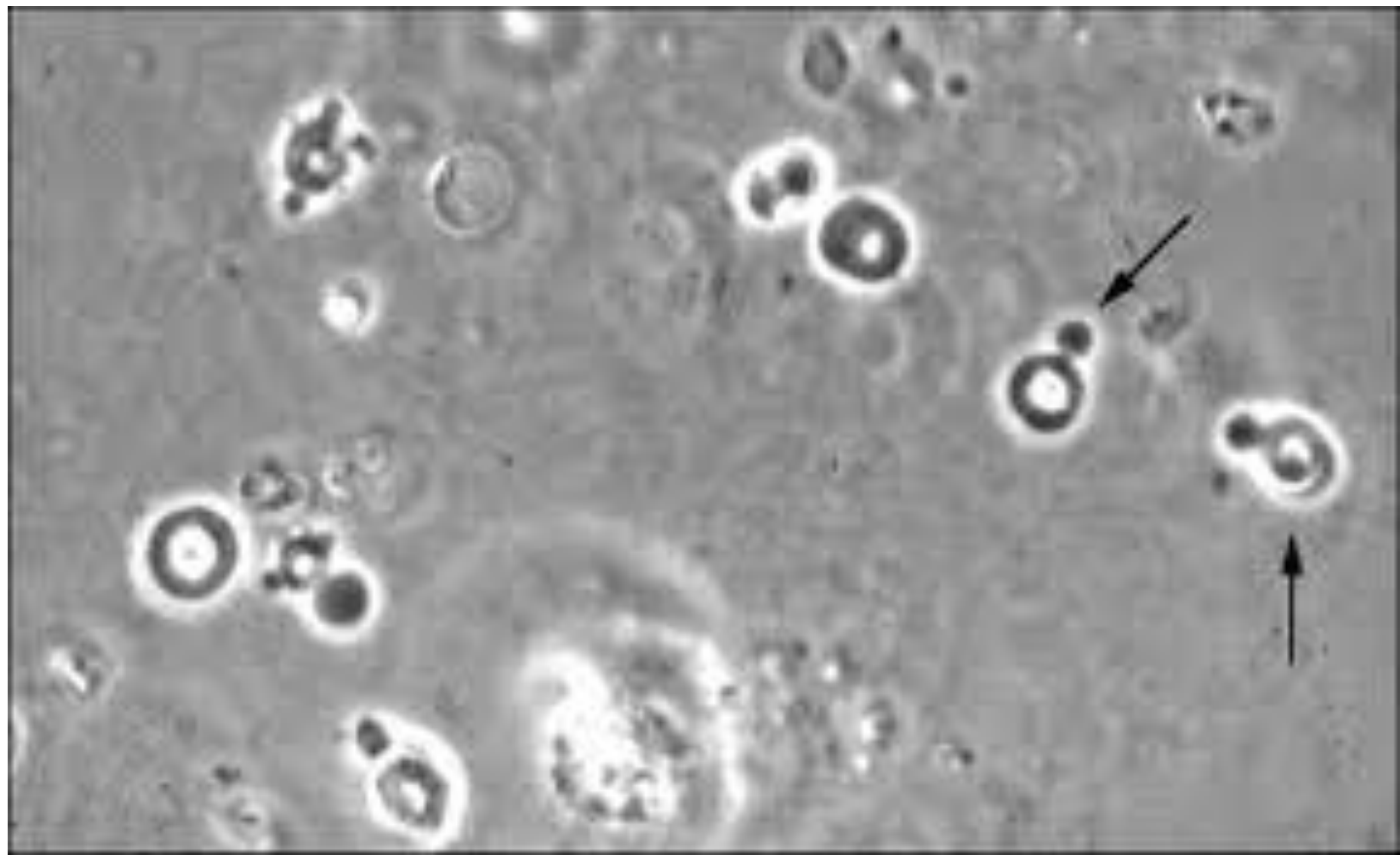


Introduction

- Granulomatosis with polyangiitis (GPA) is characterized by the classic triad of respiratory tract granulomatous inflammation, systemic small vessel vasculitis, and necrotizing glomerulonephritis.
- The gold standard for diagnosis of GPA is tissue biopsy involving the skin, lung, or kidney
- The diagnosis of GPA can be made without tissue biopsy when a patient presents with the classic symptoms for GPA and are found to be positive for cytoplasmic-ANCA (c-ANCA) and anti-proteinase 3 (anti-PR3) antibody.



