Case report

WEGENER'S GRANULOMATOSIS- CASE REPORT

Tatjana Radjenovic Petkovic, Milan Radovic, Tatjana Pejcic, Milan Rancic, Desa Nastasijevic Borovac and Ivanka Djordjevic

Wegener's granulomatosis is an uncommon multisystemic disease, characterized by necrotizing granulomatous inflammation of the upper and lower respiratory tracts and general focal necrotizing vasculitis (Commonly known as „Wegener's triad"). The lungs are involved in 72 percents of patients and the clinic and radiographic findings indicate bilateral pulmonary nodules of varying size and definition, cavitated in half of the patients, accompanied by the nodular lesion with rare involvement of the pleura.

We described a case of 62-year-old women with pansinusitis, mild azotemia and initial respiratory tract symptoms such as chronic cough and occasional haemoptysis. Due to bilateral nodular infiltrates in the lungs on the chest radiogram she was initially treated for smear negative pulmonary tuberculosis, but without expected antituberculous response. An additional diagnostic procedure pointed to Morbus Wegener.

Two patterns of ANCA positive immunofluorescence are recognized as reliable and valuable diagnostic tools in the absence of histopathology for the diagnosis of Wegener's granulomatosis. *Acta Medica Medianae 2008;47(3):78-81.*

Key words: *Wegener's granulomatosis, lung involvement, ANCA*

Clinic for Lung Disease, Clinical Center Nis

Contact: Tatjana Radjenovic Petkovic
Vizantijski bulevar 36/26
18000 Nis, Srbija
E-mail: tatjanarp@bankerinter.net

Introduction

Wegener's granulomatosis (WG) is a multi-systemic disease characterized by a necrotizing granulomatous vasculitis affecting predominantly the lower and upper respiratory tract, lung and kidneys (1). The prevalence of the disease is about 3 persons per 100.000 people, equally in both sexes (2). The German pathologist Friedrich Wegener first described the disease in 1936. In 1954, Godman and Churg more fully delineated the disease and established the three main clinical criteria of WG (vasculitis, glomerulo-nephritis, respiratory tract involvement). Clinical manifestations and organ involvement of the disease vary widely.

Case report

A 62-year-old female was admitted to the hospital with haemoptisys, polyarthralgia, fever, weight loss, night sweats. One mounth prior to the admission she had reported the nose pain, rhinorrhea and epistaxis, and she received non-specific antibiotic therapy, without any imrovement. She denied smoking and alcohol use.

At the time of hospital admission, the patient was conscious, her body temerature was 37,5°C, puls 130/min, respiration rate 20/min, blood preasure 90/60 mmHg. She was adynamic, pale, upset, with haemoptysis. Her nostrils and throat were erithematous, with coagulum on the right nostril. On her tongue, palate and bucal mucosa there were difuse aphtous ulcerations. Her neck was supple, with no meningeal signs. Rare bilateral basal rales were obsered on the lung auscultation. Normal cardial auscultation was reported. Her abdomen was neihter tender nor distended, there were no edema, cyanosis or clubbing of the exremities.

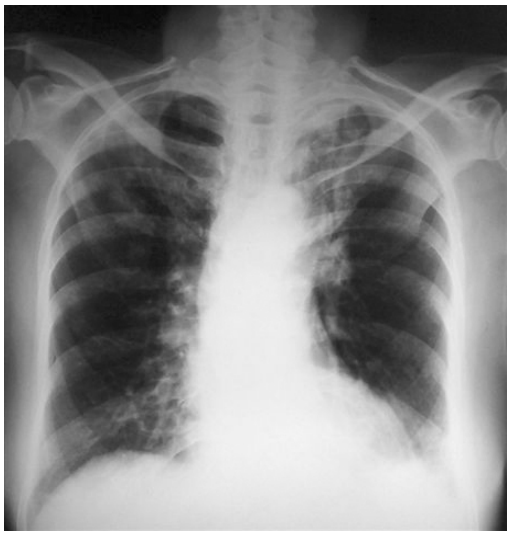

Figure 1. Chest radiograph

Table 1. Laboratory parametars

Peripheral blood	
WBC	18,4 x 10^4/µl
RBC	3,92x10^6/µl
hemoglobin	8,6 g/dL
Platelets	902x 10^3/µl
ESR	110 mm/h
Biochemical parameters	
CRP	252,2 mg/dl
glucose	4,7 mmol/l
urea	9,8 mmol/l
creatinine	135 µmol/l
alkaline phosphatase	155 U/l
AST	39 U/l
ALT	65 U/l
LDH	702 U/l
protein	64 g/l
albumin	29 g/l
Calcium	2,19 mmol/l
Sodium	l40 mmol/l
Chloride	98 mmol/L
Urine analysis	
hemoglobin	+
albumin	+
sediment	Lot of red blood cells casts

Chest CT scan showed two infiltrates in the right upper lobe, (33x24 mm and 20x19 mm) and consolidation on the left upper lobe.

