

A RARE CASE OF GRANULOMATOSIS WITH POLYANGIITIS with DIFFUSE PULMONARY HEMORRHAGE: A CASE REPORT

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INTRODUCTION

Wegner's Granulomatosis is the other name for Granulomatosis with Polyangiitis first described by German pathologist Friedrich Wegener in 1936. It is a multi-system necrotizing non caseating granulomatous vasculitis which affects small to medium-sized vessels involving any organ system, most commonly the lungs and kidneys. ^[1] The annual worldwide incidence of GPA (Granulomatosis with Polyangiitis) is estimated to be 10-20 cases per one million based upon the geographical location. ^[2] The clinical presentation includes diffuse pulmonary haemorrhage, acute glomerulonephritis, chronic sinusitis, palpable purpura and the imaging findings of nodules or cavities. The serological tests, includes the use of cytoplasmic antineutrophil cytoplasmic antibody (ANCA) and perinuclear ANCA. ^[3] Treatment includes remission induction therapy followed by remission maintenance therapy. A combination of corticosteroids and immunosuppressants (cyclophosphamide, methotrexate and rituximab) are used to treat this disease. Relapse and flares can occur during treatment and are usually controlled by corticosteroids. ^[4]

CASE REPORT

The 18-year-old child patient presented to the General Medicine OPD C.U.Shah Medical College, Surendranagar with active complaints of cough, breathlessness, low grade fever and weakness. He also complained about headache for 4 weeks. On presentation, patient was febrile to 100.7 Fahrenheit (38.2 degrees Celsius), heart rate of 110, blood pressure of 116/72 and oxygen saturation 97%. The Patient was vaccinated for COVID-19 and was tested negative for COVID-19 at the time of admission. The patient's symptoms started 1 month back when he had viral infection that remained for 5-7 days, after which he was transfused blood for two times. Later on, patient developed bilateral facial pitting oedema; soon after few days of transfusion. At this time, he started feeling progressive exertional dyspnea, cough with expectoration. The expectorant contains blood before a day of admission. He also had pleuritic chest pain on admission. Child also have had history of abdominal pain at peri umbilical region. There is itching and irritation on maculopapular rashes at the shin of tibia giving dermatological manifestation. Family history was significant for a maternal grandmother with systemic lupus erythematosus.

In laboratory tests, complete blood count test was normal. Erythrocyte sedimentation rate was 90. Bleeding time, clotting time and activated partial thromboplastin time were within normal ranges. Electrolytes and renal function tests were normal. Urine routine microscopy showed +3 Albumin, 10-12 pus cells and plenty of red blood cells. Sputum AFB (Acid fast bacilli) was done and turned negative. The patient gave negative test for S. typhi 'O' and 'H'.

Ultrasonography revealed, changes of bilateral renal parenchymal disease, mild ascites and left sided minimal pleural effusion. Chest radiograph was performed which showed bilateral (left greater than right) multifocal nodular opacity, concerning for round pneumonia. Unenhanced CT brain was performed for evaluation of headache which showed no acute intracranial abnormalities. Frothy secretions were seen in the left maxillary sinus, representing active sinus disease. Further, suspecting granulomatous disease, HRCT (High resolution computed tomography) was advised.

His CT scan showed multiple small discrete and confluent consolidatory, ground glass and nodular opacities in both lungs more marked in left lung field. No evidence of intrinsic area of cavitation. Left sided minimal pleural effusion is seen. Small atelectasis noted in posteromedial basal segment of left lower lobe. These findings are consistent with changes of Wegner's granulomatosis with mild diffuse alveolar haemorrhage involving both lungs more marked in left lung field (Figure 1 and 2).

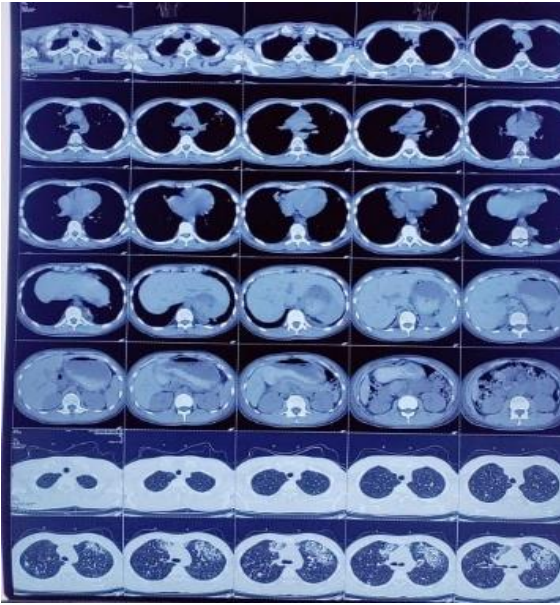


Figure 1



Figure 2

Subsequently, serum C-ANCA was positive 1:130.

