MEDICINE

INDEX COPERNICUS INTERNATIONAL

ICV value for 2023 = 74.57

Case Report

International Journal of Medical Case Report

Granulomatosis with Polyangiitis (Wegener's Granulomatosis): A Case Report

Authors:- Chia Earn Sun, Narizan Ariffin
KPJ Healthcare University, Nilai, Negeri Sembilan, Malaysia.

INTERNATIONAL JOURNAL OF MEDICAL CASE REPORTS ISSN 2455-0574

Abstract

Granulomatosis with Polyangiitis (GPA) is a rare autoimmune vasculitis affecting the respiratory tract, kidneys, and small-to-medium vessels, posing significant diagnostic challenges. We report a 61-year-old Malaysian man with prolonged fever, weight loss, respiratory symptoms, and otorrhea. Initial treatment for tuberculosis and fungal infection failed to improve his condition.

Extensive investigations revealed elevated inflammatory markers, a positive PR3-ANCA antibody, and histopathological evidence of vasculitis and granulomatous inflammation from a lung biopsy. These findings led to a revised diagnosis of GPA.

This case highlights the need to consider GPA in patients with persistent multisystem symptoms unresponsive to conventional treatment, especially in regions endemic to tuberculosis.

Keywords:- Granulomatosis with Polyangiitis, PR3-ANCA, Respiratory Tract Diseases, Vasculitis

INTRODUCTION

Wegener's granulomatosis is a rare condition, even more in the local Malaysian population. Patients usually present with non-specific, constitutional symptoms, which poses a great challenge in diagnosis. In this article, we present a patient who presented with prolonged fever and systemic symptoms, and discuss the dilemma in reaching the diagnosis.[1]

Access this Journal Online

Quick Response Code

Website: www.ijomcr.net

Email:ijomcr@gmail.com

Corresponding Author:
Chia Earn Sun
KPJ Healthcare University, Lot PT 17010, Persiaran Seriemas, Kota Seriemas, 71800 Nilai, Negeri Sembilan.
Email: summer_earn@hotmail.com

CASE REPORT

A 61-year-old Indian man presented with prolonged fever for 4 months, associated with reduced appetite and loss of weight of 6 kilograms over the past 4 months. He also had a prolonged cough with occasional haemoptysis. He denied any shortness of breath or chest pain. He had bilateral otorrhea and otalgia for 3 months. The ear discharge resolved after a course of oral levofloxacin, however, he still complained of intermittent bilateral ear fullness, tinnitus, and reduced hearing. Besides, he also had rhinorrhoea with yellowish nasal discharge, nasal congestion, and epistaxis. There were no abdominal or urinary symptoms. He had left breast cancer 20 years ago, meningioma 5 years ago in which he underwent right frontoparietal craniectomy, and latent tuberculosis infection 2 years earlier which was treated with anti-tuberculous medications.

Clinically, blood pressure was 154/80, pulse rate was 117 beats per minute, and oxygen saturation was 99% under room air. He was febrile at 39oC. General examination showed a thin gentleman with mild pallor. There was no clubbing. There was no palpable neck node. Otoscopy examination showed bilateral middle ear effusion. Nasoendoscopy revealed inflamed nasal mucosa with punctate areas of blood clots and crusting. Osteomeatal complex and nasopharynx were normal, and no mass was seen. Intraoral examination was normal. Auscultation of the lungs revealed reduced air entry over the left lower zone. Cardiovascular examination was normal. Abdomen was soft and non-tender with no palpable spleen, liver, or kidneys.

Full blood count showed normocytic normochromic anemia. White blood cell count was raised at 15.2 x 103/uL, with neutrophil predominant at 82.2%. Lactate dehydrogenase (LDH) was raised at 358 U/L. Erythrocyte Sedimentation Rate (ESR) was increased to 67 mm/hr. C-reactive protein (CRP) was raised at 199mg/L (Table 1).