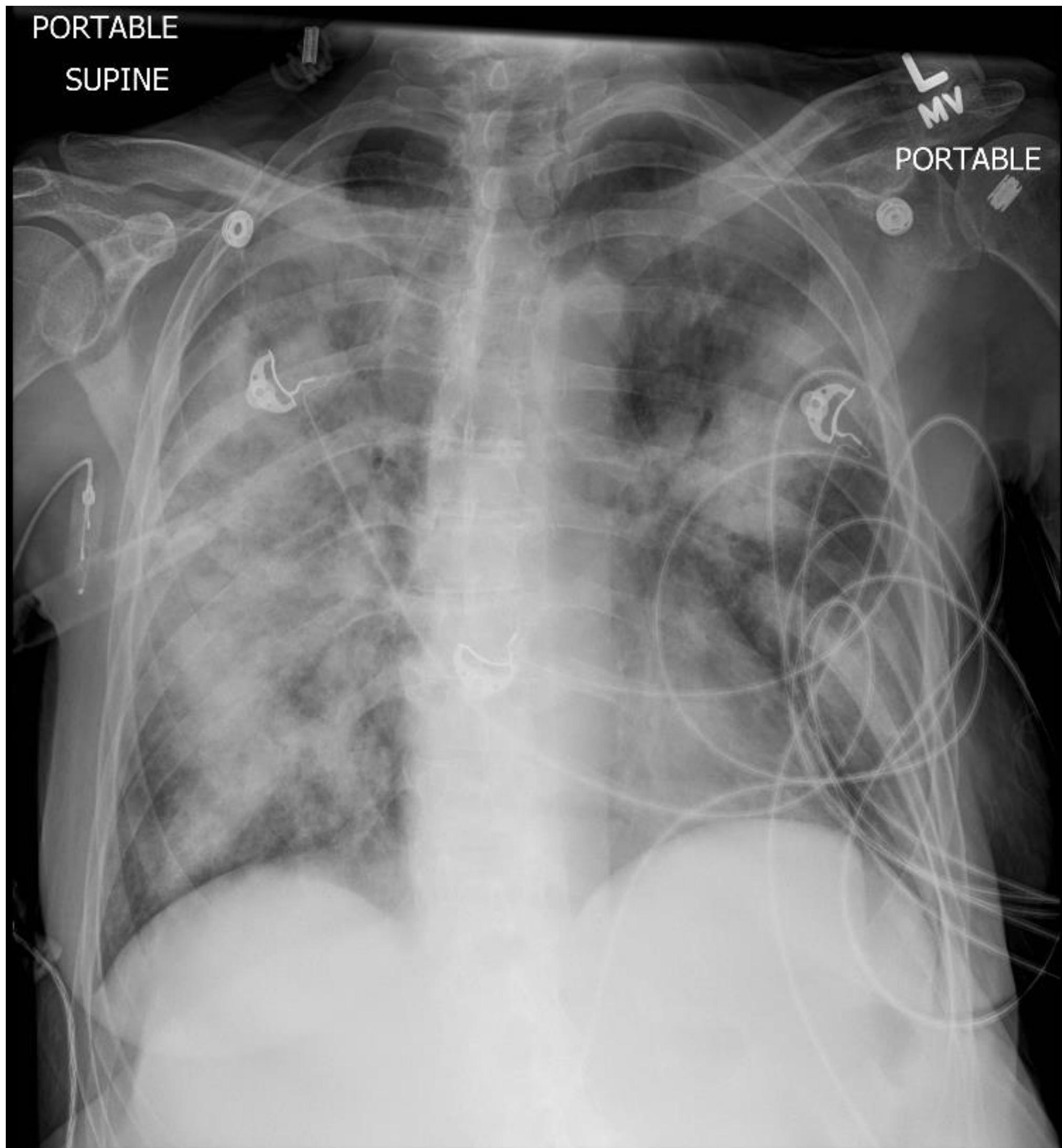
Dysmorphic red blood cells in the urine

Case Description

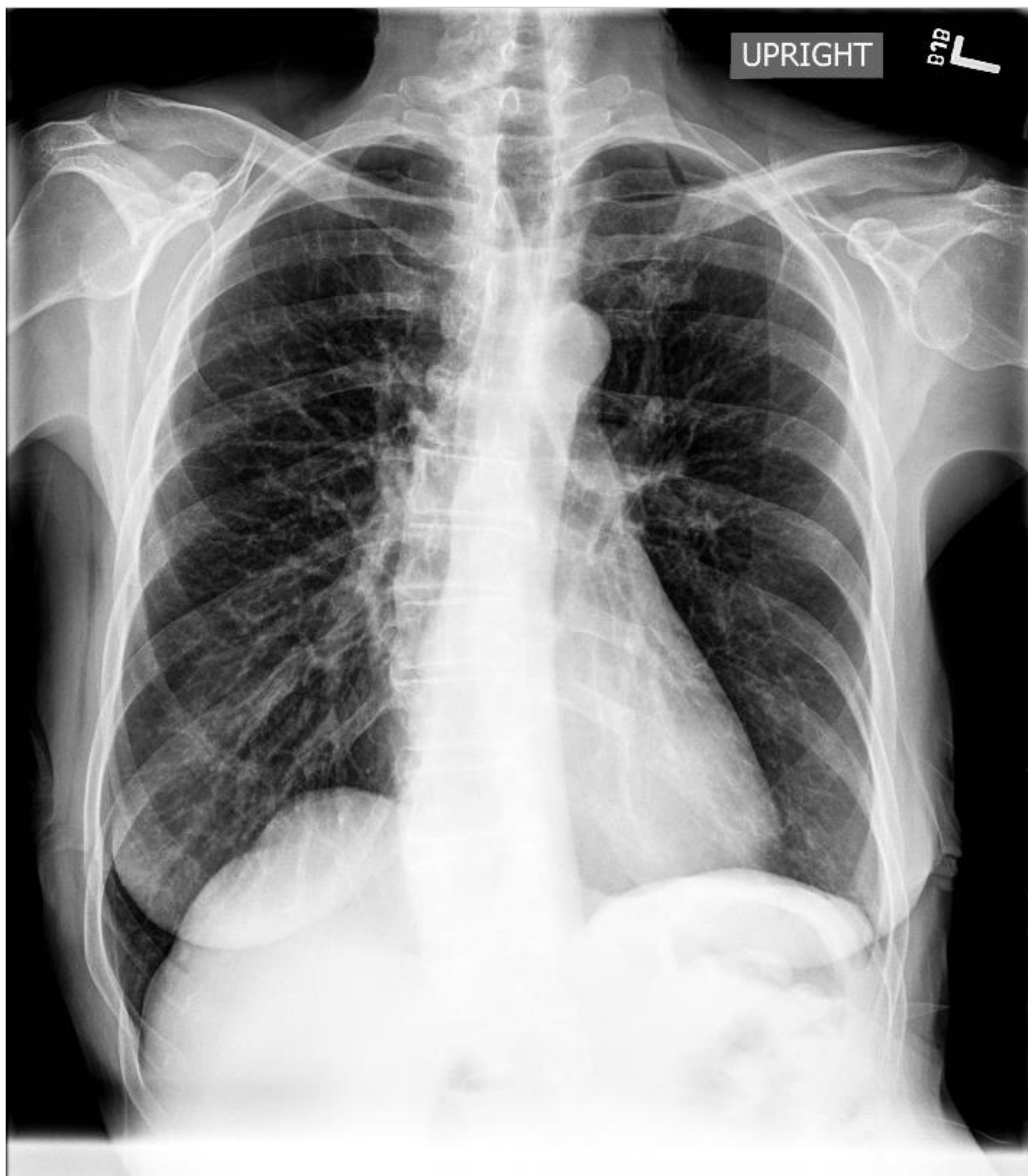
- A 64-year-old Caucasian woman presented to an outside hospital with two weeks of myalgias, arthralgias, malaise, and one week of lingual ulcers in the setting of recent sinusitis.
- Past medical history includes a Roux-en-Y for weight loss, major depressive disorder, and a former 50 pack year smoker.
- Labs at the outside hospital notable for mild leukocytosis (12.6 K/cu mm), anemia (Hgb 11 g/dL), AKI with creatinine 1.29 mg/dL, ESR 79 mm/hr, CRP 17.6 mg/dL, UA with 3+ blood, 2+ protein and 167 RBCs per HPF, and a positive ANA.
- Chest radiograph with bilateral upper and lower lobe consolidations.
- At the outside hospital, she was started on ceftriaxone and azithromycin for community acquired pneumonia and steroids for lupus pneumonitis. She subsequently developed hemoptysis with worsening hypoxia and bilateral infiltrates on chest radiograph necessitating a transfer to the OHSU ICU for management of acute hypoxemic respiratory failure.

