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Case Report

Internal Meicine

Different features in Wegener's Granulomatosis: Report of Five Cases

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ABSTRACT

Wegener's granulomatosis (WG) is an autoimmune inflammatory condition. It is often a rapidly progressive and potentially fatal disease. The clinical presentation of WG can be so diverse that the list of its differential diagnosis is vast, ranging from infectious diseases to other vasculitis (e.g. Behcet's disease), as well as malignancies. The exact aetiology of WG remains unclear. The upper airway diseases including sinusitis, oral lesions and otitis media are the most common presenting features of WG. In this paper, we have described 5 WG cases. They had different presentations and chief complaints. Some of them presented with upper airways diseases, while the others mainly suffered from the manifestations of pulmonary involvement. Although all of them were finally diagnosed as WG cases, the processes of the work up for the diagnosis as well as the outcome of the disease were not the same. So, the diversities in the presentation should be mentioned in the management of the WG suspected patients.

Key Words: Wegener's granulomatosis, manifestations, case report.

KEY MESSAGE

- The physicians need to be informed about the different manifestations of Wegener's granulomatosis and they should consider these diversities in the suspected cases.

INTRODUCTION

Wegener's granulomatosis (WG) is a rare, multi-systemic, life threatening autoimmune inflammatory condition of unknown aetiology [1]. Ninety percent of the patients with WG have head and neck involvement, mostly of the sinuses [2]. Its clinical signs vary, but its pulmonary manifestations are common. The thoracic lesions generally consist of intra-pulmonary nodules [3]. The involvement of the eye and the adnexal structures is common, occurring in 29% of the patients [1]. In this paper, we have described 5 cases which presented with various features of WG.

Case 1

A 21 year-old woman presented with dyspnoea, productive cough and fever from 10 days before admission and maculo-papular rashes on her extremities from 4 days earlier. 4 months previously, she had suffered from polyarthralgia and morning stiffness (more than 30 minutes), with rheumatic factor positivity (RF) in her laboratory studies. Her body temperature was 38ºC. Coarse rales were heard in her lung examination. There were maculopapular rashes on her upper and lower extremities and a splinter haemorrhage on her hand's nails. The dorsal and palmar flexion of her right wrist, as well as the dorsal flexion of her right ankle were limited. The results of her laboratory tests are shown in [Table/Fig 1]. Additional laboratory studies showed significant, positive serum anti-neutrophilic cytoplasmic antibodies (ANCA) and proteinase 3 antibodies (APR3), but her serum was negative for antinuclear antibodies (ANA). Her chest X-ray showed bilateral large consolidations and nodules [Table/Fig 1]. On bronchoscopy, linear superficial nodularity was seen in the bronchus intermedius and in the right middle lobe. The histological studies of the bronchial biopsies revealed non-specific bronchitis. A diagnosis of WG was made, based of the patient's history, her physical examination, significant serum C-ANCA and the chest X-ray lesions. The patient was treated with intravenous cyclophosphamide for three days, followed by oral Prednisolone. The patient's condition improved. Her arthralgia, arthritis, and cough decreased. Her haemoptysis and haematuria were removed. She was discharged on day 6 on oral antibiotics and prednisolone.

Case 2

A 24 year-old woman with an unmarkable medical history presented 2 months before admission with otalgia, otorrhoea, nasal congestion and a bloody nasal discharge. She was admitted because of poly-arthralgia in her hands and feet, otalgia and otorrhoea, headache, productive cough and bloody tinged sputum. Her vital signs were normal and her physical examination showed bilateral conjunctival erythema, otorrhoea in her left ear and an erythematous tympanic membrane in her right ear on otoscopy, gingivitis in her mouth and erythematous papules on her neck, chest and groin. Her pulmonic sounds were coarse on auscultation. The examination of her extremities showed tenderness and swelling on the olecranons and on the dorsal surface of her right hand and restriction in the dorsal and palmar flexion. [Table/Fig 1] shows the results of the laboratory tests. Her serological tests were strongly positive for C-ANCA (67.8 IU). Her lung HRCT scan revealed alveolar and parenchymal infiltration in the right lower lobe and in the lingula lobe. A diagnosis of WG was made, based of the patient's history, her physical

examination, and significant serum C-ANCA. On the third day of admission, the severity of the haemoptysis was increased and she had severe respiratory distress with rales in the lungs on auscultation. The initial treatment consisted of intravenous methyl prednisolone for three days, followed by intravenous hydrocortisone. The patient also received intravenous cyclophosamide, but the massive haemoptysis and severe respiratory distress continued. We tried to insert an intra-jugular catheter to start plasmapheresis, but it was impossible because of the patient's severe respiratory distress. The patient was transferred to the intensive care unit with a diagnosis of alveolar haemorrhage on the sixth day of hospitalization. After 2 hours, her pulse rate and blood oxygenation decreased and cardiopulmonary resuscitation was started immediately, but it was not successful and the patient died.

Case 3

A 37-year old man presented with fever, chills, sweating, productive cough, dyspnoea at the supine position and left eye proptosis, redness and blurred vision from 2 months before admission. He had a history of dyspnoea, productive cough, eye dryness and redness (despite using artificial tears), unilateral left headache and left eye pain since 2 years ago. He had dysphonic speaking. He was febrile, but his other vital signs were normal. There were echymotic lesions on the dorsal surface of his left hand and multiple petechiae on his abdomen. The examination of his left eye revealed scleritis and mild proptosis. He had reduced eye movements, visual acuity (by finger counting) and reduced colour vision. There was a non-reactive pupil. The lung sounds were coarse on auscultation. The results of his laboratory tests are shown in [Table/Fig 1]. His chest X-ray showed bilateral large nodules and cavities. The water's view X-ray revealed the involvement of the frontal, maxillary and the ethmoid sinuses and nasal septum thickness. His serological assessment revealed a strong positivity for C-ANCA. His chest CT scan showed multiple nodules and thick wall cavitations. His para nasal CT scan revealed pan sinusitis. The MRI of the orbits showed an intra and extra-chanal abnormal tissue which encased the left optic nerve that prolapsed to the left maxillary sinus. The BAL cytology was negative for malignancies. His histological studies revealed severe inflammation, vasculitis in the small venules and capillaries and a non caseous granuloma which was suggestive of WG. A diagnosis of WG was made, based of the history, physical examination, significant serum C-ANCA and the imaging and histological studies.

