

Progressive hearing loss as the leading sign of Wegener's granulomatosis

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Abstract: 57-year-old woman with a history of ischaemic heart disease, arterial hypertension and after myocardial infarction was admitted to the university hospital because of progressive hearing loss and fever of unknown origin. Shortly before hospitalization she developed cough, haemoptysis and conjunctivitis. On the basis of clinical presentation Wegener's granulomatosis was suspected. To confirm the diagnosis, CT scans of the chest, sinuses and ears were performed and revealed massive lesions especially in the tympanic cavity, mastoid antrum and cells. Infiltrations were also observed in sinuses, especially maxillary, and typical granulomas were found in the lungs. Moreover, the biopsy taken from the mucous membrane of the nose showed abnormalities typical of Wegener's granulomatosis. Anti-neutrophil cytoplasmatic antibodies (ANCA) were also examined. It is of interest that c-ANCA (cytoplasmatic) were negative and p-ANCA (perinuclear) were positive which is rare in this disease. The patient was treated with immunosuppressive drugs (intravenous methylprednisolone, oral prednisolone and cyclophosphamide). Following therapy fever, haemoptysis and conjunctivitis subsided, while inflammatory parameters normalized. This case report presents an unusual clinical manifestation of Wegener's granulomatosis with the leading sign of hearing loss.

Key words: fever of unknown origin, hearing loss, Wegener's granulomatosis

INTRODUCTION

Wegener's granulomatosis (WG) is a rare, systemic, vascular disease of so far unknown pathogenesis and various clinical presentation. According to the current classification of vasculitis syndromes based on the 1994 Chapel Hill Consensus Conference Wegener's granulomatosis is the vasculitis of small vessels with the presence of anti-neutrophil cytoplasmatic antibodies (ANCA), so called ANCA-associated vasculitis [1]. The annual incidence of the disease is 3–14 cases per million [2]. A case of WG characterized by an unusual clinical presentation has been presented below.

CASE REPORT

A 57-year-old woman, a white-collar worker, with ischaemic heart disease and arterial hypertension diagnosed 5 years earlier, and after myocardial infarction in 2006, was admitted to the General Medicine and Endocrine Department in Warsaw because of the progressive left ear hearing loss, deafness of the right ear and fever of an unknown origin. At the beginning the ototoxicity of prolonged furosemide therapy was taken into consideration as the patient had been treated

with diuretic, β -adrenolytic and angiotensin II receptor antagonist. However, after furosemide withdrawal hearing impairment still progressed. On audiometric examination prior to the hospitalization the mixed hearing loss was diagnosed – of a conductive and perceptive character. Spontaneous epistaxis also occurred.

Within a month prior to the admission a fever of 38.5°C, and, just before hospitalization, haemoptysis, cough, oedema and reddening of the conjunctivae appeared (fig. 1).

On admission a fever of 38°C and palpebral oedema were found and conjunctivitis was visible (fig. 1). Laboratory findings at the admission and after the treatment are shown in table.

On the basis of anamnesis and increased inflammatory parameters the WG was suspected. The CT scan of paranasal

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Fig. 1. Signs of conjunctivitis

sinuses, the temporal bone pyramid and chest were performed. In lung parenchyma, mainly in upper (but also in lower) lobes a few lesions up to 14 mm in diameter were seen. The outlines of these parenchymal densities were partly irregular, blurred and might be typical of the WG (fig. 2). The CT of temporal bone revealed pathological mass filling the tympanic cavity, supratympanic recess and mastoid cavity, also present in mastoid cells on the right and in the central and lower part of the left ear tympanic cavity (fig. 3).

The CT of paranasal sinuses revealed massive, parietal thickenings of nasal mucosa in both maxillary sinuses, both frontal recesses, and anterior ethmoid cells, and mild thickenings in both sphenoid sinuses. Orifice-ductal complexes were bilaterally obstructed (fig. 4).

The histopathologic examination showed abundant mixed inflammatory infiltration.