Clinical Course

- On hospital day one, she had several episodes of hemoptysis with increasing oxygen requirements and worsening opacities on chest radiograph concerning for diffuse alveolar hemorrhage.
- She was treated empirically on high dose methylprednisolone for diffuse alveolar hemorrhage. Her c-ANCA and anti-PR3 antibody were found to be positive.
- Her urine sediment showed a urine protein to creatinine ratio of 1.55 without red blood cell casts or dysmorphic red blood cells.
- Due to her minimal renal involvement and positive c-ANCA and anti-PR3 antibody results, tissue biopsy was not performed and a presumptive diagnosis of GPA was made based on the classical clinical picture.
- Her induction therapy consisted of rituximab in addition to high dose corticosteroids
- The induction therapy led to resolution of her hypoxemic respiratory failure, glomerulonephritis, and hemoptysis.
- She was able to discharge on hospital day eight.



Chest x-ray on presentation



Chest x-ray 24 days after initiation of rituximab

Discussion

- The classification of the ANCA positive pulmonary-renal syndromes typically occurs via pathology results on biopsy and/or ANCA serology.
- Microscopic polyangiitis is distinguished from GPA and eosinophilic granulomatosis with polyangiitis by the absence of granulomas on lung biopsy.
- In regards to classification by ANCA serology, microscopic polyangiitis is classically associated with perinuclear-ANCA (p-ANCA) and the myeloperoxidase antibody (anti-MPO), while GPA is often associated with c-ANCA and anti-PR3.
- The combination of positive c-ANCA and anti-PR3 antibody in the appropriate clinical picture, has a 99% specificity and a positive likelihood ratio of 73 for the diagnosis of GPA.
- The combination of positive c-ANCA and anti-PR3 antibody has a sensitivity of 73% and a negative likelihood ratio of 0.27.

Take Home Points

- The combination of positive c-ANCA and anti-PR3 antibody in the appropriate clinical picture, has a 99% specificity and a positive likelihood ratio of 73 for the diagnosis of GPA.
- The diagnosis of GPA can be made without tissue biopsy when a patient presents with the classic symptoms for GPA and are found to be positive for cytoplasmic-ANCA (c-ANCA) and anti-proteinase 3 (anti-PR3) antibody.
- Early diagnosis and initiation of immunosuppressive therapy is important in GPA, as the one year mortality rate if left untreated is 80%.

References

- Watts R et al. Development and validation of a consensus methodology for the classification of the ANCA-associated vasculitides and polyarteritis nodosa for epidemiological studies. *Ann Rheum Dis.* **66**:222-227, 2007.
- Hagen EC et al. Diagnostic value of standardized assays for anti-neutrophil cytoplasmic antibodies in idiopathic systemic vasculitis. *Kidney International* **53**:743-753, 1998.
- Walton EW. Giant-cell granuloma of the respiratory tract (Wegener's granulomatosis). *Br Med J* **2**:265–70, 1958.
- Fauci AS, Haynes BF, Katz P, *et al.* Wegener's granulomatosis: prospective clinical and therapeutic experience with 85 patients for 21 years. *Ann Intern Med* **98**:76–85, 1983.