

Case 17

J.W. is a 48 year-old man who presented to CPMC with one day of hemoptysis (coughing up blood) and a 6 month history of headache, intermittent cough, arthralgias (joint pains), 10 pound weight loss and intermittent fevers. One month prior to admission during an evaluation of his headache he was found to have sinusitis that was treated with antibiotics without success. There was no other past medical history and he denied the use of tobacco, alcohol, or other drugs. There was no known exposure to tuberculosis. On physical exam he had râles in both lower lung fields, swelling of his knees and wrists, and an ulcer in the right nares. Pertinent laboratory studies showed a Hct 25% (normal > 36%), urinalysis with 3+ protein,¹ and 25-50 RBC per high powered field;² creatinine 3.7 mg/dl (elevated); normal liver function tests. His chest X-ray showed a diffuse infiltrate in the mid-lung fields bilaterally (Fig. 1) with several cavitary lesions confirmed by chest CT (Fig. 2). Skin tests were positive for *Candida* but a PPD (test for TB) was negative.

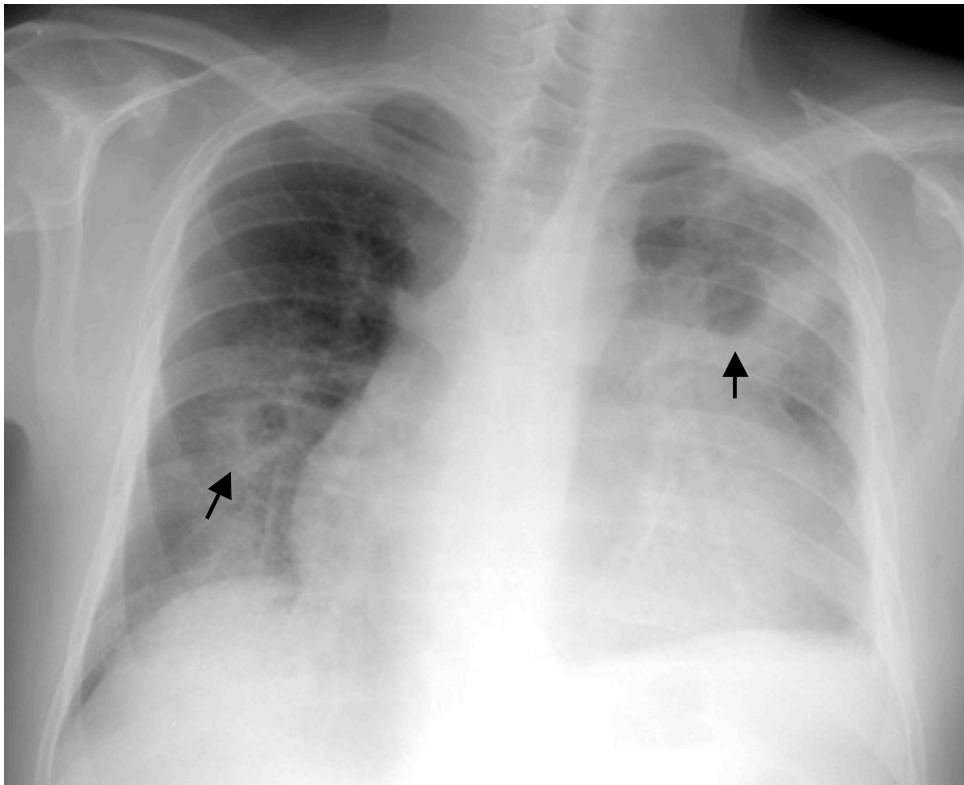


Fig. 1. PA chest chest X-ray of J.W. on presentation to CPMC. Arrows point to possible cavitary lesions.

Serological studies were negative for rheumatoid factor, ANA and anti-DNA antibodies. A c-ANCA was positive. Biopsy of the nasal ulcer and the lung yielded similar lesions showing vessel walls invaded by inflammatory cells including lymphocytes and monocytes. Some of the lesions appeared granulomatous; AFB (acid fast bacilli) and fungal stains were negative. The diagnosis of Wegener's Granulomatosis was made and the patient was treated with prednisone and cyclophosphamide. The patient improved and his renal function and chest X-ray returned to normal within several months of therapy.

