)-PAS stains were negative as well as basil stains. Acid-resistant basil (ARB) was absent in swabs taken during bronchoscopy excluding tuberculosis. On rheumatology consultation, a diagnosis of WG was established based on these findings. The rheumatologist initiated treatment with oral prednisolone and intravenous cyclophosphamide infusion once a month. One month later, bilateral otoscopy was normal and there was no air-bone gap. Bone conduction thresholds remained as before. There were no significant adverse effects caused by either prednisolone or cyclophosphamide. One year after the start of therapy, the patient is alive and doing well.

DISCUSSION

Patients with WG may remain undiagnosed for months to years, while mild and non-specific symptoms remain unrecognized, leading to delays in diagnosis. The sensitivity of ANCA test varies in relation to disease activity; sensitivities of c-ANCA testing for overall Wegener granulomatosis range from 34% to 92%, and specificities range from 88% to 100%. Results must be viewed in the context of the patient's clinical picture and disease activity.[7]

In a series of 22 patients with Wegener's granulomatosis, systemic and head/neck complaints occurred in 100% of patients studied.[8] Because of these frequent head-neck manifestations in limited forms of Wegener's granulomatosis, it must be kept in mind that a granulomatous lesion or infection not responding to treatment may be a sign of Wegener's granulomatosis even in patients lacking multiple organ system findings.[9] Similar to this patient who reported a cough only two months after her initial presentation with aural fullness, the diagnosis is less evident in patients with symptoms limited to the ear. The most common otologic involvement in WG is serous otitis media, resulting from eustachian tube obstruction and nasopharyngeal involvement;[10] followed by neurosensorial hearing loss due to a likely vasculitis of the cochlear vessels and deposition of the immune complex in the cochlea. In another study, Takagi reported chronic otitis media as the most common head and neck finding in WG.[2] The conductive hearing loss often persists because of a thickened and often perforated tympanic membrane and because of middle ear adhesions following healing of granulation tissue. Wegener granulomatosis presenting with chronic otitis media and facial palsy was even reported to follow a fatal course.[11,12] In our patient, the history, initial otoscopy and audiological findings suggested acute serous otitis media with no specific extraordinary signs or symptoms.

Overall survival rates of WG have improved over the last decades since the widespread

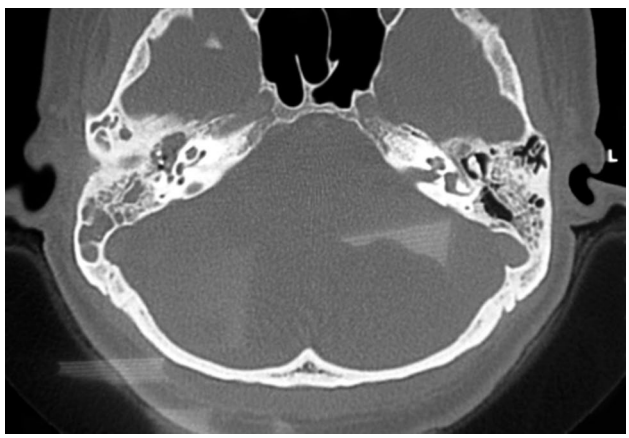

Figure 2. *Axial computed tomography scan showing mucosal thickening and loss of aeration, without bone erosion*

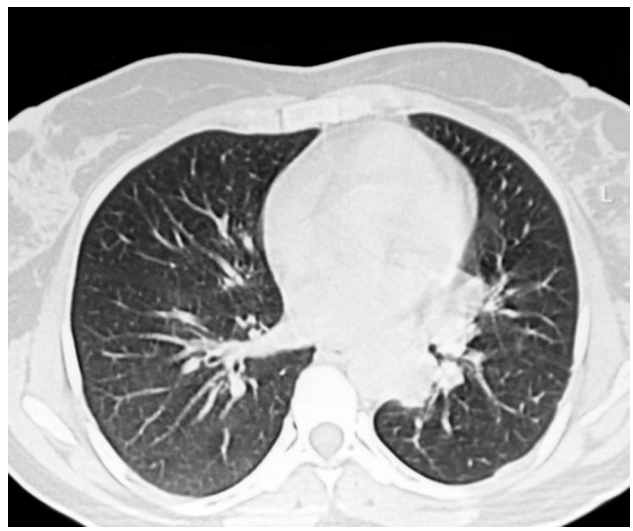

Figure 3. *Adenopathy on left hilus and multiple nodules of with central necrosis in thorax computed tomography.*

institution of early therapy with corticosteroids and cyclophosphamide, improving the success rates of treatment. Remission rates of 70-85% have been achieved, depending on the extension of disease, particularly if major renal involvement develops. In the presented case, it was observed that otologic symptoms and conductive hearing loss which were unresponsive to medical and surgical treatment, improved significantly after therapy with corticosteroids and cyclophosphamide.

In conclusion, the early diagnosis of WG is very important for starting timely appropriate treatment in order to prevent progression of this disease. We reported a case of acute otitis media with effusion progressing to suppurative otitis media and multiple perforations despite medical treatment and ventilation tube insertion, as a presenting first sign of WG. Because of high involvement in the head and neck region, we emphasize that a specific disease like WG should be kept in mind, if prolonged classic therapy for otitis media is ineffective and when otoscopic findings persist especially with granulation tissue formation.

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