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CASE REPORT

Otorhinolaryngologic Manifestations of Wegener's Granulomatosis

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Wegener's granulomatosis is a clinical form from the group of systemic vasculitis and glomerulonephritis ANCA. This disease of unknown etiology is characterized by necrotizing granulomatosis angiitis. Otorhinolaryngologic symptoms are the first symptoms of Wegener's granulomatosis in 80 to 95% of cases. Early diagnosis is very important as it enables early intensive immunosuppressive therapy, which can lead to permanent remission. Discovery of c-ANCA enables quick noninvasive serological diagnosis. The case described is a female patient suffering from Wegener's granulomatosis, aged 48, from the occurrence of the first symptoms, through diagnostic and therapy procedures until the final diagnosis was made.

Keywords: otorhinolaryngologic symptoms, Wegener's granulomatosis, c-ANCA

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Competing interests
The authors declare no competing interests.

INTRODUCTION

In 1931, Klinger published a case study involving a patient who was suffering from nasal destruction and renal failure. Autopsy showed diffuse granulomatous inflammation, glomerular lesion and arthritis. In 1939, Friedrich Wegener published a clinical histopatological description of the syndrome as a separate entity [1].

Wegener's granulomatosis (WG) is an idiopathic systemic disease characterized by necrotizing granulomatous vasculitis of upper and/or lower airways, glomerulonephritis and vasculitis of small blood vessels of different spread and degree [1-3]. As in other autoimmunity diseases, numerous factors have different roles in the occurrence of this form of vasculitis.

The prevalence of WG is up to 50 per one million of inhabitants in Europe. The disease can occur at any age, but it is most frequent in adults after the age of 40 [1].

WG is a form of systemic vasculitis, characterized by the presence of anti-neutrophil cytoplasmic antybodies with a cytoplasmic distribution (c-ANCA), detected by indirect immunofluorescence or enzyme immunoassay [4]. These antibodies are specific for neutrophil proteinase 3, a component of cytoplasmic netrophil azurophil granule [5]. Presence of c-ANCA in circulation is strongly associated with WG. Specific presence of c-ANCA in proving WG is up to 96%, and sensitivity depends on the spread and activity of the disease and is 50% in patients with the initial phase and up to 100% in patients with the active generalized form of the disease [1-3,6]. Discovery of c-ANCA (van der Woude 1985.), offers a new approach in examining the pathogenesis of necrotizing vasculitis, enables a quick noninvasive serological diagnosis and plays a role in the differential diagnosis of systemic vasculitis and glomerulonefritis [1-6]. A growing antibody titer can be the predictor of a relapse of the disease and can help differentiate a relapse from opportunistic infections [6]. WG belongs to the group of the severest forms of necrotizing primary systemic vasculitis and unless treated it leads to a lethal outcome. Early diagnosis is very important as it enables early intensive immunosuppressive therapy, which can lead the disease into the state of permanent remission. Clinical manifestations of the disease are shown in Table 1.

Otorhinolaryngologic symptoms are often the first symptoms of WG and can be the only sign of the disease in case of a localized form of WG or be part of a wide spectrum of symptoms in a generalized form [1]. Otorhinolaryngologic manifestations of WG are shown in Table 2.

CASE STUDY

A patient, aged 48, was admitted to the Department of Maxillofacial Surgery at the Clinical Centre in Banja Luka in July 2006, due to nasal blockage, nasal purulent discharge and facial pain. Upon admission, a sinus x-ray showed homogenous shadowing of the right maxillary sinus, while computerized tomography of sinuses showed expansive proliferative change in the form of a soft tissue mass that destroyed the medial wall of the right maxillary sinus, which expanded into the right nasal cavity

Table 1. Clinical manifestations of Wegener's granulomatosis [7]

Organ affected	Main symptoms	Incidence
Glomerulonefritis	microhematuria	80%
Lungs	dyspnea, hemoptysia	85%
Head and neck (rhinitis, sinusitis)	secretion from the nose, epistaxis, crusts, hearing loss, subglottic stenosis	95%
Joints	arthralgia, myalgia, arthritis	70%
Eye	conjunctivitis, episcleritis,	>50%
General symptoms	weight loss, fever night sweats	60%
Skin	purpura, necrosis, nodules	50%
Peripheral nervous system	Paraestesia	20%
Central nervous system	epilepsy, psychosis	<10%
Gastrointestinal tract	bloody diarrhea, tenesmi	<10%

and the ethmoid sinus. A chest x-ray was negative. After clinical and radiographic examinations the patient underwent surgical treatment (Caldwell-Luc radical antrostomy of right maxillary sinus). Pathohistological findings showed chronic granulomatous inflammation, with the note that the inflammation infiltrate contained scattered granulomas built from epithelioid cells. One month after the surgical treatment the patient was again admitted to the same department due to nasal purulent discharge and facial pain. CT of the sinuses was performed, showing visible destruction of the medial wall of the right maxillary sinus and ethmoid sinus (figure 1).