Case 17, cont'd

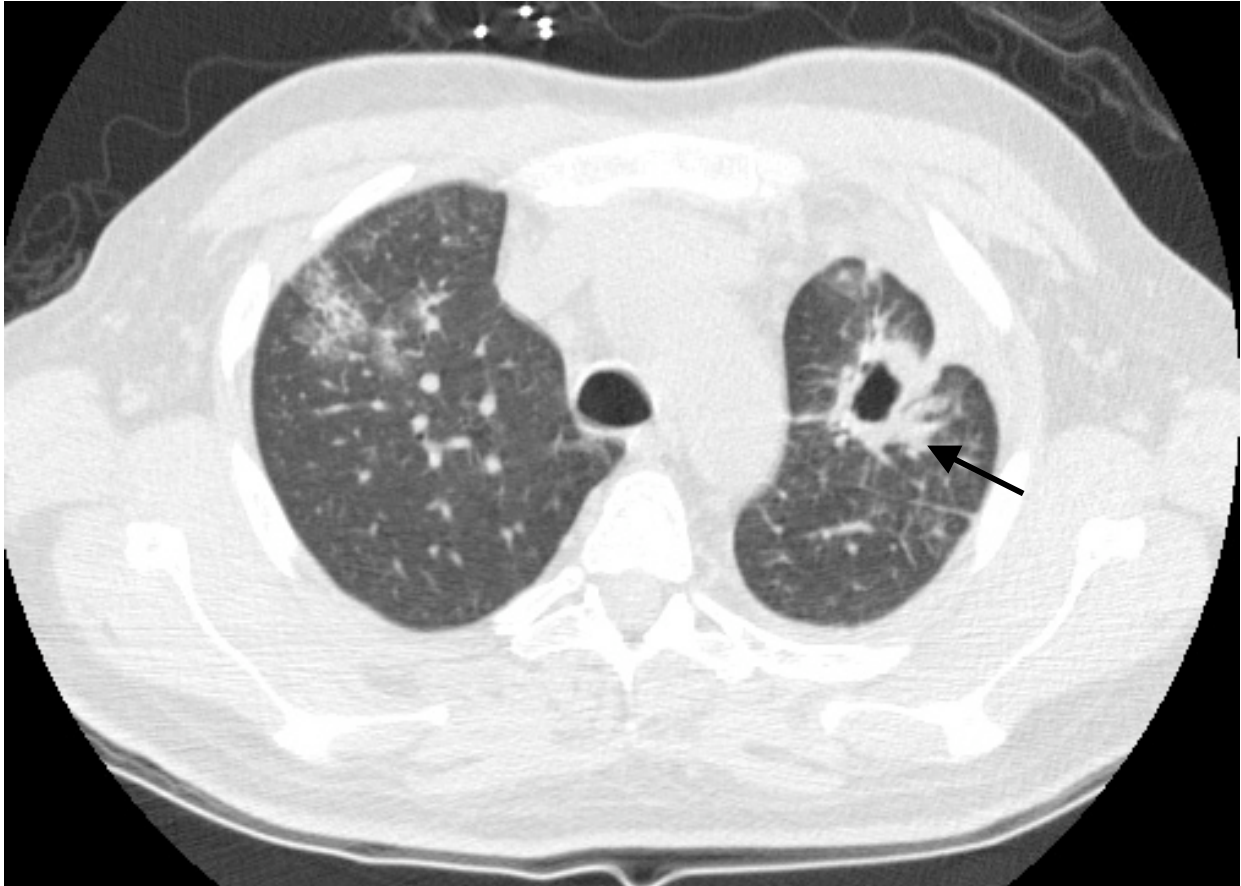


Fig. 2. Chest CT of J.W. demonstrating cavitory lesion in left upper lobe of the lung (arrow).

¹Indicative of renal disease characterized by abnormal loss of protein in the urine

²Hematuria, or blood in the urine, usually indicating intrinsic renal disease

Questions for Case 17

- (1) How does the immunopathology of Wegener's granulomatosis differ from SLE or polyarteritis nodosa?
- (2) What is known about the mechanism of granuloma formation? What is the differential diagnosis of granulomas in a pathological lesion?
- (3) What is a c-ANCA and describe briefly how it is performed. How does it differ from p-ANCA?

(4) A recent study emphasized the critical role of ANCA in the pathogenesis of vasculitis (Xiao et al, *J. Clin. Invest.* 110:955, 2002). In this study, the authors immunized mice lacking the gene that encodes myeloperoxidase (MPO) with MPO. Splenocytes from these mice were injected intravenously into *Rag2*^{-/-} mice; all developed severe necrotizing glomerulonephritis, granulomatous inflammation and systemic necrotizing vasculitis. Additional studies show that direct intravenous injection of anti-MPO antibodies, derived from MPO-immunized MPO-deficient mice, into wild-type or *Rag2*-deficient mice, resulted in focal necrotizing glomerulonephritis. What do these results say about the possible role of auto-antibodies in Wegener's granulomatosis?