



## Case report

# Massive hemoptysis: A rare case with uncommon presentation and rapid response – A case report

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## ABSTRACT

We report an unusual case of massive haemoptysis in young patient with mass lesion in left upper lobe. Bronchoscopic biopsy, percutaneous CT guided biopsy & serum marker confirmed the lesion to be granulomatous with polyangiitis (GPA). Rarity of the case was endoluminal bronchial lesion in GPA and radiographic presentation of mass lesion on the Computed Tomography. Also this case highlights that massive haemoptysis can be a sole and initial manifestation of GPA. Prompt diagnosis & pulse therapy led to dramatic symptomatic, clinical & radiological improvement, emphasizing the fact that GPA can present as acute emergency and rapid diagnosis with early treatment initiation with pulse steroid therapy & rituximab can be life saving measure.

## 1. Introduction

Granulomatosis with polyangiitis (GPA) is an uncommon systemic ANCA-associated vasculitis with estimated prevalence of 3 per 100 thousand populations. It is characterized by necrotizing granulomatous inflammation and typically involves small arteries and veins either intravascular or extravascular. Mean age at time of newly diagnosis of limited GPA is about  $47 \pm 16$  years. Despite their younger age, patients with limited disease had a longer mean time since diagnosis compared with those with severe disease [1]. Involvement of upper and lower respiratory tract and kidney are classical triad of GPA, however virtually any organ can be involved.

Tracheobronchial involvement, a less common GPA manifestation, comprises stenosis of the tracheobronchial tree, which can lead to upper airway obstruction and bronchial stenosis & collapse. The diagnosis of GPA is mainly made by the histological demonstration of vasculitis, necrosis, and granulomatous inflammation. Systemic necrotizing vasculitis represents a major challenge in critical care units, thus, early and accurate diagnosis and aggressive treatment are essential to improve outcome. The occurrence of diffuse alveolar haemorrhage sometimes leading to massive haemoptysis in such disorders is a sign of severe disease. Because the associated mortality is high & treatment of GPA is more specific, it is important to differentiate diffuse alveolar haemorrhage from other causes of haemoptysis [2].

## 2. Case report

A 25-year-old male presented with blood stained expectoration of about 300 ml/day since 2 days and chest pain since one week with no similar complaints in past. He had history of shortness of breath and wheeze during childhood with no significant past and family history. On examination patient had tachypnea & tachycardia and saturation (SPO<sub>2</sub>) of 96% on room air. On auscultation left upper lobe crackles were heard. Laboratory findings were Haemoglobin 13.6 gm/dl, total leucocyte count of 15,500 cells/mm<sup>3</sup>, ESR 44 mm/hr, Serum IgE 800IU/ml, sputum AFB stain and gene expert were negative. Liver function test, urine routine, renal function tests were within normal limits. Chest radiograph PA view (Fig. 1) revealed non homogenous opacity left upper and mid-zone. CECT chest (Fig. 2A and B) was suggestive of heterogeneously enhancing lesion measuring  $6.4 \times 6.8 \times 5.6$ cm with internal areas of necrosis and surrounding ground glass attenuation in apico-posterior segment of left upper lobe with narrowing and partial occlusion of left apicoposterior segmental bronchus with few enlarged intrapulmonary lymphnodes. Videobronchoscope showed soft tissue endoluminal lesion completely occluding left upper lobe segments which bleeds on biopsy (Fig. 3). Bronchoscopic lavage, brushings and biopsy were done from left upper lobe lesion. Subsequently CT guided percutaneous biopsy was also performed from left upper lobe lesion.

Pending the reports patient was discharged. He got re-admitted after 5 days with persistent haemoptysis of about 100–200 ml, worsening of

