A Rare Cause of Diffuse Alveolar Haemorrhage

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37 years old male, labourer, non smoker

Chief complaints:

1. *Breathlessness* - 4 days
   - mMRC grade IV
   - No orthopnoea and PND
2. *Cough* - 5 days
   - Dry in nature
3. *Hemoptysis* - 5 days
   - Frank blood
   - 15-20ml each episode
4. *Fever* -1 day
   - Low grade

Past history:

Migratory Polyarthritis - 3 months back involving large and small joints

Clinical Examination

Vitals :

- Pulse rate: 140/min
- Respiratory rate: 50/min
- Blood pressure: 110/90 mmHg
- SpO2: 64% on room air

General physical examination: -NAD

Systemic Examination

Respiratory system – B/L diffuse inspiratory crackles

Musculoskeletal system – no local joint swelling
no restriction of movement

Other systems - NAD

Laboratory Investigations

HEMOGLOBIN	6.60 g/dL	**LFT**	WNL
TLC	12,700	**PT/INR**	13.4/1.13
PLATELETS	1,28,000	**RFT**	WNL
PBS	Microcytic hypochromic -Iron deficiency anaemia	**URINE MICROSCOPY**	Protein, Glucose } Trace RBCs- 4-5
CRP	16.15	**URIC ACID**	4.60
ESR	30	**UPCR**	0.05

Investigations. . .*contd*

ABG

s/o Acute Hypoxemic Respiratory Failure (type I)

Fio2- 44%
PaO2/Fio2 - 95 → Severe ARDS

pH	7.43
pCO2	40
pO2	42
Hco3	26.5
SpO2	87

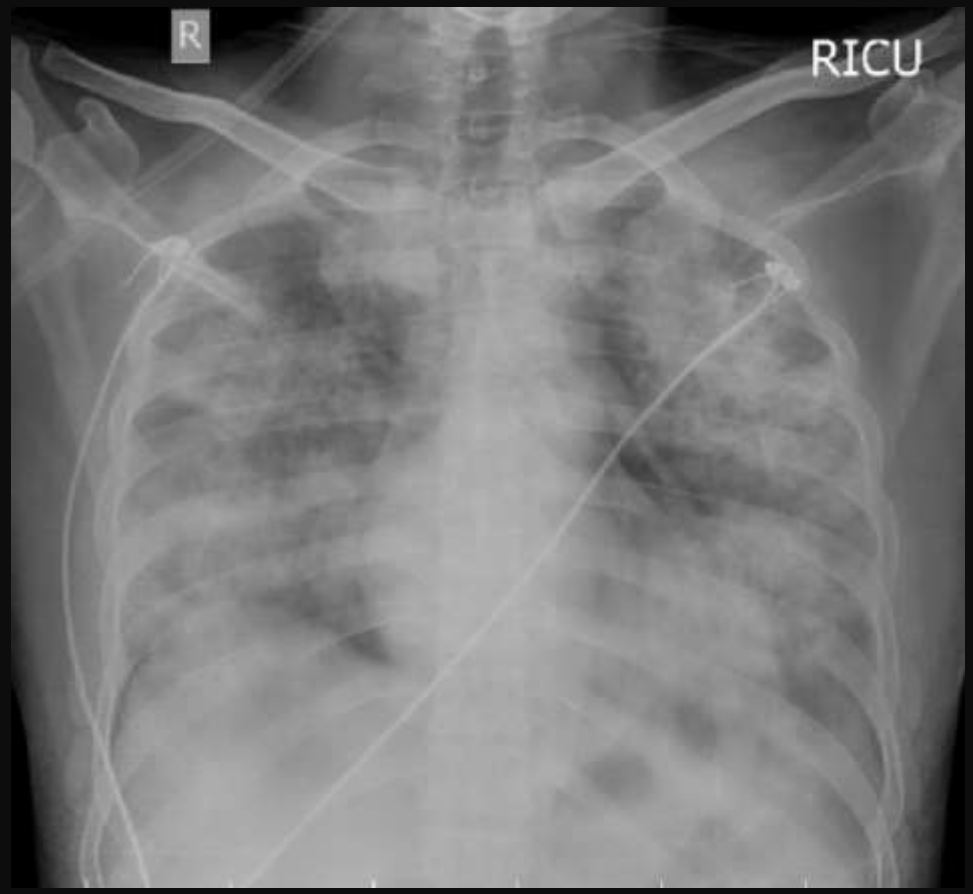
2D ECHO

LVEF-60%, mild PAH, no RWMA

Radiological Investigations

Chest Xray:

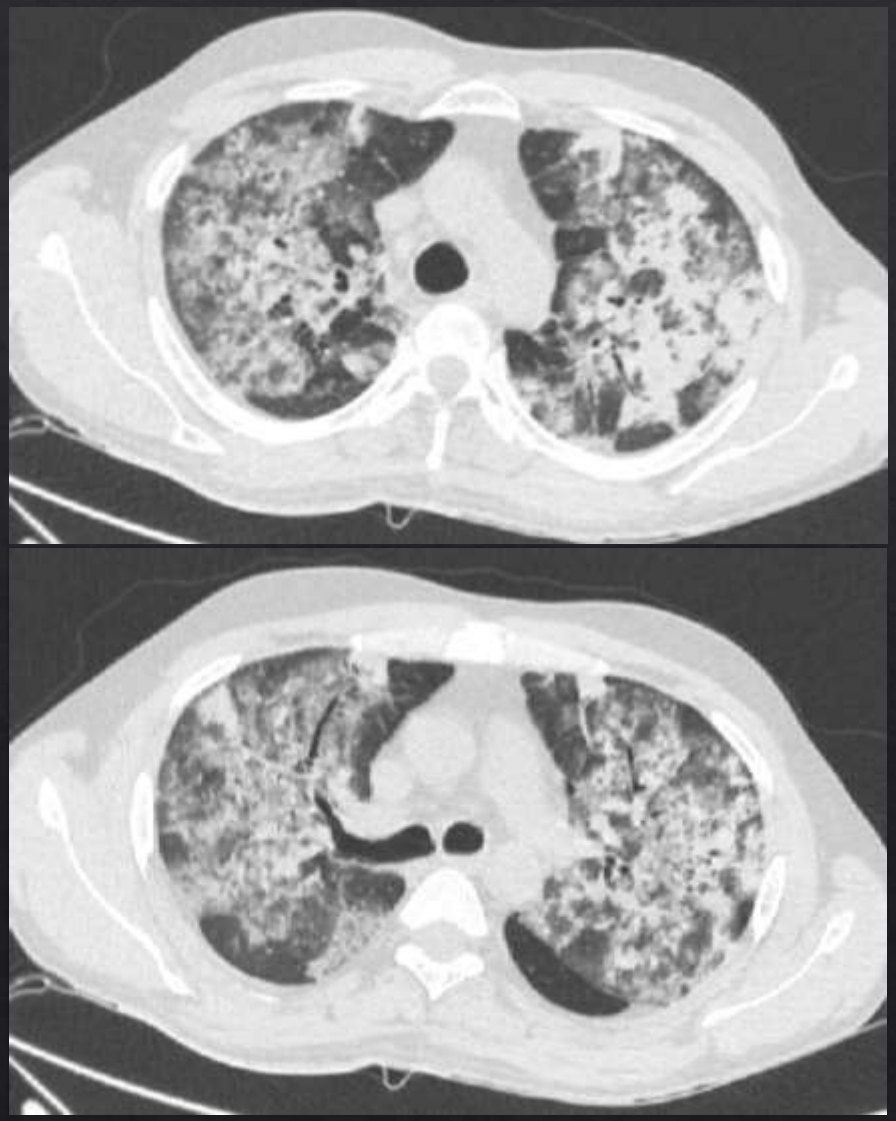
Bilateral diffuse alveolar opacities



Radiological Investigations. . . *contd*

HRCT thorax:

Bilateral multiple ill-defined diffuse GGOs with early alveolar consolidations -central to peripheral involvement with few areas of sparing.