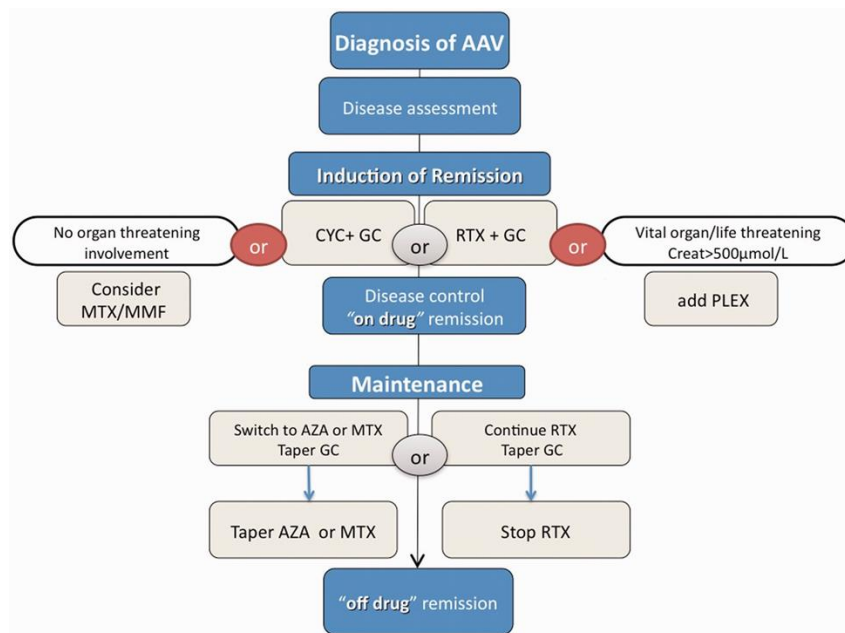
DISCUSSION

Wegener granulomatosis also known as granulomatosis with polyangiitis is a small-medium vessel necrotizing vasculitis, which is a part of wide ranges of disorders entitled the anti-neutrophil-cytoplasmic-antibody (ANCA) associated vasculitides (AAV). AAV includes granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA or Churg Strauss syndrome). This classification on the Modern Nomenclature of Systemic Vasculitides was laid down at the Chapel Hill Consensus Conference in 2012. [5] They are characterized by necrotizing vasculitis and positive ANCA titers. The titers are reactive to proteinase-3 (PR3-ANCA), C-ANCA or myeloperoxidase (MPO-ANCA) – pANCA. [1] Environmental pathogens triggers immune system to produce infections or autoantigens by releasing excessive cytokines (Th1 and Th17), which in turn leads to inflammatory granulomatous vascular lesion. Neutrophils granulocytes have an enzyme called proteinase 3 which when reacts with ANCA, induces adherence to endothelium, damaging the endothelium by degranulation. Cytoplasmic-ANCA (c-ANCA) with autoantibodies directed against proteinase 3 antibodies is seen in 80%-90% of the cases with GPA. Other predisposing factors includes genetic association, medications and various infections. [2]

GPA is characterised by necrotising granulomatous lesions of the respiratory tract, vasculitis and glomerulonephritis. [6] In our patient significant involvement of the upper and lower respiratory tract with elevated inflammatory markers and a positive ANCA are consistent with the classic presentation of GPA. A positive c-ANCA is not diagnostic of GPA and requires consideration of the clinical findings, history, and further confirmatory testing such as the ELISA and tissue biopsy. In our case, clinical history and radiological findings are suggestive of vasculitic process. Pulmonary-renal syndromes or lung-kidney syndromes are clinical syndromes defined by a combination of diffuse alveolar haemorrhage (DAH) and glomerulonephritis. It is seen in wide ranges of diseases, including various forms of primary systemic vasculitis (especially Wegener's granulomatosis and microscopic polyangiitis), Goodpasture's syndrome, and systemic lupus erythematosus. [7] In our patient, the pulmonary manifestations are prominent showing diffuse alveolar haemorrhage in both lungs and the renal syndrome manifest parenchymal disease. Dermatologic involvement is reported in 50%-60% of the patients with GPA with purpura commonly involving the lower extremities. [2] Further this study correlates with the clinical symptoms of patient having maculopappular rashes on the shin of the tibia. Other organ system involvement includes nervous system, musculoskeletal system, eye and cardiac system. A thorough histopathological investigation can help confirming the diagnosis.

