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P438 -A young female with classical kidney biopsy appearances of anti-glomerular basement membrane disease in addition to thrombotic microangiopathy: a case report

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Introduction:
Anti-glomerular basement membrane (anti-GBM) disease typically presents with rapidly progressive glomerulonephritis (RPGN) with or without pulmonary haemorrhage. The classic histological features on kidney biopsy include glomerular crescents with linear IgG staining along the GBM. Interestingly, several case reports on patients with anti-GBM disease mention this classic histology in rare association with features of thrombotic microangiopathy (TMA) (1, 2, 3, 4). We report a case of a young female with anti-GBM disease, who demonstrated TMA on biopsy and subsequently bled post-biopsy.

Case Report:
A 27-year-old female presented to Accident and Emergency with a 3-week history of fatigue, vomiting and loose stools. She had returned from South Africa a few weeks ago having taken malaria prophylaxis. She denied experiencing lower urinary tract symptoms but had visited her GP 3-4 days before presenting to hospital and had been prescribed Nitrofurantoin for a presumed UTI. She reported no fevers, rashes, joint pains, breathlessness or haemoptysis. Her past medical history included asthma and episcleritis. Her family history consisted of ankylosing spondylitis (father), rheumatoid arthritis (mother) and T1DM (both brothers). She was a non-smoker.

On admission, she had a stage 3 AKI (Creatinine 1267umol/L, Urea 40mmol/L from a presumed normal baseline), anaemia (Hb 82g/L, MCV 83fL), low-normal platelets (202,000/ml) and normal eosinophils. Her haemolysis screen was equivocal (bilirubin 9umol/L, LDH 430 IU/L, Coomb's test negative). Her blood film demonstrated occasional red cell fragments. Her ADAMTS13 level was 78% excluding TTP. Her malaria screen was negative as was her pregnancy test. Her stool culture was negative including for E.Coli serotype, E0157. Her urine dip showed haematoproteinurea. Her kidneys were unobstructed and of normal size on ultrasound. Her CXR was clear.

Subsequent investigations revealed a very high anti-GBM titre (298U/ml) with negative MPO/PR3 antibodies. She was started on high-dose steroids and oral cyclophosphamide at 2mg/kg. In addition, she was commenced on 14 consecutive plasma exchange (PEX) sessions, three times/week haemodialysis and received blood product support. She continued to pass good volumes of urine. Her case was discussed with our colleagues at the National Renal Complement Therapeutics Centre who advised against use of eculizumab.

A kidney biopsy was performed following the second PEX session which revealed 48 glomeruli of which 44 were obsolete. Of the remaining 4 glomeruli, 3 were abnormal and demonstrated cellular crescents with fibrinoid necrosis. Linear staining with C3 and IgG, consistent with anti-GBM disease, was demonstrated on immunofluorescence. Interestingly a second pathology of TMA was also noted in the form of red cell fragmentation, foam cells and arteriolar thrombosis. Despite FFP cover for abnormal clotting pre-biopsy, she had a delayed bleed with haematoma formation and a 3 g/L drop in Hb.

Discussion:

Several case reports document anti-GBM histology with superimposed TMA features; the implication being that the TMA is secondary to anti-GBM disease (1, 2, 3, 4). The complement system has been implicated in both these pathologies (4). It has been suggested that TMA compounds renal failure and anaemia in these patients (5).