Clinical Impression

1. Diffuse Alveolar Haemorrhage
2. Viral Pneumonia
3. Bilateral Community Acquired Pneumonia

Initial Management

- The patient was started on broad spectrum antibiotics (ceftriaxone) and antiviral therapy.
- High dose Inj Methylprednisolone was initiated.
- Due to persistent tachypnoea and impending respiratory failure, patient was taken on Non-invasive mechanical ventilation.

Investigations…*contd*

Throat swab for viral panel – Negative

RA
Anti CCP
ANA by IF
ANA blot

} Negative

pANCA (MPO)- Negative
cANCA (PR3)- POSITIVE

- Plan:
  Bronchoscopy: BAL with TBLB

BRONCHOSCOPY

- Persistent bloody fluid
- Cytology of the alveolar lavage

⇩

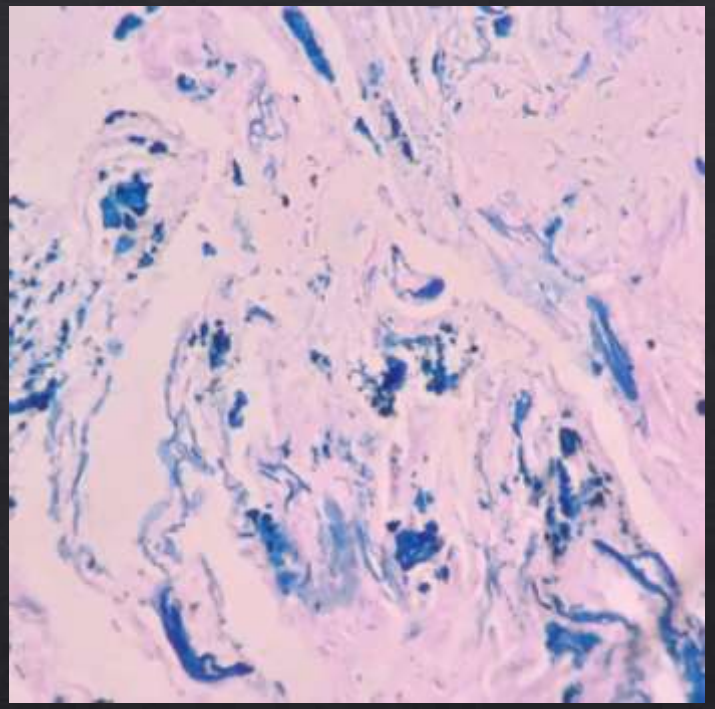
Hemosiderin-laden Macrophages

with no atypical cells

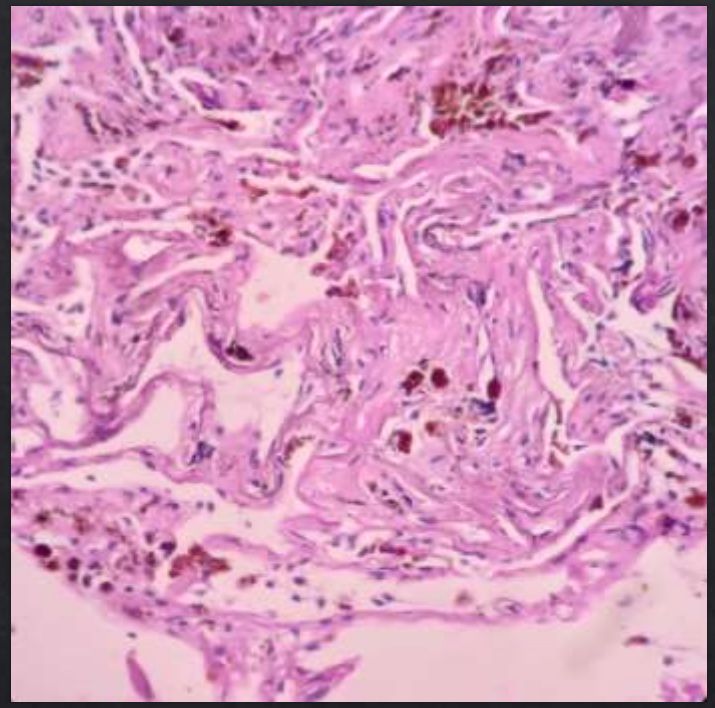
⇩

s/o Alveolar haemorrhage

Transbronchial Lung Biopsy



Prussian blue stain for hemosiderin
Blue granules of hemosiderin



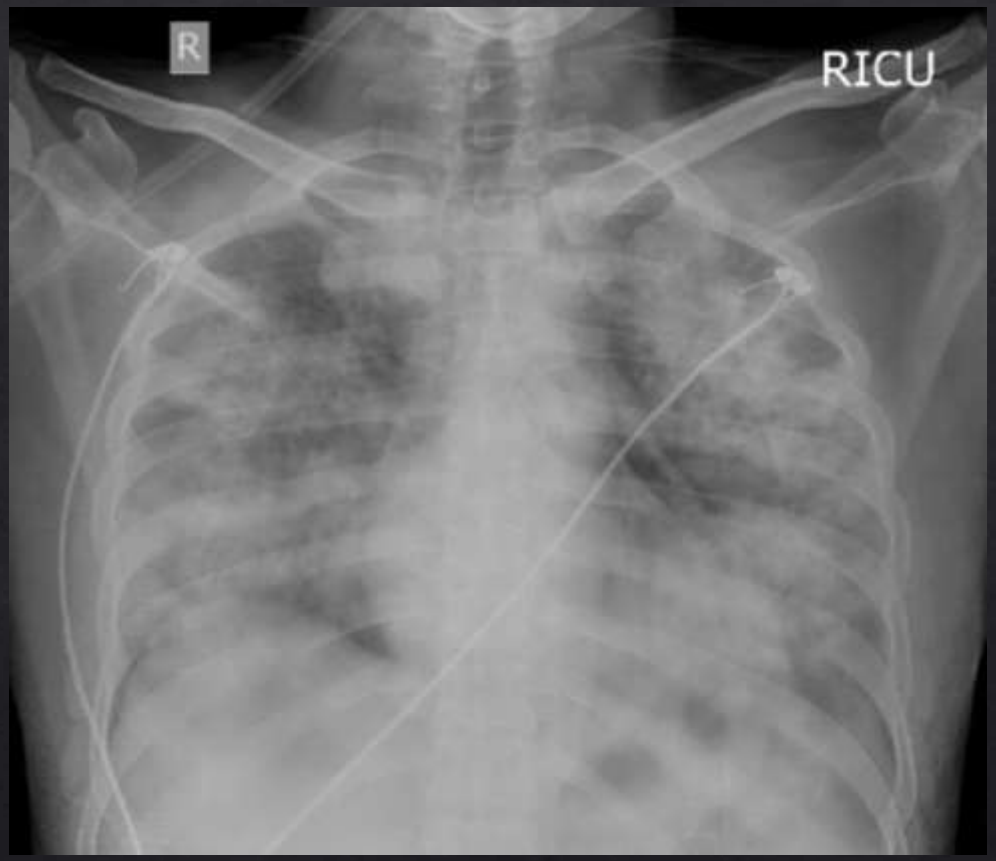
Lung with pigmented macrophages
in alveoli

