c-ANCA Positive Necrotizing Crescentic Glomerulonephritis with Linear Immunoglobulin Staining

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Learning Objectives

1. Patients presenting with suspected pulmonary-renal syndrome should be tested for both anti-MPO (p-ANCA) and anti-PR3 (c-ANCA)
2. Pulmonary renal syndromes present with a spectrum of immunohistochemical features, with rare instances of overlap.
3. Immunohistochemical patterns of overlap may have prognostic implications for patients.

Introduction

Necrotizing crescentic glomerulonephritis is found in anti-glomerular basement membrane (GBM) disease (Type 1), immune complex (Type 2) deposition and anti-neutrophil cytoplasmic (ANCA)-related disease (Type 3).

ANCA positive glomerulonephritis is typically characterized on renal biopsy as pauci-immune, with mild or absent glomerular staining for immunoglobulin, or complement staining by immunofluorescence.

Rare cases of concomitant p-ANCA plus linear immunofluorescence pattern staining have been discussed, however none with prior association with c-ANCA.

We report a case of systemic c-ANCA pulmonary-renal syndrome with anti-GBM-disease-typical linear staining on renal biopsy immunofluorescence.

Case Presentation

A 63 year-old man with a 60 pack-year smoking history presented to a community hospital complaining of shortness of breath, non- exertional chest pain and recent history of hemoptysis on a background history of chronic non-productive cough lasting many years. He had not been seen by a doctor in several years, had no known medical problems, and took no medications. He denied edema, weight gain, orthopnea or paroxysmal nocturnal dyspnea.

Physical exam was significant for hypertension and course bilateral breath sounds with expiratory wheeze.

Laboratory investigation revealed proteinuria, a creatinine of 11.4 mg/dL, and positive circulating c-ANCA antibodies. Protein/ creatinine ratio 3.52.

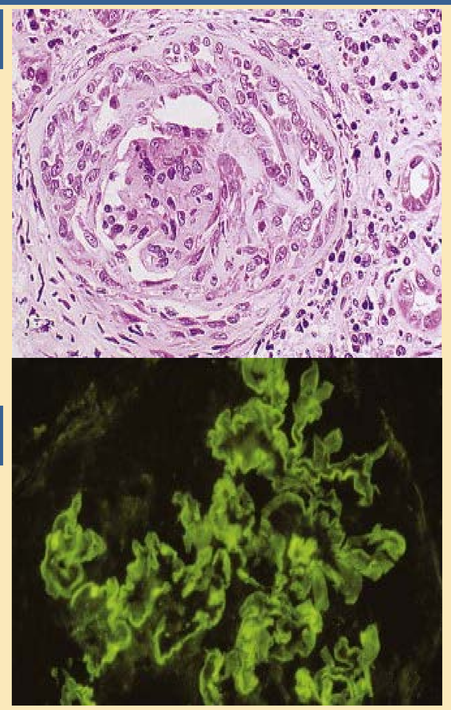

Figure1: Renal biopsy. A. Crescentic glomerulonephritis on Light Microscopy. B. Linear staining on immunofluorescence

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CT Chest showed multiple bilateral pulmonary nodules, biopsy of which showed only hemosiderin-laden macrophages. Renal biopsy showed linear IgG staining suspicious for Goodpasture syndrome and necrotizing crescentic glomerulonephritis with 70% interstitial fibrosis on immunofluorescence microscopy.

The patient was treated with hemodialysis, 7 rounds of plasmapheresis, rituximab, and solumedrol, complicated by upper gastrointestinal bleed requiring admission to the intensive care unit. After resolution he was continued on oral prednisone.

The patient improved and was discharged on 10 mg of oral prednisone daily and hemodialysis to out-patient follow-up with rheumatology and nephrology.

Condition	Renal Biopsy Findings
Goodpasture Syndrome	Anti-GBM antibodies, Linear IgG immunofluorescence staining on renal biopsy, +/- crescentic glomerulonephritis
Granulomatosis with Polyangiitis	PR3/c-ANCA antibodies, pauci-immune or complement immunofluorescence staining on renal biopsy +/- crescentic glomerulonephritis
Eosinophilic granulomatosis with Polyangiitis	MPO/p-ANCA antibodies, pauci-immune staining on renal biopsy, necrotizing crescentic glomerulonephritis with granulomas
Microscopic Polyangiitis	MPO/p-ANCA antibodies, pauci-immune or complement immunofluorescence staining on renal biopsy +/- crescentic glomerulonephritis, crescents consist of fibrin and plasma proteins
Systemic Lupus Erythematosus	Granular immunofluorescence, diffuse proliferative glomerulonephritis, wire looping on light microscopy
Sarcoidosis	Multiple findings of noncaseating granulomatous interstitial nephritis, membranous nephropathy, or nephrocalcinosis
Tuberculosis	Tubulointerstitial nephritis with granulomas.
Metastatic lung cancer	Metastatic carcinoma infiltrating renal parenchyma with the same positive tumor biomarkers as the lung sample.

Table 2: Differential Diagnosis for Pulmonary-Renal Syndromes and their typical immunohisto-chemical features

Discussion

The differential diagnosis of Pulmonary-Renal Syndromes comprise Goodpasture syndrome, granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis, microscopic polyangiitis, SLE, sarcoidosis, TB and metastatic lung cancer. The typical presenting features of GPA vs GBM are hemoptysis with worsening renal function.

Rare cases have been seen with ANCA positive antibodies and linear immunofluorescence in necrotizing crescentic glomerulonephritis, the majority of which are p-ANCA/MPO positive.

Patients presenting with suspected pulmonary-renal syndrome should be tested for both anti-MPO and anti-PR3 ANCA-related disease and anti-GBM-disease .

Further study of pulmonary- renal syndromes with ANCA vasculitis and linear immunoglobulin staining without anti-GBM serum antibodies are necessary to understand the pathogenesis and develop necessary treatment protocols.

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