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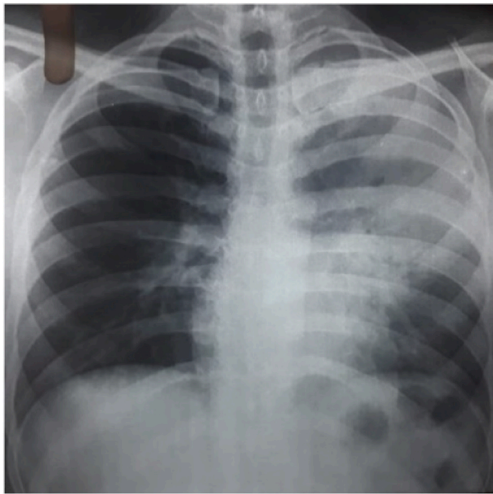
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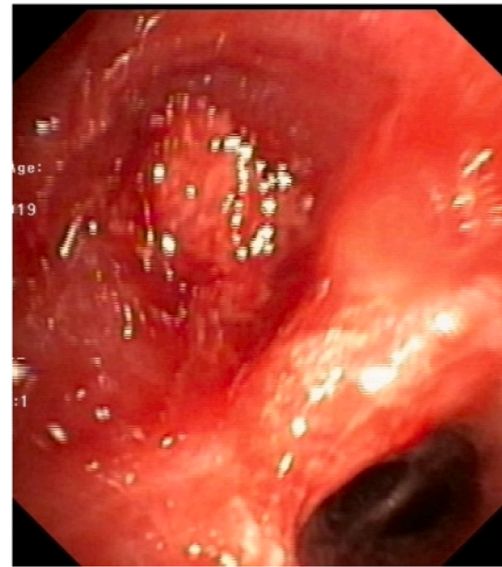


**Fig. 1.** Chest X-ray PA view revealed non-homogenous radio dense opacity in left upper and midzone.

breathlessness and hypoxia with saturation of 88% on room air. His chest radiograph showed significant worsening of left upper lobe lesion. Patient was started on oxygen through nasal canula @ 2 L per minute, haemostatic agents & parenteral antibiotics.

Bronchial lavage was negative for AFB stain by Ziehl-Neelsen stain and on Gene Xpert, Mycobacterium TB was not detected. Bronchial lavage was also negative for malignant cells on cytological analysis with no growth on aerobic culture. On histopathology (Fig. 4A and B) endobronchial biopsy was suggestive of capillaritis with leucocytoclasia and infiltration by both acute and chronic inflammatory cells and occasional multinucleated giant cells. Histopathology of both bronchoscopic and CT guided biopsy showed granulomatous inflammation with multinucleated giant cells and microscopic haemorrhage suggestive of vasculitis. Further laboratory findings revealed a strongly positive value by enzyme-linked immunosorbent for antibodies anti PR3 autoantibodies (9.9IU/ml) and negative for MPO (<0.2IU/ML).

A diagnosis of Granulomatosis with polyangiitis was made on basis of clinico-histopathological and serological evidence. Our patient was classified as having limited disease on basis of fulfilment of modified American College of Rheumatology criteria [3] for the classification of GPA. Following the diagnosis, patient was started on intravenous methylprednisolone 1000mg in 250ml NS over 2 hours 3 days. Rituximab was given intravenously as four doses of 375 mg/m<sup>2</sup> at weekly intervals (plus prednisolone 100mg on the day of infusion). Chest x-ray (Fig. 5) after one week of therapy showed significant clearance of left upper zone lesion along with clinical improvement with amelioration of breathlessness and haemoptysis.

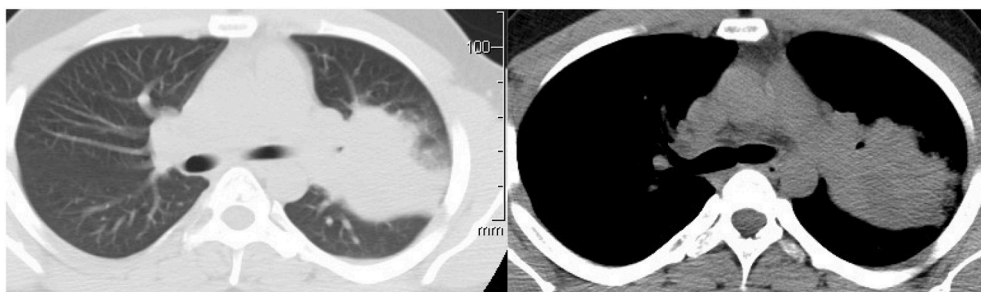


**Fig. 3.** Bronchoscopic findings revealed soft tissue endoluminal lesion completely occluding left upper lobe segments.