The biopsy did not show any evidence of granuloma, capillaritis or vasculitis

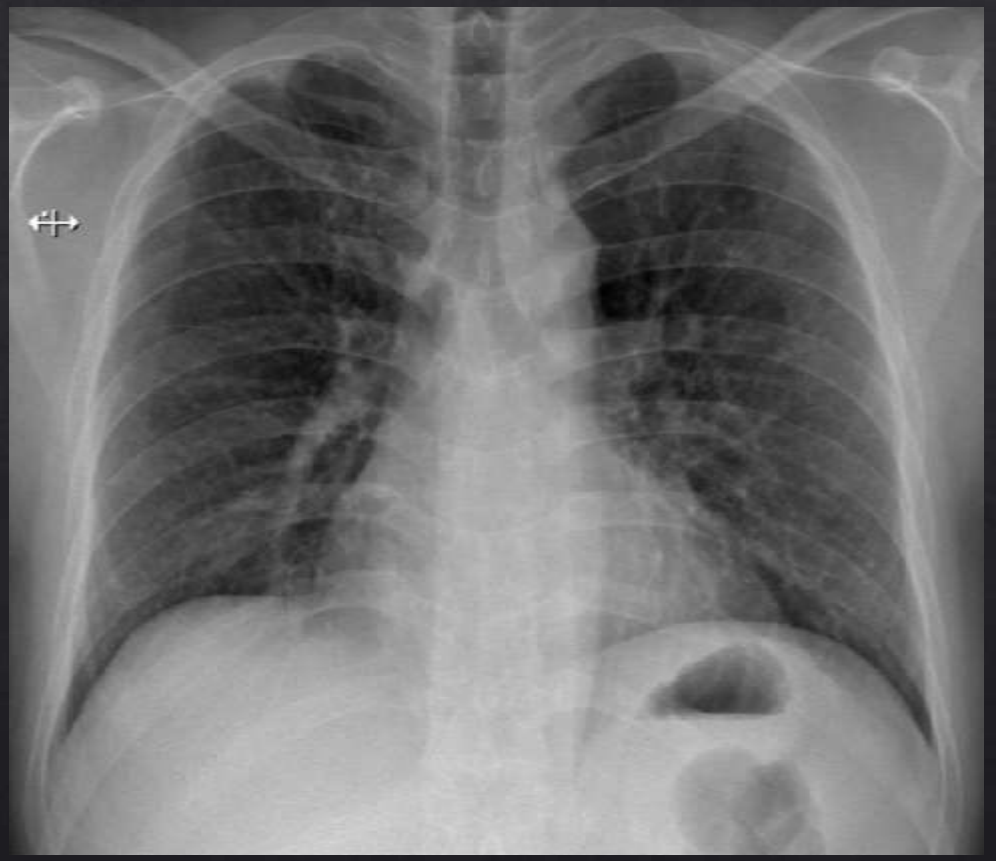
Course in hospital

- Nephrology and ENT consultation was taken, no evidence of renal and ENT involvement.
- 2 weeks after starting on steroids - satisfactory clinical and radiological improvement was noted.
- Oxygen requirement reduced to 4-5L/min, patient was shifted to ward and planned for discharge.