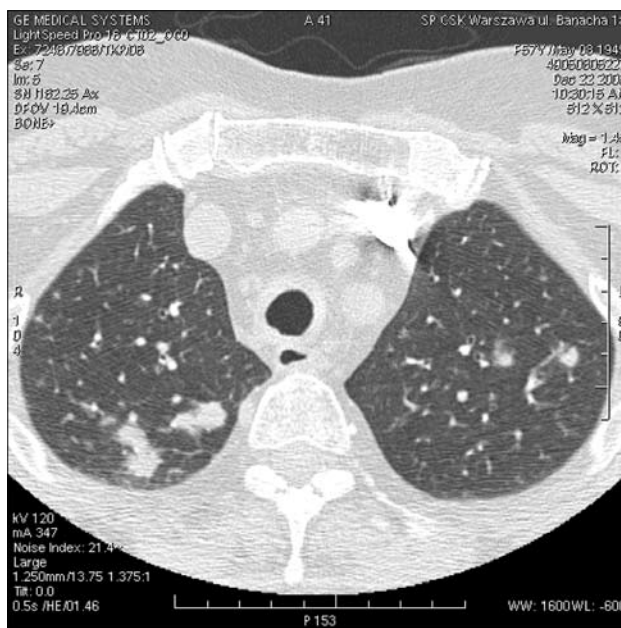


Fig. 2. Parenchymal density typical of Wegener's granulomatosis

The ANCA assays showed as follows: c-ANCA (cytoplasmatic) against proteinase 3 within a normal range and p-ANCA (perinuclear) against myeloperoxidase elevated – 0.8 U/ml for c-ANCA (reference range 0-6) and 16.8 U/ml for p-ANCA (reference range 0-3), respectively. Creatinine clearance and renal function parameters remained normal. In urinary sediment erythrocytes covered the whole vision field. As the WG was suspected the patient was referred to the Systemic Vasculitis Centre in the Czerniakowski Hospital for further diagnosis and treatment where a detailed differential diag-

Table. Laboratory findings

| Parameter (unit) | Before treatment | After treatment | Norm range |
|--------------------------------------|----------------------|---------------------|------------|
| Sedimentation rate after 1 hour (mm) | 70 | 10 | 0–10 |
| CRP mg/l | 200 | 13.17 | 0–10 |
| hemoglobin (g/dl) | 12.4 | 12.0 | 12–16 |
| erythrocytes (T/l) | 4.28 | 3.8 | 5,5–5,2 |
| leukocytes (G/l) | 13.4 | 10.4 | 4–11 |
| neutrophils t/ μ l | 10.76 | 7.2 | 2–6,9 |
| platelets (G/l) | 799 | 289 | 150–400 |
| fibrinogen (mg/dl) | 563 | 371 | 200–400 |
| Na (mmol/l) | 131 | 136 | 137–149 |
| K (mmol/l) | 4.4 | 4.5 | 3,6–5,0 |
| creatinine (μ mol/l) | 61.8 | 60.9 | 44,2–115 |
| urine erythrocytes | many in visual field | 5–6 in visual field | |
| urine protein | absent | absent | |
| CRP – C-reactive protein | | | |



Fig. 3. Ears lesions



Fig. 4. Sinuses lesions

nosis was performed in the field of infectious, neoplastic, systemic diseases, including connective tissue diseases and primary systemic vasculitis.

The re-evaluation of histopathological material taken from nasal mucous tissue revealed diffuse inflammatory infiltration in stroma composed mainly of mononuclear cells (plasmacytes) with addition of neutrophils and eosinophils. Neutrophils were concentrated around vascular fissures infiltrating their

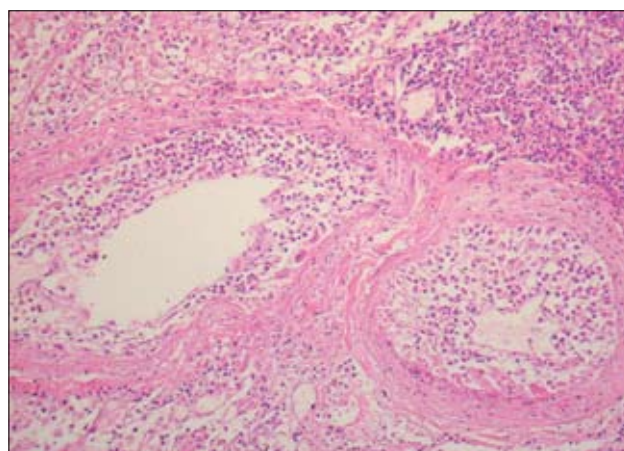


Fig. 5. Histopathology suggesting Wegener's granulomatosis

walls and creating the leucocytoclastic image. Sparse clusters of granulocytes (pus follicles) and diffuse nasal epithelium ulceration were visible – the image suggesting and typical of the WG. (fig. 5).

On the basis of clinical presentation, the histopathological image and serological findings, the diagnosis of primary systemic vasculitis MPO-positive WG was established. After obtaining informed consent the immunosuppressive (methylprednisolone intravenously, prednisolone orally) and cytotoxic (cyclophosphamide orally) treatment regimen adjusted to age and weight was administered. Afterwards a significant clinical improvement was achieved: normalization of body temperature, bilateral hearing improvement. The right-side complete recovery was confirmed in audiometric examination. At present the patient is on immunosuppressive and cytotoxic drugs and remains under control of the Out-Patient Department in the Czerniakowski Hospital Systemic Vasculitis Centre.

DISCUSSION

The classic Wegener triad consists of infiltration of upper and lower respiratory tracts and necrotic glomerulonephritis [3]. However, clinical manifestations of the disease may include several signs resulting from infiltration of different organs [4]. Most signs depend on the grade and spectrum of vasculitis, which is histologically characterized as necrotic inflammation with granulocytic infiltration. Each organ may be affected and consequently a course of the disease may have a different character. Moreover, the grade of the inflammatory process may be differentiated – from mild to fulminant, which also depends on the number of infiltrated organs [5]. The most frequently affected organs are skin, eyeballs, upper and lower respiratory tracts, the peripheral and central nervous system, joints, kidneys, rarely the digestive tract and mucous membranes [6].