Examination	Result	Unit	Reference range
Haematology			
Haemoglobin	10.7	g/Dl	13.0-18.0
Red cell count	3.8	10^{12}/L	4.5-5.9
Haematocrit (PCV)	32	%	41-53
Mean Cell Volume (MCV)	85	fL	76-103
Mean Corpuscular Haemoglobin (MCH)	28	pg	26-34
Mean Corpuscular Haemoglobin Concentration (MCHC)	33	g/dL	31-36
Red Blood Cell Distribution Width (RDW)	12.4	%	8.0-14.6
Platelet Count	487	10^3/L	150-450
Mean Platelet Volume (MPV)	8.5	fL	5.8-12.0
White blood cell count	15.2	10^3/Ul	4.3-10.5
White Blood Cell Differential Count			
Neutrophil	77.3	%	40-75
Lymphocyte	8.0	%	20-45
Eosinophil	6.8	%	0-6.0
Monocyte	7.5	%	1-11
Basophil	0.4	%	0-2
Erythrocyte Sedimentation Rate (ESR)	67	mm/hr	0-20
Lactate dehydrogenase (LDH)	358	U/L	135-225
C-reactive protein	199	mg/L	<5.0
Renal Function Test			
Creatinine	45	umol/L	59-104
Urea	3.3	mmol/L	2.0-6.8
Sodium	136	mmol/L	135-155
Potassium	4.0	mmol/L	3.5-5.5
Chloride	91	mmol/L	95-111
Calcium	1.96	mmol/L	2.14-2.55
Phosphate	0.89	mmol/L	0.78-1.50
Anti-nuclear antibody (ANA)	Positive (1:80)		Negative
Anti-dsDNA	66.7 (Reactive)	IU/Ml	<50
Complement factor, C3	1.41	g/L	0.90-1.80
Complement factor, C4	0.29	g/L	0.15-0.45
Myeloperoxidase (MPO) – pANCA antibody	0.2	IU/mL	<3.5
Proteinase 3 (PR3) – cANCA antibody	110.0	IU/mL	<2.0

Table 1. Relevant laboratory investigations.

Computed tomography showed mucosal thickening of the right sphenoid sinus. The rest of the paranasal sinuses are normal. There was a large minimally enhancing heterogeneous hypodense mass at the posterior-basal segment of the left lower lobe with multiple lung nodules of varying sizes scattered in both lung fields. There was also left hilar lymphadenopathy.

In view of his previous history of latent tuberculosis infection, he was treated empirically for tuberculosis with Akurit-4 4 tablets daily and table Pyridoxine 20mg once daily. However, he had persistent fever and did not show clinical improvement. Sputum culture and sensitivity grown Pseudomonas Aeruginosa, sensitive to Meropenem. He was given intravenous Meropenem 2g TDS subsequently. Serum Aspergillus Antigen (ELISA) test was positive with an index of 4.019. Intravenous Amphotericin B was thus initiated for fungal infection.

Despite empirical anti-tuberculous, targeted intravenous antibiotics and antifungal, he did not show clinical improvement. Other investigations were not conclusive. Blood culture and sensitivity showed no growth. Ear swab aerobic, anaerobic, and mycobacterial cultures did not grow any organism. Tuberculosis work-up including sputum Acid-Fast Bacilli x 3 and tuberculosis quantiferon were negative. CT-guided biopsy of the left lower zone mass was performed, in which initial pathological examination revealed acute on chronic fibro inflammatory changes with no evidence of malignancy or tuberculous granuloma. This led to a diagnosis dilemma.

On Day 7 of hospitalization, serum PR3-ANCA (Antineutrophil Cytoplasmic Antibodies) came back high positive at 110 IU/L, and Myeloperoxidase (MPO)-pANCA antibody was negative. Anti-double stranded DNA (Anti-dsDNA) was reactive at 66.7 IU/ml. Antinuclear antibodies (ANA) were also positive (1:80). Complements C3 and C4 were normal. Rheumatoid factor was raised at 56.7 IU/ml. This sheds light on the possibility of autoimmune or connective tissue disease.

Previous lung biopsy specimens were reviewed. Periodic Acid-Schiff (PAS) stains confirmed the presence of vasculitic damage. Histological features depict an acute or chronic fibroinflammatory process. Acute inflammatory infiltrate of polymorphs, eosinophils, and histiocytes was seen; with areas of central necrosis. Focal areas of coagulative type necrosis were seen, with infiltration of inflammatory cells seen in the intima of some of the arterioles. Tuberculoid granulomata was not observed. Fragments of lung parenchyma included showed septal edema and acute alveolitis. There was no evidence of malignancy.

Given the histological evidence of granulomata, ischemic type coagulative necrosis, and highly positive c-ANCA, the diagnosis was revised as Granulomatosis with Polyangiitis(GPA)/ Wegener's granulomatosis. He was referred to a rheumatologist for further management.