On admission

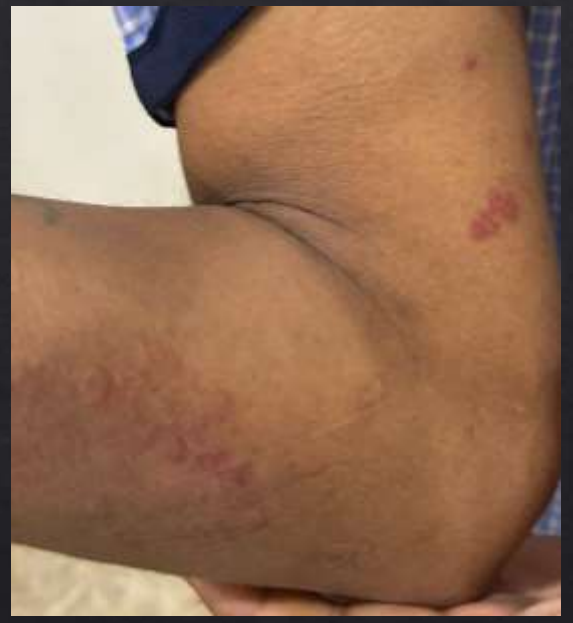


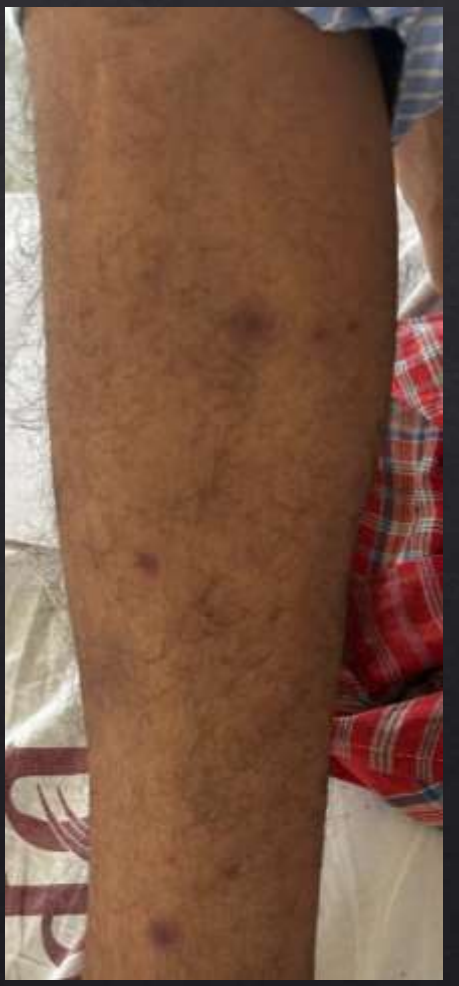
2 weeks later



Course in hospital…*contd*

The patient developed *multiple erythematous purpura and ecchymosis* on the extensor aspects of the upper limbs and lower limbs