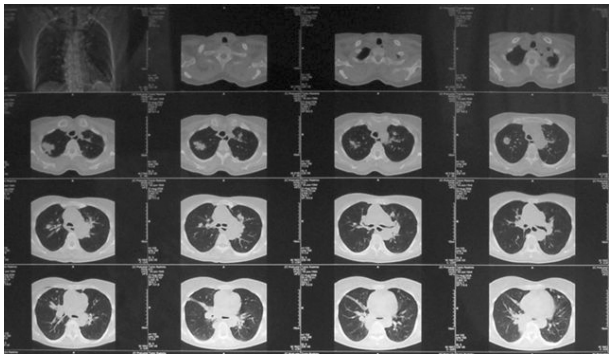

Figure 2. Chest CT scan

CT sinuses scan showed mucosal thickening in the right maxilar sinus, and nasal septum deviation.

Sputum culture showed Streptococcus pneumonia. Ziehl-Neelsen stain and culture for acid-fast bacilli were negative.

Urinoculture showed providentia on mass.

Chemo-culture was sterile.

Results of the test for human immunodeficiency (HIV) virus were negative.

Sputum cytology showed a lot of red blood cells and polymorphonuclear cells.

Hematological examination showed leukocytosis and hypochromic anemia.

Ultrasonography of the abdomen showed the pyelon dilatation in both kidneys, with splenomegaly (125x82 mm), and unechogenic zone in the liver.

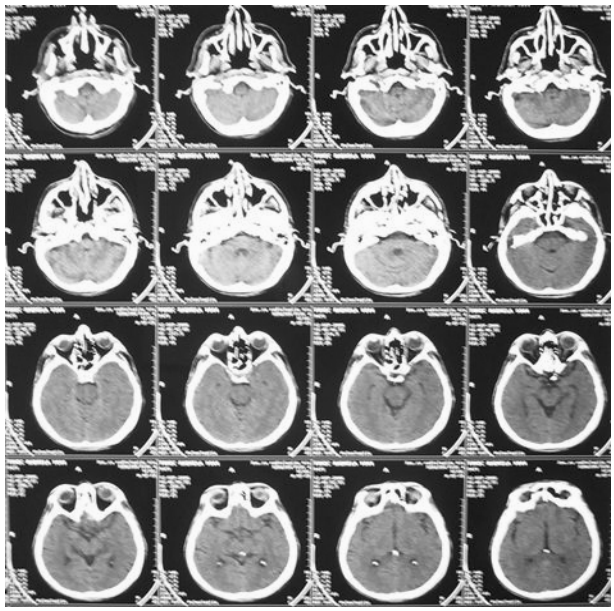

Figure 3. Paranasal sinuses CT

ORL examination showed multiple mucosal varices in the nostrils' mucosa.

Flexibile fiberoptic bronchoscopy revealed mucosal erythema and oedema suspected to malignancy (differential diagnosis: WG, or other granulomatous disease).

The admission diagnosis was sputum non confirmatum tuberculosis, and the patient underwent the treatment with antituberculosis drugs (Isoniasid, Rifampicin, Pyrasinamide), by protocol for the third category of patients.

In spite of the therapy, the patient was under mild distress, adynamic, upset, with frequent haemoptysis, with elevated values of laboratory parametars. Radiological finding was unchanged. At day 17, the patient developed palpable purpura on the lower extremitas. Dermatologist was consulted, and suspected of purpura Choenoch Shoenlain.

We suspected of WG, and some immunological investigations were performed.

Table 2. Immunological analysis

Immunological parametars	
Antinuclear antibodies	negativna
Immune complexes	>135 mg%
IgG	18,81g/l
IgM	1,24 g/l
IgA	4,47 g/l
C_3	1,54 g/l
cANCA	24 U/ml
pANCA	9 U/ml

We discontinued antituberculous and started with pronison therapy (40 mg/daily).

