Linear anti-glomerular basement membrane IgG but no glomerular disease: Goodpasture’s syndrome restricted to the lung

Sanjeev Sethi¹, Matthew Lewin¹, Lauren Lopez² and Donna Lager¹

¹Department of Laboratory Medicine and Pathology, Mayo Clinic, 55905 Rochester, MN and ²Department of Medicine, Elmbrook Memorial Hospital, Brookfield, WI, USA

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Introduction

We present an unusual case of Goodpasture’s syndrome with pulmonary manifestations and no renal function abnormalities and normal urinalysis, although there was intense linear staining for anti-glomerular basement membrane (GBM) antibodies.

Case presentation

C.V. is a 22-year-old woman, who presented to the emergency room (ER) with shortness of breath, coughing and frank haemoptysis. She had been seen in the ER twice over the previous 3 weeks for similar symptoms, but with only mild blood-tinged sputum. Chest X-ray showed bilateral infiltrates. She was treated with Zithromax and subsequently Biaxin for a presumed pneumonia. There was no history of fevers, chills or weight loss. However, the haemoptysis persisted with increasing shortness of breath, forcing her back to the ER. Her history was significant in that she is a smoker and works as a bartender in a smoky restaurant. Laboratory investigations at admission: haemoglobin 10 gm/dl, platelet count 309 × 10³/µl, sodium 138 mEq/l, potassium 3.8 mEq/l, serum creatinine 0.7 mg/dl, blood urea nitrogen 11 mg/dl, total bilirubin 1.5 mg/dl, PCO2 34, PO2 48. Urinalysis was unremarkable. Chest X-rays showed worse diffuse alveolar infiltrates compared with the previous X-rays. The clinical diagnosis was that of acute interstitial lung disease with haemoptysis and included a differential diagnosis Wegner’s granulomatosis, lupus, sarcoidosis, pneumonitis. Goodpasture’s disease, etc. Titres for anti-GBM antibodies returned high positive (>32 U/ml, normal <3 U/ml). Remaining serological tests were negative. A renal biopsy was done to confirm Goodpasture’s disease and to document whether renal disease was present or not.

Renal biopsy findings

The renal biopsy showed an essentially normal-appearing renal parenchyma on light microscopy. There were five glomeruli present, none were sclerosed. The glomeruli did not show any evidence of crescents, fibrinoid necrosis or karyorrhexis (Figure 1). The mesangium was not expanded, the capillary loops were patent and there was no evidence of endocapillary proliferation. There was also no evidence of thrombosis, emboli or double contours. The interstitium was well preserved and the vessels were unremarkable. Five glomeruli were present for immunofluorescence studies. The glomeruli show bright linear staining (3+) for IgG, λ and κ light chains along the glomerular basement membranes (Figure 2A). There was mild linear staining for C3 (1+). Staining for IgA, IgM and C1q was negative. Staining for subtypes of IgG showed predominantly bright linear staining for IgG4 subclass (Figure 2C) with milder staining for IgG1 subclass (Figure 2B), while IgG2 and IgG3 were negative. Electron microscopy was unremarkable.

Renal biopsy diagnosis

Linear IgG deposition along the GBMs, with no evidence of a crescentic or necrotizing glomerulonephritis.

Clinical follow-up

She was treated with steroids and plasmapheresis. Plasmapheresis was continued until anti-GBM titres
returned negative. The steroids were continued for 6 months. The steroids are being tapered off at the time of submission of the manuscript. At this time, she is essentially asymptomatic. Chest X-rays are negative and anti-GBM antibody titres are negative. Throughout the course the renal function remained normal.

Discussion

Goodpasture’s syndrome is due to anti-GBM antibodies against antigens in the basement membranes. Hudson et al. [1,2] have identified α3 NCI domain of collagen IV as the target antigen. The antigen is present in both pulmonary and GBMs and patients usually present with the pulmonary-renal syndrome. The α3 (IV) NCI epitope is hidden within the α3.α4.α5 (IV) protomer and for binding of the anti-GBM antibody, exposure to an environmental agent (such as cigarette smoke, hydrocarbons, etc.) is often required in order to reveal these epitopes[3]. Renal biopsy in patient’s with Goodpasture’s syndrome shows a necrotizing and crescentic glomerulonephritis, the diagnosis is confirmed on immunofluorescent microscopy which demonstrates linear IgG antibody staining along the GBMs.

We present a case of a young lady with Goodpasture’s syndrome restricted to the lung. The patient was a heavy smoker, and as stated earlier, cigarette smoking and working in a smoke-filled environment may have led to the onset of Goodpasture’s syndrome. The case is unusual in that the renal biopsy showed bright linear staining for anti-IgG on immunofluorescent microscopy, yet there were no morphological changes of anti-GBM glomerulonephritis on light microscopy. In addition, urinalysis and renal function was essentially normal throughout the course. From the clinical standpoint, the patient was treated with steroids and plasmapheresis, given the high anti-GBM antibody titres and the acute pulmonary symptoms from pulmonary haemorrhage. The patient is doing well, has quit smoking, symptoms have resolved and anti-GBM titres have gradually become negative. From the pathology standpoint, the case was perplexing in that, although there was bright linear anti-GBM staining of the GBMs, there was no evidence of a crescentic or necrotizing glomerulonephritis. A possible explanation is that while the anti-GBM antibodies were pathogenic in the lung, they did not have the same pathogenic characteristics in the kidney. In a study of the subtypes of anti-GBM IgG antibodies in Goodpasture’s syndrome, Noel et al. [4] found that the most predominant was IgG1 (91%), followed by IgG4 (73%). IgG1, unlike IgG4, can fix complement and activate macrophages. Sub-typing of the anti-GBM IgG antibodies of our case showed predominantly IgG4 linear staining, with much milder staining for IgG1. Therefore, in our case, since the predominant IgG sub-type was IgG4, it likely that the binding of the IgG4 antibodies to the GBM did not result in significant complement activation and renal injury. This is supported by the finding of only very mild complement deposition along the GBMs.

A search of the literature revealed few reports of similar biopsy findings, although in most cases, while renal function was normal in the setting of Goodpasture’s syndrome, the urinary sediment showed haematuria [5–8]. It is also possible that kidneys with
normal renal histology and normal renal function may represent an early form of Goodpasture’s syndrome, and early recognition and treatment results in no significant renal injury. The case also illustrates the fact that Goodpasture’s syndrome should be in differential diagnosis of haemoptysis, even in the setting of normal renal function.

Conflict of interest statement. None declared.

References


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