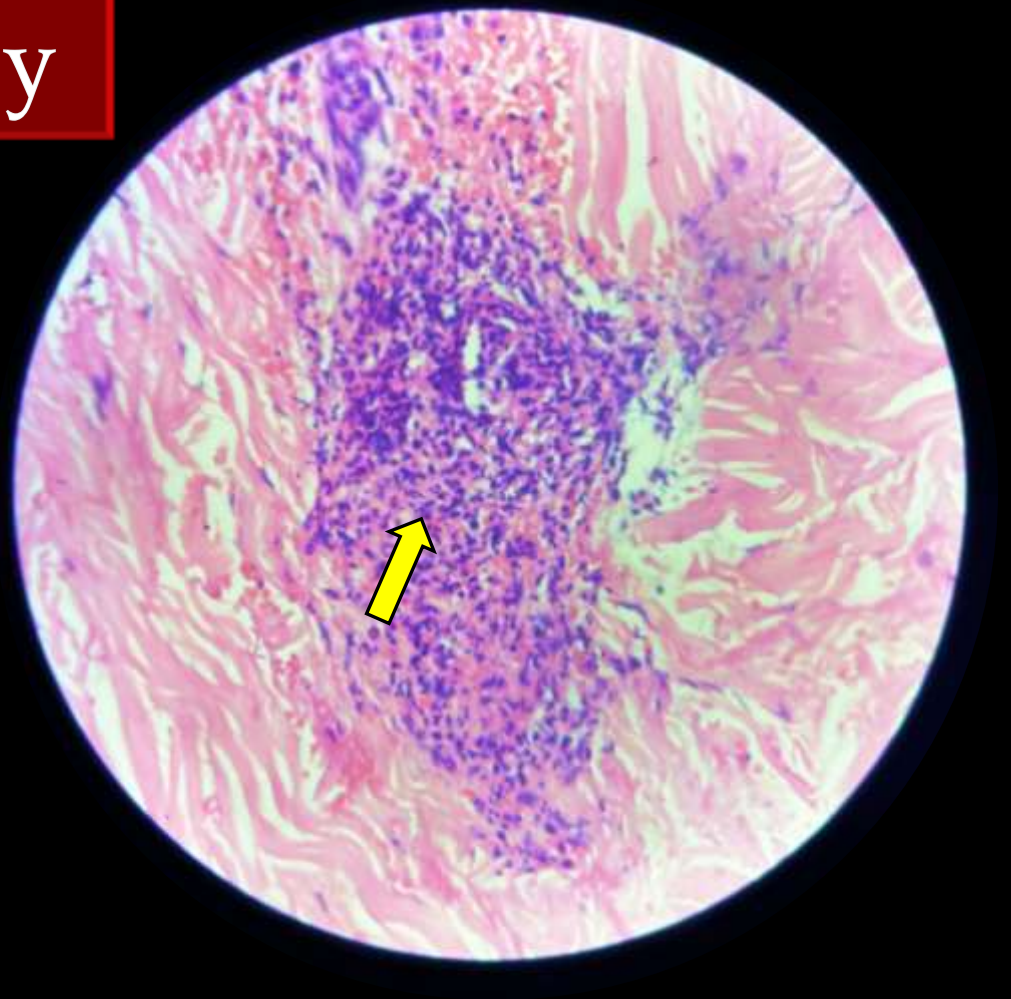




Skin biopsy

Cutaneous Leukocytoclastic Vasculitis

[Small Vessels]



Disruption of small vessel wall lumen with red cell extravasation. Significant infiltration of the vessel with neutrophils, lymphocytes, plasma cells were seen.

Final Diagnosis

Granulomatosis With Polyangiitis (ANCA associated Vasculitis)

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CLASSIFICATION CRITERIA FOR **GRANULOMATOSIS WITH POLYANGIITIS**

CONSIDERATIONS WHEN APPLYING THESE CRITERIA

- **These classification criteria should be applied to classify a patient as having granulomatosis with polyangiitis when a diagnosis of small- or medium-vessel vasculitis has been made**
- **Alternate diagnoses mimicking vasculitis should be excluded prior to applying the criteria**

CLINICAL CRITERIA

Nasal involvement: bloody discharge, ulcers, crusting, congestion, blockage, or septal defect / perforation	+3
Cartilaginous involvement (inflammation of ear or nose cartilage, hoarse voice or stridor, endobronchial involvement, or saddle nose deformity)	+2
Conductive or sensorineural hearing loss	+1

LABORATORY, IMAGING, AND BIOPSY CRITERIA

Positive test for cytoplasmic antineutrophil cytoplasmic antibodies (cANCA) or antiproteinase 3 (anti-PR3) antibodies	+5
Pulmonary nodules, mass, or cavitation on chest imaging	+2
Granuloma, extravascular granulomatous inflammation, or giant cells on biopsy	+2
Inflammation, consolidation, or effusion of the nasal/paranasal sinuses, or mastoiditis on imaging	+1
Pauci-immune glomerulonephritis on biopsy	+1
Positive test for perinuclear antineutrophil cytoplasmic antibodies (pANCA) or antimyeloperoxidase (anti-MPO) antibodies	-1
Blood eosinophil count ≥ 1 x10^9/liter	-4

Sum the scores for 10 items, if present. A score of ≥ 5 is needed for classification of GRANULOMATOSIS WITH POLYANGIITIS.

Follow Up

- The patient in on regular OPD follow up and asymptomatic.
- Oral steroids were tapered on over the period of 2 months.
- Repeat chest Xray shows complete radiological resolution.
- Nephrology review was done and all repeat renal parameters are in normal limits.

Discussion

DAH is characterized by bleeding into the alveolar spaces of the lungs due to disruption of the alveolar-capillary basement membrane.

Classical presentation :

- Dyspnoea
- Cough
- Haemoptysis
- Fall in haematocrit

Causes of diffuse alveolar hemorrhage syndromes (DAH) based on histologic appearance

Capillaritis
Systemic vasculitides
Behçet syndrome
Cryoglobulinemia
Granulomatosis with polyangiitis (Wegener)
Henoch-Schönlein purpura
IgA nephropathy
Microscopic polyangiitis
Pauci-immune glomerulonephritis
Rheumatic diseases
Mixed connective tissue disease
Anti-GBM (Goodpasture) disease*
Isolated pulmonary capillaritis (ANCA positive)
Polymyositis
Primary antiphospholipid antibody syndrome
Rheumatoid arthritis
Systemic lupus erythematosus*