The patient was treated with intravenous cyclophosphamide for three days, which was followed then by oral prednisolone and oral methotrexate. The patient's general condition improved, but no significant improvement was seen in the visual acuity, colour vision and in the papillary response of the left eye.

Case 4

The patient was a 46 year-old woman with a history of chronic sinusitis and cough, who was referred to our hospital because of fever and frontal headache that did not respond to antibiotic therapy. Her physical examination was normal except for asthenia and some neurological signs included bilateral toe paresthaesia and dysesthaesia.

The results of her laboratory tests are shown in [Table/Fig 1]. Her serum C-ANCA was positive. Electromyography (EMG) showed sensory-motor poly-neuropathy which suggested lumbar discopathy. The histological study of her trans-bronchial specimen revealed ulcerative bronchitis and squamous metaplasia which suggested WG vasculitis.

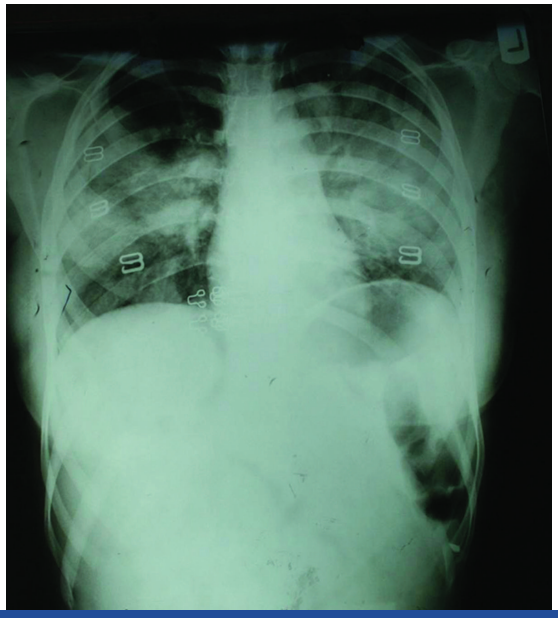
A diagnosis of WG was made, based of the patient's history, histopathology, and significant serum C-ANCA. The patient was treated with intravenous cyclophosphamide and intravenous methyl prednisolone, followed by oral prednisolone, oral cyclosporine and oral co-trimoxasol. Her condition improved during 3 months of follow up.

Case 5

The patient was 16 year-old woman with a history of recurrent epistaxis and severe polyarthralgia for 2 years. On examination, she was found to have mild nasal crusting. The examinations of her chest as well as her other systems were normal. Her serological studies showed a significant rise in the ANA and anti ds-DNA, while her serum ANCA (C-ANCA and P-ANCA) was negative. The results of her other laboratory tests are shown in [Table/Fig 1]. Her nasal biopsy and histological studies showed necrotizing granulomatosis inflammation with ulcer, which was suggestive of WG. A diagnosis of WG was made, based of the patient's history

Tests	Case 1	Case 2	Case 3	Case 4	Case 5
WBC /µl	7900	16500	13500	11600	12400
Hemoglobin gr/dl	7.4	12.8	9.5	13.1	12.6
Hematocrit %	25	39	27	39	38
Platelet /µl	545000	340000	620000	410000	200000
ESR	84	42	82	73	36
CRP	+++	+++	+++	++	Negative
ANA	_	Negative	Negative	Negative	+++
RF	+++	_	_	_	Negative
C-ANCA	+++	+++	+++	+++	Negative
C3	Normal	Normal	_	_	_
C4	Normal	Normal	_	_	_
CH50	Normal	Normal	_	_	_

[Table/Fig-1]: Results of laboratory tests in 5 cases of Wegener's granulomatosis.



[Table/Fig-2]: Chest X-ray of case 1 diagnosed as Wegener's granulomatosis. Bilateral large consolidation and nodules are seen.

and her histopathological findings.

She was treated with oral steroids, methotrexate and co-trimoxasol. Her condition improved during 6 months of follow-up.

DISCUSSION

Our WG cases had different presentations and chief complaints. Some of them presented with upper airways diseases, while others mainly suffered from the manifestations of pulmonary involvement. WG is currently characterized as ANCA which is associated small vessel vasculitis. WG often is a rapid progressive and potentially fatal disease. Its exact aetiology remains unclear. Five different features of WG have been described here, but often it is a multisystem disease. Fever and weight loss maybe reported at the onset of the disease and more frequently during the course of the illness [4]. The upper airway diseases including sinusitis are the most common presenting features of WG [5]. Pulmonary involvement is one of the cardinal features of WG. The diagnosis is based on the clinical criteria, including oral ulcers and an abnormal chest X-ray, which is supported by histopathological findings which reveal granulomatous inflammation and positive C-ANCA and PR3 in the laboratory studies. Immunosuppressive agents such as cyclophosphamide or azathioprine, combined with steroids, were suggested for the treatment, with a remission rate of up to 90% [4].

Although all of our cases were finally diagnosed as WG cases, the processes of the work up for the diagnosis, the treatments, as well as the outcome of the disease, were not the same. So, the diversities in the presentation should be mentioned in the management of the WG suspected cases.

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