Management includes immunosuppressants (cyclophosphamide, methotrexate and steroids). Rituximab is as effective as cyclophosphamide for remission induction of previously untreated patients and is preferable when cyclophosphamide avoidance is desirable. Other drug modalities in use are methotrexate, mycophenolate mofetil, glucocorticoids, plasma exchange. [8] In the presented case, injection rituximab therapy was the chosen treatment, showing clinical and laboratorial remission, but cyclophosphamide was not administered in the form of pulse therapy due to a suspicion of pulmonary infection, which would worsen the clinical condition.

Figure 3: Algorithm of the treatment guideline for AAV [8].



CONCLUSION

GPA has complex multifactorial pathology, with different clinical manifestations that leads to early diagnosis and timely start of treatment. Diagnosis is confirmed on biopsy with raised c-ANCA levels. A negative c-ANCA, however, does not exclude the disease. Treatment includes a combination of corticosteroids and immunosuppressants. The correlation of nasal, pulmonary and renal symptoms is important to confirm the diagnosis. A proper pattern-based approach to the radiological findings is required to shorten the list of the differential diagnosis of various pulmonary vasculitides. Inter association between clinical, laboratory, and radiological findings are mandatory for making a reasonably specific diagnosis. With advances in treatment, they have a higher long-term survival rate and have been able to lead a relatively normal life.

REFERENCES:

- Lakhani DA, Balar AB, Adelanwa A, Gross A, Mohamed R, Smith KT, Kim C. Granulomatosis with polyangiitis: A case report and brief review of literature. *Radiol Case Rep.* 2021 Sep 5;16(11):3445-3450. doi: 10.1016/j.radcr.2021.08.028. Erratum in: *Radiol Case Rep.* 2023 Jan 24;18(3):1394-1395. PMID: 34527120; PMCID: PMC8429614.
- Garlapati P, Qurie A. Granulomatosis With Polyangiitis. [Updated 2022 Dec 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK557827/>.
- Chung, Man Pyo et al. "Imaging of pulmonary vasculitis." *Radiology* vol. 255,2 (2010): 322-41. doi:10.1148/radiol.10090105.
- Maqbool U, Maqbool A, Maqbool A, Qadeer A, Mehmood MF, Loon M. An atypical presentation of granulomatosis with polyangiitis: A case report. *Radiol Case Rep.* 2023 Apr 14;18(6):2245-2248. doi: 10.1016/j.radcr.2023.03.023. PMID: 37113631; PMCID: PMC10126852.
- Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, Flores-Suarez LF, Gross WL, Guillevin L, Hagen EC, Hoffman GS, Jayne DR, Kallenberg CG, Lamprecht P, Langford CA, Luqmani RA, Mahr AD, Matteson EL, Merkel PA, Ozen S, Pusey CD, Rasmussen N, Rees AJ, Scott DG, Specks U, Stone JH, Takahashi K, Watts RA. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum.* 2013 Jan;65(1):1-11.
- Greco A, Marinelli C, Fusconi M, et al. Clinic manifestations in granulomatosis with polyangiitis. *International Journal of Immunopathology and Pharmacology.* 2016;29(2):151-159. doi:10.1177/0394632015617063.
- Brusselle, G G. "Pulmonary-renal syndromes." *Acta clinica Belgica* vol. 62,2 (2007): 88-96. doi:10.1179/acb.2007.016.
- Eleana Ntatsaki, David Carruthers, Kuntal Chakravarty, David D'Cruz, Lorraine Harper, David Jayne, Raashid Luqmani, John Mills, Janice Mooney, Michael Venning, Richard A. Watts, on behalf of the BSR and BHRP Standards, Guidelines and Audit Working Group, BSR and BHRP guideline for the management of adults with ANCA-associated vasculitis, *Rheumatology*, Volume 53, Issue 12, December 2014, Pages 2306–2309, <https://doi.org/10.1093/rheumatology/ket445>