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P312 -Diffuse Alveolar Haemorrhage Secondary to Lung Biopsy Proven Anti-GBM Disease with Negative Circulating Anti-GBM Antibodies by Standard ELISA – Case Report –

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Background: Anti Glomerular Basement Membrane (GBM) disease is a rare disorder characterised by auto-antibodies against alpha 3-chain of type IV collagen in the basement membrane of the glomeruli and alveoli. Presentation is typified by a rapidly progressive glomerulonephritis with crescent formation and in 40-60% of cases will have concurrent pulmonary haemorrhage. Isolated pulmonary haemorrhage without renal involvement is rare but is often associated with additional factors such as smoking, infection, cocaine inhalation or hydrocarbon exposure.

Case Report: A 21-year old white British female presented to local hospital with acute shortness of breath requiring admission to intensive care for respiratory support. She had no significant past medical history, was an active smoker and had recently used intranasal cocaine recreationally. She denied haemoptysis, fever or contact with unwell persons. Haemoglobin was found to be 55 g/L with raised CRP and normal creatinine. Urine dip was negative for blood and protein. Chest X-ray and subsequent CT chest showed bilateral lung infiltrates in keeping with possible pulmonary haemorrhage. She was commenced on pulse Methylprednisolone and transferred to our unit for plasma exchange. Serology including ANA, ANCA, complements and anti-GBM antibody were negative on numerous occasions. Bronchoscopy and subsegmental biopsy confirmed diffuse alveolar lung haemorrhage with linear alveolar staining for IgG supporting the diagnosis of anti-GBM disease. She received 7 sessions of plasma exchange and 4 doses of I Cyclophosphamide with gradual weaning of corticosteroids. She made an excellent response and was strongly advised to stop smoking.

Discussion: We present an unusual case of anti-GBM disease diagnosed by lung biopsy, in absence of detectable circulating anti-GBM antibodies or urinary abnormalities. In clinical practice; we rely on ELISA to detect circulating anti-GBM antibodies; however, there are case reports of renal biopsy proven anti-GBM disease in absence of these antibodies. Lung biopsies are seldom used to diagnose anti-GBM disease where detection of linear IgG staining pattern is less reliable than in glomeruli. There are several possible explanations for negative anti GBM testing using standard ELISA. Half life of bounding antibodies could be longer than those in circulation thus circulating antibodies could have disappeared when serum sample is collected. Salama et al were able to detect circulating antibodies in 2 cases using a biosensor technique although both ELISA and Western blot analyses were negative. Anti-GBM antibodies are usually IgG1, however other IgG subclasses can be detected. Ohlsson et al reported 4 young women with severe alveolar haemorrhage and IgG4 anti-GBM antibodies who showed low or negative result in regular anti-GBM ELISA testing; although in our case lung biopsies were negative for IgG4 staining. Presence of IgA or IgM anti-GBM antibodies or antibodies reacting to an usual antigen or epitope compared with the typical well-defined epitope region of NC1-domain of alpha 3-chain of type IV collagen are other possible explanations.

Conclusion: Anti-GBM disease without circulating autoantibodies is rare but should be considered in patients with unexplained pulmonary haemorrhage. This case emphasizes the importance of obtaining a tissue diagnosis in these settings and that patients can present with isolated lung involvement.