DISCUSSION

Granulomatosis with polyangiitis (GPA), previously known as Wegener's granulomatosis (WG), is an uncommon autoimmune disease. It is characterized by pauci-immune necrotizing vasculitis of small and medium-sized vessels.[2] It is distinguished clinically by its predilection for affecting the upper and lower respiratory tracts and kidneys. Histologically, it is characterized by the presence of necrosis, granulomatous inflammation, and vasculitis.1 Diagnosis of GPA in our patient was challenging, as he presented with nonspecific symptoms. Tuberculosis was the initial working diagnosis in our patient as it is endemic in our country, along with his previous history of tuberculosis. Given his previous history of left breast cancer and meningioma, malignancy also has to be excluded.

GPA most commonly occurs in Caucasian population while it is rarely seen in non-Caucasians. Patients typically develop onset of symptoms between 45 to 65 years old. At the time of diagnosis, two organ systems are involved on average. Most patients are diagnosed 3-12 months from the onset of symptoms. Patients usually present initially with unexplained constitutional symptoms. Fever was described as the first

symptom in 33% of patients.[2] Head and neck involvement in the initial phase of GPA accounts for 70-95% of the cases. Nose and paranasal sinuses are the most commonly involved sites (60-90% of cases). 19% -70% of patients reported ear disorders in the form of unilateral or bilateral otitis media. Middle ear disease developed secondary to the formation of granulation tissue in the nasopharynx and Eustachian tube, resulting in secretory changes.[3] Larynx, oral cavity, orbit, and parotid gland are other h ead and neck regions that may be involved. Pulmonary involvement is one of the cardinal features of Wegener's granulomatosis. It affects 45% of patients at presentation, and 87% during the course of the disease.1 Pulmonary symptoms include cough, haemoptysis, pleuritis. Radiographic findings include pulmonary infiltrate (67%) and nodules (58%). Lung parenchymal disease is the most frequent manifestation which produces multiple nodules and masses. Airway involvement in GPA does not show a typical radiographic pattern, ranging from segments of bronchial stenosis, and intraluminal soft tissue mass to lobar or segmental atelectasis and lung nodules.[4]

Our index patient presented with constitutional symptoms for 4 months. He had respiratory tract symptoms, such as prolonged cough, haemoptysis, rhinorrhoea, nasal congestion, and epistaxis. Clinical examination revealed bilateral middle ear effusion. Nasoendoscopy showed nonspecific areas of inflammation, punctate hemorrhage, and crusting in the nasal cavities.[5] His nasal mucosa was intact, and paranasal sinus CT showed no abnormal findings except for mild mucosal thickening in the sphenoid sinus; therefore, a nasal biopsy was not performed. Computed tomography of the thorax revealed a left lung mass with multiple lung nodules and hilar lymphadenopathy. Initial histological examination of the left lung mass was non-conclusive. Blood investigations were non-specific with raised inflammatory markers. Tuberculosis workups were negative. He was treated empirically for tuberculosis in consideration of his previous medical history. Antibiotic and antifungal were also initiated based on his sputum culture and sensitivity, and Aspergillus antigen test. However, he did not show clinical improvement.

This led to a diagnosis dilemma. The initial diagnosis was re-visited. Further laboratory investigations later revealed a high positive PR3-ANCA of 110 IU/L, while MPO-ANCA was negative. This aided in the diagnosis of ANCA-associated vasculitis. A pathological specimen from the lung biopsy was reviewed, which showed vasculitis changes, granulomata, and ischemic coagulative necrosis.

The diagnostic criteria established by the American College of Rheumatology in 1990 include the following: haematuria, abnormal chest radiography, ulceration in mouth/ nose, and positive histopathological evaluation, in which at least two of these have to be stated to establish the diagnosis. Approximately one-third of patients may present with a limited, locoregional form of the disease, without renal involvement. Our patient fulfilled the diagnostic criteria for GPA. He had abnormal chest radiography, and ulceration in the nose, alongside a positive histopathological examination. The final diagnosis was GPA.