Examination of the specimen obteined from bronchoscopy showed granulomatous inlammation, displastic changes gr I.

Abdomen CT scan was normal, with little infrasplenical fluid.

Kidney biopsy speciemens were suspected on WG.

Patient was sent to the Institute for Immunology, Clinical Center Serbia, and started with Cixlophoshamide therapy (Endoxan 100 mg/2daily).

After six mounts of therapy, the patient was stabile, without any simptoms of WG. The six-month follow-up was recommended.

Discussion

WG was first described by Klinger in 1933, followed by Wegener in 1936 and 1939, and Ringerts in 1947.

WG is classified as ANCA positive vasculitis, mostly localized on the small and medium-sized blood vessel. It mostly affects the upper and lower respiratory airways and kidneys (3). According to literature data, the lungs are affected in 90 percents of patients (4). Typical radiological presentations of the lung involvement are multiple, bilateral, nodular infiltrations, with or without cavities. According to some data, in 20-50% of patients it is manifested with pleural effusion (4). Atypical presentations are interstitial lung disease, hilar mass or pneumotorax (5,6). In 1990, the American College of Reumatology (ACR) established the criteria for the classification of WG (7): nasal or oral inflammation, radiologically demonstrated pulmonary infiltrates, abnormal urinary sediment (red cell cast, haematuria), granulomatous inflammation on biopsy. Patient shall be said to have Wegener's granulomatosis if at least 2 of these 4 criteria are present. The presence of autoantibodies to proteinase 3/ cANCA is not requried for diagnosis of WG, by either ACR or Chaper Hill consensus Conference (CHCC) deffinition (7). Occasionaly, patients with infection, inflammatory bowel disease, rheumatic disease, neoplasm develop ANCA (8).

Sex distribution of the disease is equal, most of the patients present in the fifth decade, although the disease can occur at any age. Clinical presentation can be so diverse that the list of differential diagnoses is vast, ranging from infection, neoplasm, tuberculosis, malignancy, other forms of vasculitis (sarcoidosis, Behcet disease, purpura Choenoch Shoenlain) (9).

In our case, we described an unusual radiological presentation of WG. Pulmonary consolidation is not a typical finding in WG, and can pose a diagnostic problem (10). Transbronchial biopsy specimens are insufficient to make a diagnosis of vasculitis. In case of atypical presentation, the diagnosis in these patients poses a great clinical problem, bearing in mind a small number of positive pathohistological findings, as well as the possibility of positive ANCA antibodies in some other diseases. Differential diagnosis of tuberculosis and Wegener's granulomatosis is a great problem. In both cases, the clinical findings include haemoptysis, subfebrile temperature, haematuria (11). Radiological presentation can be the same in both disases. Even histopatologic finding can make confusion, since both diseases have granulomatous changes. In addition, the cases of positive ANCA antibodies have been described in those suffering from tuberculosis (12). Sometimes, patients with WG were mistakenly treated for pulmonary tuberculosis, and Wegener granulomatosis was diagnosed when the patients failed to respond to antituberculosis drugs (13).

Toyoshima et al. (14) presented a case of good therapeutic response and restitution of granuloma after the applied antituberculosis therapy. However, in our case, therapy response was obtained after the applied immunosupressive therapy.

Even though classified in the group of rare pulmonary diseases, early diagnostics and the timely beginning of clinical management may considerably influence the further course of disease. Therefore, the application of additional diagnostic tests may be crucial for the prognosis of disease. For the clinical menagment, early identification of disease is of particular significanse for prognosis in the patients with Wegener's granulomatosis.