The patient underwent antibiotics and decongestive therapy and was released with satisfactory general condition. After a certain period due to shortness of breath and prolonged coughing new diagnostic procedures were performed. Bronchoscopic findings done in May 2007 showed a white fatty plaque on the mucosa of the right main bronchus, and the cytological findings described respiratory cells as partly damaged with metaplastic changes. The patient was released from the Clinic for Respiratory Diseases with the diagnosis of Infiltratio pulmonum. In May 2007 the patient was admitted to the Clinic for Internal Diseases at the Clinical Centre Banja Luka, the Department of Nephrology with the symptoms and signs of renal failure and also with-dry irritated cough and haemoptysis. Laboratory hematological and biochemical blood analysis and urine analysis were done, and based on nephrological parameters chemodialysis was performed. A chest x-ray was done showing both-sided pulmonary nonhomogenous, smeary, stripy shadowing of lung fields indicating interstitial infiltrative substrate. A renal biopsy was performed and it showed granulomatous inflammation. Immunology analysis confirmed higher value of c-ANCA (>100 U/mL), ANA (34 IU/mL) was negative, which confirmed diagnosis of Wegener's granulomatosis. She was started on treatment cyclosphosphamide 250 mg and methylprednisolone 500 mg intravenously as a bolus dose, followed by oral cyclosphosphamide 150 mg and prednisolone 20 mg per day. For the first time the patient was examined by an otorhinolaryngologist, who established the saddle-nose deformity (figure 2).

Nasoscopy showed a perforation of the nasal septum, a defect of the lateral wall of the nasal cavity on the right side with the absence of the inferiorturbinate, and large part of the middle turbinate. Examination showed red, thick mucosa, with eroded surfaces, covered with crusts and purulent discharge (figure 3). Antibiotics were given, dictated by culture and sensitivity tests. Recommended was nose cleaning by douching several times a day with dilute salt water.

A nephrologist released the patient with satisfactory general condition with the recommendations about the

Table 2. Otorhinolaryngologic manifestations of Wegener's granulomatosis (disease picture, symptoms and clinical findings) [1]

Salivary Glands	Ear	Pharynx, oral cavity	Nose, PNS	Larynx
sialadenitis	SNHL chronic otitis glue ear	gingivitis	rhinitis, sinusitis chronic, meningitis	subglottic stenosis
swelling pain	tinnitus, conductive hearing loss, vertigo otorrhea	hypertrophic gingival ulcerations	nasal obstruction, crusts, epistaxis, granulomatous-inflammation septal perforation, saddle-nose, hyposmia, anosmia,	stridor, dysphonia, dyspnoea

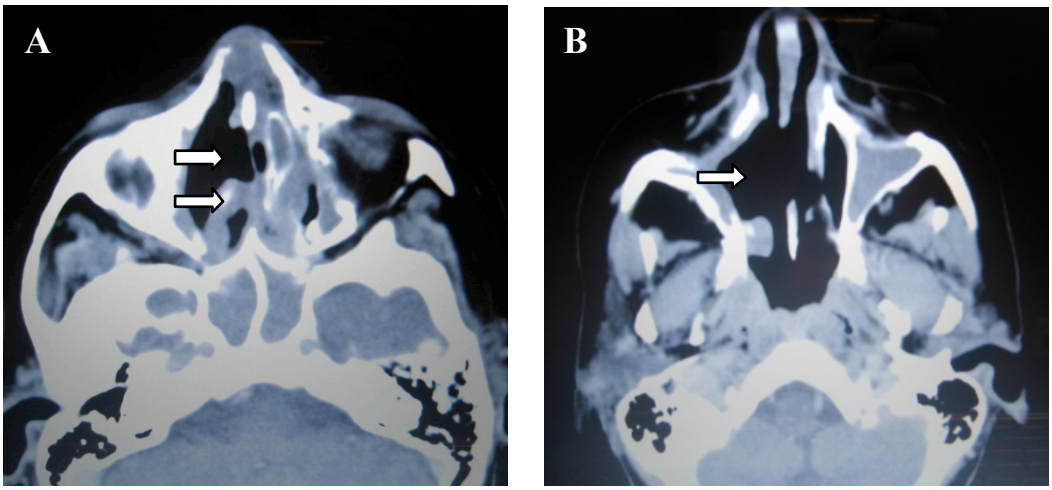

Figure 1. Computerized tomography findings
A- the upper arrow shows the defect of the septum, and the lower the rest of the middle turbinate (tail)
B- the arrow shows that the inferior turbinate and the medial wall of the maxillary sinus are missing

continuation of the treatment with regular check-ups. The patient is still in the state of remission.

DISCUSSION

In most patients upper and lower respiratory tract are first affected (initial granulomatous phase). This limited form, unless treated, develops into generalized vasculitis, necrotizing glomerulonephritis and pulmonary capillaritis, which present a severe, life threatening phase of the disease. In our case the first occurrence of the symptoms was localized in the nose and sinuses, after which the symptoms occurred in the lower airways. After less than a year, with bad general condition, the patient was admitted to the Department for Nephrology at the Clinic for internal diseases with the picture of acute renal insufficiency and hemoptysia.

