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A JOURNEY FROM THROMBOCYTOSIS TO NEPHROLOGY: UNMASKING AMYLOIDOSIS

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CASE PRESENTATION

A 62-year-old construction worker, presented with incidental thrombocytosis of 587 × 10^9/L during a GP visit in March 2022. His symptoms also included myalgia, chronic constipation, intermittent cough with exertional dyspnoea. He also complained of frothy urine since 2019. He was referred to the nephrology team for worsening proteinuria starting in February 2024. On physical examination, blood pressure was 140/80, the patient was noted to be cachexic but with normal lung findings, no hepatosplenomegaly and no pedal oedema. There was also incidental finding of palpable cervical lymph nodes.

INVESTIGATIONS

Initial blood tests during the nephrology clinic review showed mild anaemia (Hb 11 g/dL), elevated platelet count (517 × 103/uL) and a total white cell count of 11.5 x 103/uL. A full blood picture in Sept 2022 revealed mild normochromic, normocytic anaemia and leukocytosis with neutrophilia. Diabetic screening was negative. Urine protein-to-creatinine index (UPCI) progressively worsened from 3.23g/day (February 2024) to 5.8g/day (July 2024). Chest X-ray showed no obvious lung lesions and heart size appeared normal. A renal ultrasound demonstrated bilateral renal parenchymal disease with normal kidney sizes of 10cm, while an echocardiogram showed grossly normal ventricles and normal cardiac function. Serological tests showed low C3 levels (0.86 g/L) and normal C4 (0.26 g/L), raised ESR at 50 mm/hr. Otherwise, the ANA and ANCA were negative. JAK2 mutation was not detected during the workup of thrombocytosis in July 2023. A thorough malignancy workup, including OGDS and colonoscopy, was normal; tumour markers were mostly normal. FNAC of the left cervical lymph node done revealed reactive lymph nodes. Serum plasma electrophoresis and urine plasma urine electrophoresis showed IgA lambda paraproteinemia with no immunoparesis and IgA lambda paraproteinuria.

DIFFERENTIAL DIAGNOSIS

Membranous nephropathy (primary or secondary), Membranoproliferative glomerulonephritis or renal amyloid deposition disease.

HISTOPATHOLOGICAL EXAMINATION

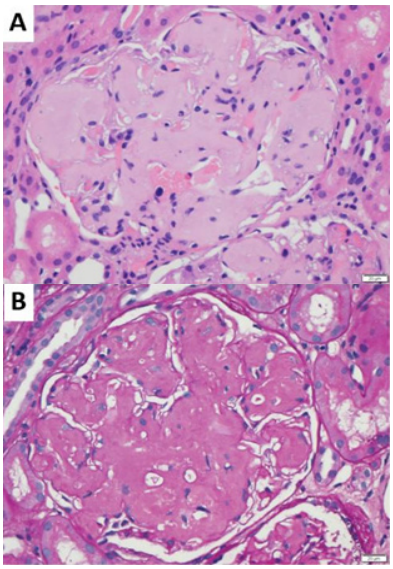

Fig 1. (A) Glomeruli show marked expansion of mesangium and thickening of capillary walls by amorphous eosinophilic material *(H&E, 400x)*. (B) The material is pale/weakly PAS positive *(Periodic acid-Schiff (PAS), 400x)*.

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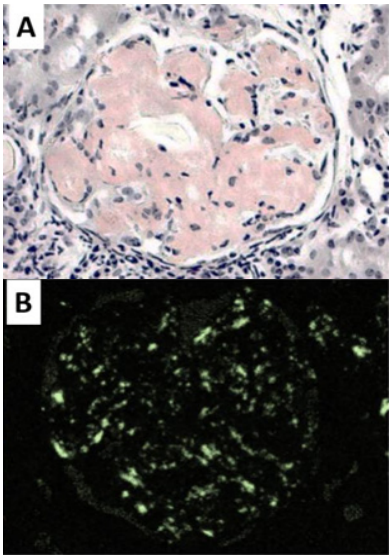

Fig 2. Congo red stain is positive, showing orangeophilic material on bright-field examination (A) that has apple green birefringence under polarized light (B), consistent with amyloid deposition *(Congo red, 400x)*.

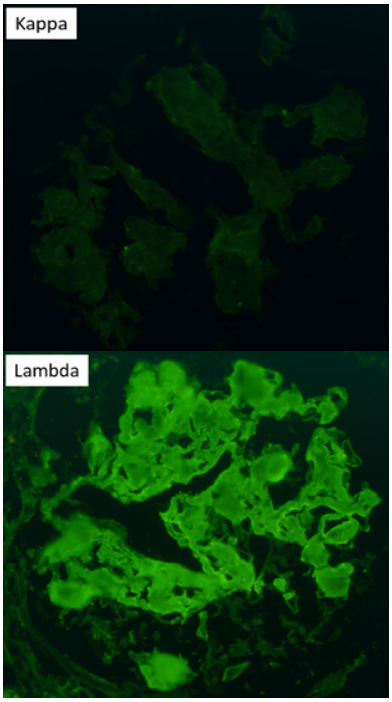

Fig 3. Lambda light chain restriction on immunofluorescence studies, *400x*

FINAL DIAGNOSIS

Features are consistent with AL Lambda subtype of amyloidosis. The patient was referred to the hematology team for further workup. Trephine biopsy showed positive amyloid deposits. Bone marrow aspirate immunophenotyping via flow cytometry showed 0.3% suspicious clonal plasma cell population. These findings are suggestive of systemic amyloidosis.

LEARNING POINTS

1. Thrombocytosis as a Red Flag: Incidental thrombocytosis can be a sign of underlying systemic disease. In this case, it led to the discovery of progressive proteinuria and renal involvement due to amyloidosis
2. Multisystem Approach in Diagnosis: The involvement of multiple specialities, including nephrology, haematology, and gastroenterology, was essential in this patient's workup. Despite initial malignancy concerns, a comprehensive diagnostic approach led to the correct diagnosis of amyloidosis
3. Importance of renal biopsy to achieve diagnosis of proteinuria: Renal amyloidosis, was diagnosed after renal biopsy, which is critical in cases of unexplained proteinuria. The Congo Red staining with apple green birefringence under polarized light along with immunofluorescence studies remains a key diagnostic tool for amyloid deposition