Although the diagnostic sensitivity and specificity of PR3-ANCA and MPO-ANCA for ANCA-associated vasculitis are very high, a minority of patients with GPA have MPO-ANCA.4 PR3-ANCA was reported to be found in 70%-90% of patients with active GPA, whereas MPO-ANCA was observed in only 5%-10% of patients with GPA.5 MPO-ANCA positive GPA patients were shown to manifest less organ involvement as compared to PR3-ANCA positive GPA patients.[6]

Histopathological evidence of vasculitis remains the gold standard for diagnostic purposes.[7] Histologically, GPA consists of ischemic necrosis with the formation of a nonmicrobial neutrophilic abscess (microabscess) and a polymorphic granuloma containing polymorphonuclear leukocytes, lymphocytes, plasma cells, dendritic cells, eosinophils, and multinucleated giant cells. Vasculitic changes may affect small-sized and middle-sized vessels, capillaries, and venules. These changes were demonstrated in our patient during further histological examination. markers of hemolysis is essential to guide treatment adjustments and assess response.[7]

CONCLUSION

Autoimmune hemolytic anemia is a rare but serious condition in children that requires prompt recognition and treatment. This case illustrates the typical clinical and laboratory findings of warm antibody AIHA and underscores the importance of corticosteroids as the primary treatment. Early diagnosis and appropriate management are crucial to improving outcomes and preventing complications.

Conflict of interest
None
Source Of Funding
None

REFERENCE

5. Shafiei K, Luther E, Archie M, Gulick J, Fowler MR. Wegener granulomatosis: case report and brief literature review. J Am Board Fam Pract. 2003 Nov-Dec;16(6):555-9. doi: 10.3122/jabfm.16.6.555. Erratum in: J Am Board Fam Pract. 2004 Mar-Apr;17(2):163-4. PMID: 14963084.
6. Terebelo S, Chen I. Granulomatosis with Polyangiitis Presenting as Pyrexia of Unknown Origin, Leukocytosis, and Microangiopathic Haemolytic Anemia. Case Rep Rheumatol. 2017;2017:6484092. doi: 10.1155/2017/6484092. Epub 2017 Jul 24. PMID: 28811951; PMCID: PMC5546083.
7. Wawrzecka A, Szymańska A, Jeleniewicz R, Szymański M. Granulomatosis with Polyangiitis with Bilateral Facial Palsy and Severe Mixed Hearing Loss. Case Rep Otolaryngol. 2016;2016:5206170. doi: 10.1155/2016/5206170. Epub 2016 Jul 14. PMID: 27493820; PMCID: PMC4963591
4. Nishiuma T, Ohnishi H, Yoshimura S, Kinami S, Sakamoto S. A case of granulomatosis with polyangiitis (Wegener's granulomatosis) presenting with marked inflamed tracheobronchial mucosa. Case Rep Med. 2013;2013:208194. doi: 10.1155/2013/208194. Epub 2013 Sep 30. PMID: 24198834; PMCID: PMC3806251
5. Fujimoto S, Watts RA, Kobayashi S, Suzuki K, Jayne DR, Scott DG, Hashimoto H, Nunoi H. Comparison of the epidemiology of anti-neutrophil cytoplasmic antibody-associated vasculitis between Japan and the U.K. Rheumatology (Oxford). 2011 Oct;50(10):1916-20. doi: 10.1093/rheumatology/ker205. Epub 2011 Jul 28. PMID: 21798892.
6. Schönermarck U, Lamprecht P, Csernok E, Gross WL. Prevalence and spectrum of rheumatic diseases associated with proteinase 3-antineutrophil cytoplasmic antibodies (ANCA) and myeloperoxidase-ANCA. Rheumatology (Oxford). 2001 Feb;40(2):178-84. doi: 10.1093/rheumatology/40.2.178. PMID: 11257154.
7. Masiak A, Zdrojewski Z, Pęksa R, Smoleńska Ż, Czuszyńska Z, Siemińska A, Kowalska B, Stankiewicz C, Rutkowski B, Bułło-Piontecka B. The usefulness of histopathological examinations of non-renal biopsies in the diagnosis of granulomatosis with polyangiitis. Reumatologia. 2017;55(5):230-236. doi: 10.5114/reum.2017.71638. Epub 2017 Oct 28. PMID: 29332961; PMCID: PMC5746633.

Author Contribution:- CS: Conceptualized, supervised, revised, and edited the manuscript. NA: Acquisition of data. Wrote the original draft, revised, and edited the manuscript.

Received : 09-11-2024 Revised: 01-12-24 Accepted : 25-12-24