Bland hemorrhage
Connective tissue disease
Anti-GBM (Goodpasture) disease*
Systemic lupus erythematosus*
Drugs
Anticoagulant therapy
Platelet glycoprotein IIB/IIIA inhibitors
Other
Thrombocytopenias (ITP, TTP, HUS)
Idiopathic pulmonary hemosiderosis
Leptospirosis
Mitral stenosis
Promyelocytic leukemia

Diffuse alveolar damage
Infection
Any infection causing ARDS (bacterial, viral)
Opportunistic infections in immunocompromised host
Rheumatic diseases
Polymyositis
Systemic lupus erythematosus
Drugs and toxins
Amiodarone
Amphetamine
Crack cocaine
Cytotoxic drugs
Isocyanates
Nitrofurantoin
Penicillamine
Propylthiouracil
Sirolimus
Trimellitic anhydride

Miscellaneous
Angiosarcoma
Choriocarcinoma
Epithelioid hemangioepithelioma
Metastatic renal cell carcinoma
Pulmonary vein stenosis
Pulmonary veno-occlusive disease/pulmonary capillary hemangiomatosis
Tuberous sclerosis/ Lymphangioleiomyomatosis

However, the transbronchial lung biopsies have shown to be often unhelpful when compared to renal biopsy.

Reumatologia. 2017;55(5):230-236. doi: 10.5114/reum.2017.71638. Epub 2017 Oct 28.

The usefulness of histopathological examinations of non-renal biopsies in the diagnosis of granulomatosis with polyangiitis

Anna Masiak [1], Zbigniew Zdrojewski [1], Rafał Pęksa [2], Żaneta Smoleńska [1], Zenobia Czuszyńska [1], Alicja Siemińska [3], Bożena Kowalska [4], Czesław Stankiewicz [4], Bolesław Rutkowski [5], Barbara Bułło-Piontecka [5]

Affiliations + expand

PMID: 29332961 PMCID: PMC5746633 DOI: 10.5114/reum.2017.71638

DAH is a rare clinical syndrome, with an incidence rate of 2%, and it is a potentially life-threatening condition.

Da Silva RC, Adhikari P. Granulomatosis With Polyangiitis Presenting With Diffuse Alveolar Hemorrhage: A Systematic Review. Cureus. 2022 Oct 4;14(10):e29909. doi: 10.7759/cureus.29909. PMID: 36348918; PMCID: PMC9632681.

4.9 to 10.5 per million cases of GPA are noted annually worldwide.

Stoller, J. K. (2015). Murray & Nadel's Textbook of Respiratory Medicine, 6th Edition. Annals of the American Thoracic Society, 12(8), 1257–1258. https://doi.org/10.1513/annalsats.201504-251ot

The incidence of pulmonary involvement in GPA varies between 62 to 90%, DAH is seen in only *5-15%* of cases.

Stoller, J. K. (2015). Murray & Nadel's Textbook of Respiratory Medicine, 6th Edition. Annals of the American Thoracic Society, 12(8), 1257–1258. https://doi.org/10.1513/annalsats.201504-251ot

Discussion…*contd*

3 Case reports in India

Our case is the 4th case reported in India!!

Diffuse alveolar hemorrhage in Wegener's granulomatosis

Mahajan, Vineet; Whig, Jagdeep; Kashyap, Anil; Gupta, Sushil[1]

Author Information

Lung India 28(1):p 52-55, Jan–Mar 2011. | *DOI:* 10.4103/0970-2113.76302

Case Report

Massive alveolar haemorrhage: a rare life threatening complication of Wegener's granulomatosis—report of a rare case

Richa Arora

Combined diffuse alveolar hemorrhage and venous thrombosis in a patient with granulomatosis with polyangiitis: Case report and systematic review of literature

Madan, Manu; Iyer, Hariharan; Tiwari, Pawan; Mohan, Anant; Madan, Karan; Hadda, Vijay; Mittal, Saurabh; Guleria, Randeep

Clinical Pearls

Though rare, DAH can be the sole and primary presentation of vasculitis.

Bronchoalveolar lavage and biopsy of the effected organ are the key tools in diagnosis of DAH in vasculitis.

Early recognition is crucial and timely intervention is indicated for prompt management.

Thankyou