References

1. Frankel SK, Cosgrove GP, Fischer A, Meehan RT, Brown KK. Update in the Diagnosis and Management of Pulmonary Vasculitis. Chest. 2006; 129:452-465.
2. Schwarz MI, Brown KK. Small vessel vasculitis of the lung. Thorax 2000; 55:502-10.
3. Seo JB, Im JG, Chung JW, Song JW, Goo JM, Park JH, Yeon KM. Pulmonary vasculitis: The spectrum of radiological findings. The British J. of Rad. 2000; 73: 1224-31.
4. Jolly M, Molta C, Hoffman G. Wegener's granulomatosis: pitfalls in the management of pulmonary disease: A case of Wegener's granulomatosis with a hilarmass. J Rheumatol. 2000;27 (10):2511-2.
5. Belavic Z, Vitas B, Doko A, Baskot A, Polovic A, Mlinac-Lucijanic M. Multiple nodose shadows of the lungs as a differential diagnosis problem. Acta Med Croatica 2006; 60(3):265-71.
6. Leavitt RY, Fauci AS, Bloch DA, Michel BA, Hunder GG, Arend WP, et al. The American College of Rheumatology 1990 criteria for the classification of Wegener's granulomatosis. Arthritis Rheum 1990; 33:1101-7.
7. Sorensen SF, Slot O, Tvede N, Petersen J. A prospective study of vasculitis patients collected in a five years period evaluation of the Chapel Hill nomenclature. Ann Rheum Dis 2000;59:478–82.
8. Al Maini M, Carette S. Diagnosis of Wegener's Granulomatosis in the ANCA Era. The Journal of Rheumatology 2006; 41:S48–S59
9. Javaud N, Belenfant X, Stirnemann J, Laederich J, Ziol M, Callard P, Ronco P, Rondeau E, Fain O. Renal granulomatoses: a retrospective study of 40 cases and review of the literature. Medicine (Baltimore). 2007;86(3):170-80.
10. Shin MS, Young KR, Ho KY. Wegeners granulomatosis upper respirathory tract and pulmonary radiographic manifestations in 30 cases with pathogenetic consideration. Clinical Imaging. 1998; 22:99–104.
11. Langford CA. Wegener's granulomatosis: current and upcoming therapies. Arthritis Res Ther 2003, 5:180-91.
12. Khilnani GC, Banga A, Sharma SC, Gupta SD. Wegener's granulomatosis: an isolated lung mass responding to antituberculosis therapy and atypical course. J Assoc Physicians India. 2000; 51:731-3.
13. Pradhan VD, Badakere SS, Ghosh K, Pawar AR. Spectrum of anti-neutrophil cytoplasmic antibodies in patients with pulmonary tuberculosis overlaps with that of Wegener's granulomatosis. Indian J Med Sci. 2004;58 :283-8.
14. Toyoshima M, Chida K, Suda T, Imokawa S, Nakamura H.. Wegener's granulomatosis responding to antituberculous drugs. Chest. 2001; 119(2):643-5.

WEGENER-OVA GRANULOMATOZA - PRIKAZ SLUČAJA I PREGLED LITERATURE

Tatjana Rađenović Petković, Milan Radović, Tatjana Pejčić, Milan Rančić, Desa Nastasijević Borovac i Ivanka Đorđević

Wegener-ova granulomatoza je multisistemska bolest nepoznatog uzroka, u čijoj osnovi je nekrotizujuća granulomatozna inflamacija sluzokože gornjeg i donjeg respiratornog trakta, nekrotizujući fokalni vaskulitis malih krvnih sudova različitih organa i fokalni nekrotizujući glomerulonefritis (tzv. Wegener-ova trijada). Plućne promene su neretko uzrok prvih manifestacija bolesti, a klinički tok je u zavisnosti od odgovora na imunosupresivnu terapiju nepredvidiv, neretko sa lošom prognozom. Radiološki se prezentuju promene na plućima u vidu nodularnih, migrirajućih infiltrata, mada su opisani i slučajevi pneumoničnih konsolidacija izgleda mlečnog stakla, pleuralnih izliva i hilarne limadenopatije. Patomorfološki, radi se o vaskulitisu krvnih sudova arterija, vena i kapilara, što dovodi do ishemije, infarkcija i perivaskularnih infiltrata, koji se radiološki prezentuju kao nodularne senke.

Radom se prikazuje 62-godišnja bolesnica sa bilateralnim variksima i devijacijom nosnog septuma, umerenom azotemijom i purpuroidnim promenama po koži potkolenica, sa bilateralnim migrirajućim nodularnim infiltratima u plućima, koje su prvobitno shvaćene kao specifične, a nakon nezadovoljavajućeg početnog efekta na antituberkulotike. U dopunskom dijagnostičkom postupku verifikovano je oboljenje Morbus Wegener.

Iako predstavljaju dopunsku dijagnostičku metodu, ANCA antitela predstavljaju značajnu pomoćnu metodu u dijagnostikovanju Wegener-ove granulomatoze u odsustvu pozitivnog patohistološkog nalaza. *Acta Medica Medianae 2008;47(3):78-81.*

Ključne reči: *Wegener-ova granulomatoza, pluća, ANCA*