External and medial otitis and mastoiditis are the uncommon first manifestations of the WG, but according to some

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data hearing impairment may affect 56% of patients [7]. Other studies suggest that the WG should be taken into consideration in either prolonged [8] or acute [9] hearing loss. The most serious complication of ear infiltration is hypoacusia and deafness [10].

Similarly to the patient described by Ozawa et al. [11] the progressive hearing loss and sudden deafness were the main signs of the disease also in our case. In the study conducted by Kempf et al. ear involvement was observed in 13 out of 19 patients (10 women and 9 men) with the diagnosis of WG. Audiometric examination carried out in this group revealed perceptive hearing loss (13 patients). Only one patient presented a normal basal tone in audiometric examination [12]. Perceptive hearing loss is usually of a reversible character if immunosuppressive and cytotoxic therapy (cyclophosphamide and steroids) is introduced; such improvement was also observed in the described case. Less toxic drugs – metotrexat and azathioprine – are recommended as the maintenance treatment [13]. The WG should be taken into account as a potential cause of sudden deafness when differential diagnosis is being carried out [14].

Cytoplasmatic antibodies (c-ANCA) are specific to the WG (sensitivity 65%, specificity 95%). Perinuclear antibodies (p-ANCA) are found in microscopic polyangiitis (MPA), but sporadically in the WG. The Enzyme-linked immunosorbent assay (ELISA) enables the separation of antibodies depending on the antigen location in cytoplasm of granulocytes: proteinase 3 (c-ANCA – specificity 99% for WG) and myeloperoxidase (p-ANCA – specificity 80% for MPA). In the described case anti-MPO antibodies were found, which made the diagnosis more difficult.

It should be remembered that in about 10% of the cases of WG and MPA with typical clinical presentation, the ANCA antibodies may be negative. The reason for that is so far unknown. The absence of ANCA antibodies does not exclude the diagnosis of WG.

REFERENCES

1. Szczeklik A, Musiał J. Układowe zapalenia naczyń. Złoty standard. In: Szczeklik A, red. Choroby wewnętrzne. T. 2. Kraków, Medycyna Praktyczna. 2006; 1687-1690.
2. Mahr AD, Neogi T, Merkel PA. Epidemiology of Wegener's granulomatosis: Lessons from descriptive studies and analyses of genetic and environmental risk determinants. Clin Exp Rheumatol. 2006; 24: S82-S91.
3. Woywodt A, Haubitz M, Haller H, et al. Wegener's granulomatosis. Lancet. 2006; 367: 1362-1366.
4. Wardyn K, Olędzka-Oreziak M, Życińska K. Zapalenia naczyń od rozpoznania do rokowania – nowe możliwości diagnostyczne i terapeutyczne. Nowa Klinika. 2001; 8: 1027-1032.
5. Thomeer M, Bacon PA, Blockmans D, et al. Clinical manifestation, approach to diagnosis and treatment of pulmonary vasculitis. Eur Respir Mon. 2005; 34: 69-90.
6. Wardyn KA, Życińska K. Pierwotne systemowe zapalenia naczyń. Pol Arch Med Wewn. 2004; 111: 757-767.
7. Bakthavachalam S, Driver MS, Cox C, et al. Hearing loss in Wegener's granulomatosis. Otol Neurotol. 2004; 25: 833-837.
8. Goktas O, Hiepe F, Paschen C. Wegener's granulomatosis (WG) presented with hearing loss and without positive ANCA. Laryngorhinootologie. 2004; 83: 180-184.
9. Otrebowski A, Sekula A, Mlynarczyk W, et al. Diagnostic problems in a rapid course of Wegener's disease with sudden sensorineural hearing loss. Otolaryngol Pol. 2000; 54 (Suppl 31): 118-119.
10. Życińska KA, Wardyn KA. Złoty standard. In: Wardyn KA, Życińska K, red. Pierwotne układowe zapalenia naczyń. Wrocław, Urban & Partner, 2004.
11. Ozawa H, Saitou H, Mizutani K. Sensorineural hearing loss from suspected Wegener's granulomatosis: report of 2 cases. Practica Oto-Rhino-Laryngologica 2003; 96: 397-404.
12. Kempf HG, Bootz F, Berg PA. Wegener's granulomatosis: otological and immunological aspects. Laryngo-Rhino-Otologie. 1992; 71: 26-30.
13. Lynch JP, White E, Tazelaar H, et al. Wegener's granulomatosis: evolving concepts in treatment. Semin Respir Crit Care Med. 2004; 25: 491-521.
14. Stone JH, Francis HW. Immune-mediated inner ear disease. Curr Opin Rheumatol. 2000; 12: 32-40.