### 3. Discussion

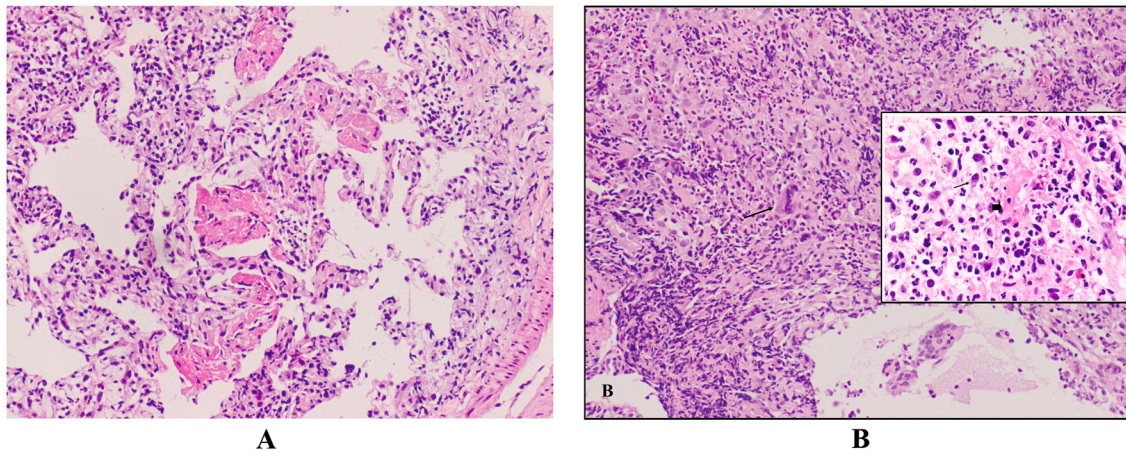
Granulomatous polyangiitis frequently presents with severe upper respiratory tract clinical manifestations like paranasal sinus pain and drainage, purulent or bloody discharge, deafness, cough, and skin lesions (such as vasculitic rash or mucosal ulcers) [2]. Pulmonary involvement manifests as asymptomatic infiltrates or may be clinically expressed as cough, breathlessness and hemoptysis. Hemoptysis when present is usually due to cavitating nodules or diffuse alveolar haemorrhage (DAH). Our case was unusual as presentation was of recurrent massive hemoptysis due to endobronchial vascular mass lesion of GPA causation. Endobronchial disease is less common than tracheal lesions and either presents as active form or as result of fibrous scarring that often results in obstruction with atelectasis.

Antineutrophil cytoplasmic antibodies (c-ANCA) with specificity for proteinase 3 (PR3) are a defining feature of this disease. Usually c-ANCA testing is a screening test for diagnosis. Positivity is not conclusive also a negative c-ANCA test does not exclude the diagnosis, and biopsy remains the standard means of diagnosis, though not feasible in few cases. Positive findings at immunofluorescence testing for c-ANCA should always be confirmed with enzyme-linked immunosorbent for antibodies directed against proteinase [3]. Pulmonary involvement of granulomatous polyangiitis typically presents as multiple, bilateral, nodular cavitary infiltrates, which on biopsy invariably reveal histopathological hallmarks like necrotizing vasculitis of small arteries and veins in form of granulomas. Renal involvement is characterized by focal and segmental glomerulitis with absence of immune complex deposition that



**Fig. 2.** Chest CT showed heterogeneously enhancing lesion measuring 6.4 × 6.8 × 5.6cm with internal areas of necrosis and surrounding ground glass attenuation in apico-posterior segment of left upper lobe with partial occlusion of left apicoposterior segmental bronchus.





**Fig. 4.** Endobronchial biopsy was suggestive of capillaritis with leucocytoclasia and infiltration by both acute and chronic inflammatory cells and occasional multinucleated giant cells.



**Fig. 5.** Follow-up chest X-ray PA view suggestive of complete radiological clearance after one week of steroid therapy.

may end up in rapidly progressive crescentic glomerulonephritis. ANCA are present in 75–87.5% of cases, of these 90% are directed against proteinase 3 (PR3) being highly specific for GPA [4].

The typical radiological finding of GPA include bilateral, multiple rounded opacities either nodules or masses ranging up to 10 cm in diameter [5]. Acute air space consolidation or ground glass opacities secondary to pulmonary haemorrhage is the second most common radiographic finding and may occur with or without the presence of nodules [6]. With progressive disease, nodules and masses tend to increase in size and coalesce. Most nodules are larger than 2 cm and tends to cavitate. These Cavities are usually thick walled with irregular inner margin. The halo sign (a rim of ground-glass opacity surrounding the pulmonary lesion) is seen in up to 15% of cases [7]. Airspace patchy consolidations and diffuse ground-glass opacities are the second most common radiographic finding (20%–50% of cases) and may be seen with or without associated lung nodules. Solitary mass lesion on CT is an uncommon & rarely reported radiological manifestation of GPA. Solitary mass lesions mimicking malignancy and diagnosed after post-operative resections as GPA have been described in the literature similar to our case [8]. There has been a report of pulmonary pseudotumor as a presentation of GPA too [9].