Importance of otorhinolaryngologist in early diagnostic is based on the fact that the first clinical manifestations of WG in 80% to 90% cases occur in the head and neck, that is in the upper respiratory ways. Otorhinolaryngological symptomatology can appear in the early stage of WG without affecting other organs, but it can also occur as part of a generalized vasculitis. In the case shown here, the patient was examined by an otorhinolaryngologist for the first time in the later stage of the disease when one could identify the nose deformity as a consequence of necrosis of the septum and granulomatous inflammation in the nasal cavity. In 1990, the American Rheumatology Society defined clinical and pathologic criteria for WG: 1) oral ulcers or nasal discharge, 2) abnormal findings on chest radiograph (nodules, cavities, or fixed infiltrates), 3) abnormal urinary sediment, 4) granulomatous inflammation on biopsy. Unfortunately, in the case shown here, positive results of the biopsy of

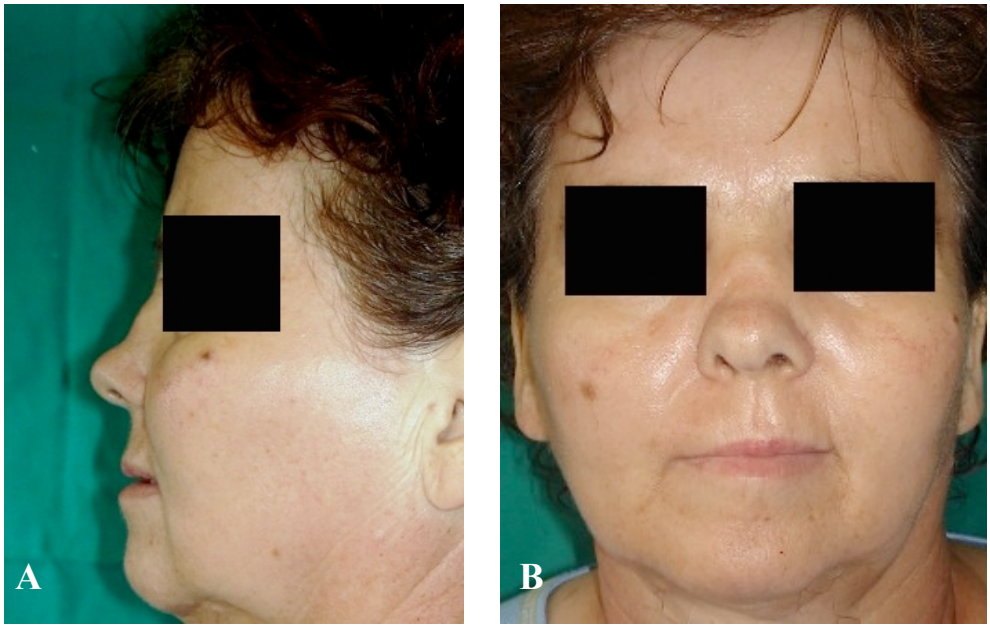

Figure 2. Saddle-nose deformity A-profile, B-an face

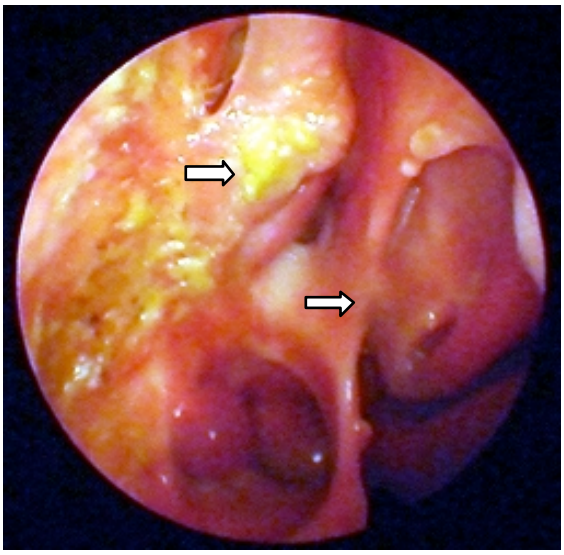

Figure 3. Endoscopic findings of the right nasal cavity (0 degrees, 4 mm)
The upper arrow shows the rest of the middle turbinate (tail) and dry purulent discharge and crusts, and the lower a perforation of the septum and wide communication with the left nasal cavity

the organs affected in terms of granulomatous inflammation did not suggest the diagnosis of the disease. Although it is possible to get falsely negative results of biopsy, positive results of biopsy have a positive predictive value of 100% [3]. Positive values of c-ANCA along with positive results of renal biopsy strongly suggested the final diagnosis, and consequently a specific treatment, which led the patient into the state of permanent remission. Combination of corticosteroids and cyclophosphamide is a widely accepted choice of therapy and it results in improvement in 90% of patients [2,3].

CONCLUSION

Otorhinolaryngological examination is obligatory in all patients with suspected Wegener's granulomatosis, and each patient with pus mixed with blood and crusts in the nose should be suspected of this disease.

In case of suspected WG, clinical picture should be completed with positive results of biopsy and positive values of c-ANCA.

C-ANCA is a decisive test in making the diagnosis, but the negative results do not exclude this disease, nor do the negative results of biopsy.

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