Pulmonary tissue offers the highest diagnostic yield by demonstrating necrotizing granulomatous vasculitis with or without

granuloma. Bronchoscopy usually shows increasingly blood stained aspirates on sequential lavage, and hemosiderin laden macrophages may be present [2]. Involvement of the airways can be the only manifestation in 25% of the GPA [10] and it can cause alterations in any segment of the airways including inflammation, ulceration, pseudomembranes, tracheobronchomalacia, destruction of cartilages, endobronchial masses, and laryngeal tracheobronchial stenoses [11]. Bronchial abnormalities in form of bronchial wall thickening in the segmental and sub segmental bronchi have been reported in 40%–70% of patients [12]. Bronchiectasis is seen less frequently (10%–20%) [13,14]. There have been isolated cases reports of lobar atelectasis caused due to endobronchial lesions [15]. Our case showed endoluminal soft tissue vascular lesion completely occluding left upper lobe segments. Bronchoscopy helps in the diagnosis and follow up of such alterations, as well as treatment to re-establishment of the functional airway patency.

Granulomatous polyangiitis is universally fatal within a few months of diagnosis if left untreated. Glucocorticoid alone are effective in symptomatic improvement, with little effect on the ultimate course of the disease. The destruction of nasal cartilage in GPA is mainly mediated by fibroblasts that can be blocked by corticosteroids [16]. The combination of high-dose corticosteroids and cyclophosphamide is the mainstay of treatment for the vasculitis, and disease resistance to this combination is rare [17]. Marked improvement can be seen >90% of patients with cyclophosphamide and complete remission in 75% & >80% five-year survival rate. Combination of cyclophosphamide with corticosteroids daily dosage has been proven for effective remission and prolong survival.

Rituximab (RTX), an anti-CD20 chimeric monoclonal antibody, provides an alternate option to cyclophosphamide in the induction therapy and DAH caused by GPA. RTX induction and low-dose maintenance can effectively and safely induce sustained remission in GPA [18]. Mild-to-moderate infusion reactions can occur during or after treatment with RTX, and prophylactic intravenous methylprednisolone and antihistamine are advised. We treated our patient with rituximab 375 mg/m<sup>2</sup> with high dose corticosteroid with dramatic radiological melting of the lung lesion and improvement of dyspnea and stoppage of haemoptysis. Patient is presently on follow treatment with good response.

Our patient presented with complaints of haemoptysis, lung mass like appearance and endobronchial lesion. Patient had limited GPA with atypical presentation resulted in difficulty diagnosis. Pulmonary haemorrhage reflects severe active vasculitis and the risk of death is high. Prompt aggressive treatment is crucial and referral to a specialist centre should be considered at an early stage.

#### 4. Conclusion

Granulomatous polyangiitis should also be considered as one of the differential diagnosis for heterogeneous lung mass with massive haemoptysis and polypoidal endobronchial lesion with segmental stenosis. Vasculitis markers like MPO & PR3 antibodies have a crucial role in diagnosing such cases early in conjunction with biopsies which may not be feasible in all cases due to acute nature of disease or massive haemoptysis. Early diagnosis is crucial to disease outcome, since aggressive therapy with high-dose corticosteroids and cytotoxic agents is life-saving in this condition.

##### 4.1. Clinical pearls

1. Massive haemoptysis can be a sole & primary manifestation of GPA & should be considered as one of the differential diagnosis in young patients with haemoptysis.
2. Mass lesion on CT can be atypical radiological manifestation of GPA.
3. Rarely GPA can be limited to lung without systemic involvement and endobronchial soft tissue vascular lesions can also be an uncommon bronchoscopic presentation.
4. In patients with haemoptysis on unclear aetiology there is a role for screening with MPO & PR3 antibodies for early diagnosis.
5. GPA can present as a fulminant disease with rapid progression and is a medical emergency. However accurate, timely diagnosis and prompt therapy can make a significant impact in terms of disease outcome.

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