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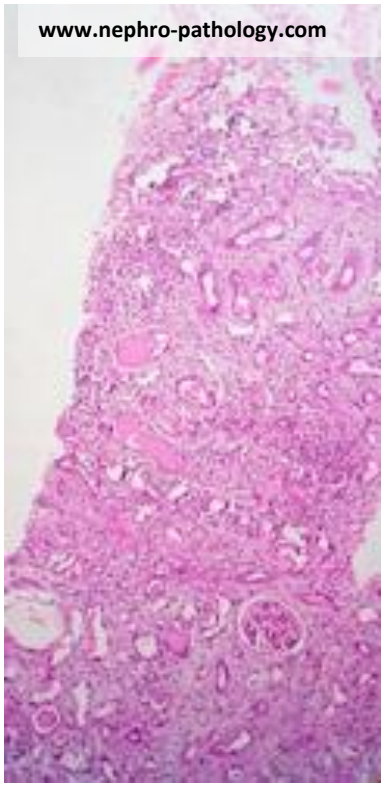
Image Quiz 7

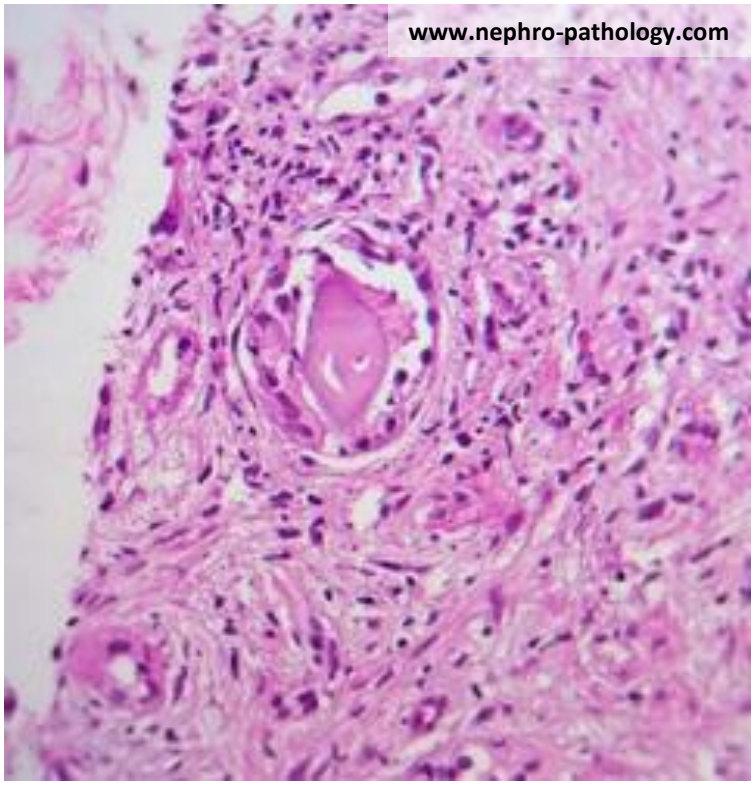
CLINICAL HISTORY:

A 51 year old male, not a known diabetic or hypertensive, presented with anorexia & feeling of generalized weakness since 3 weeks. Preliminary evaluation revealed renal impairment with serum creatinine of 4.1 mg% (362.4 micro mol/L). Urine albumin 1+, RBC 2-3/hpf and WBC 8-10/hpf. Haematological parameters showed Hb of 9 g% and ESR of 88 mm/1st hour. Viral serologies, ANA, ANCA and anti GBM antibodies were negative.

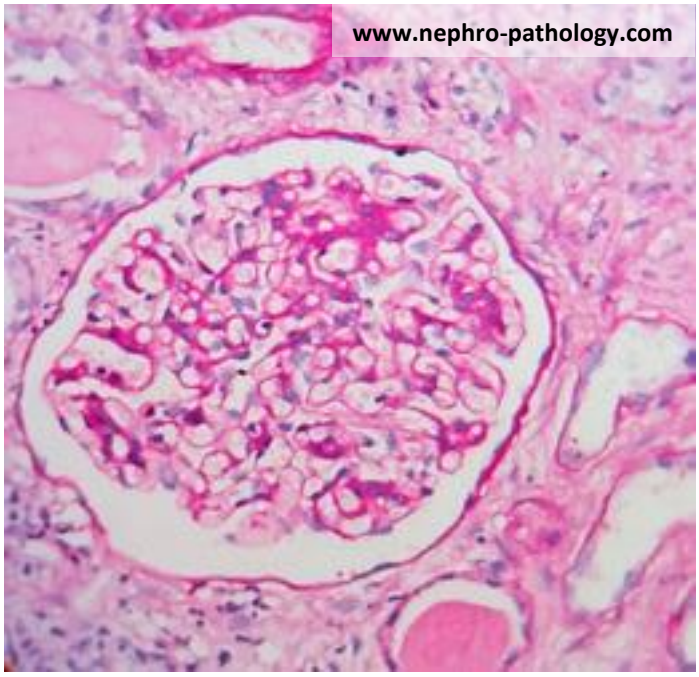
Pending/awaiting results of other investigations, a renal biopsy was performed in view of unexplained renal failure.

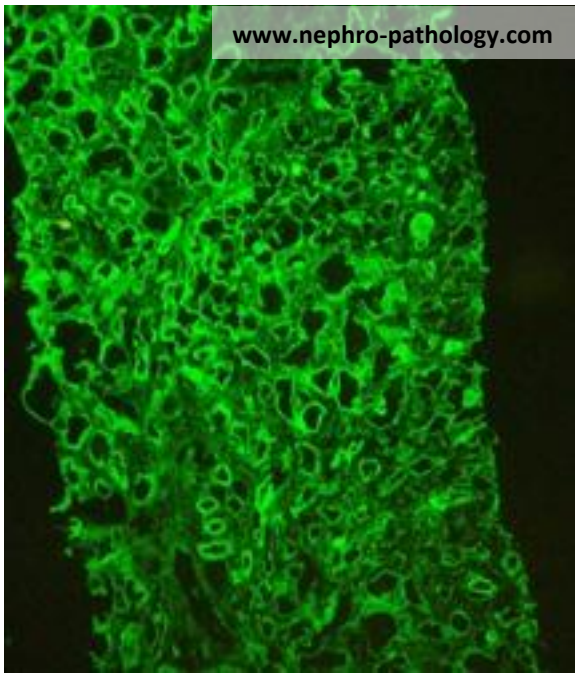
MICROSCOPY:



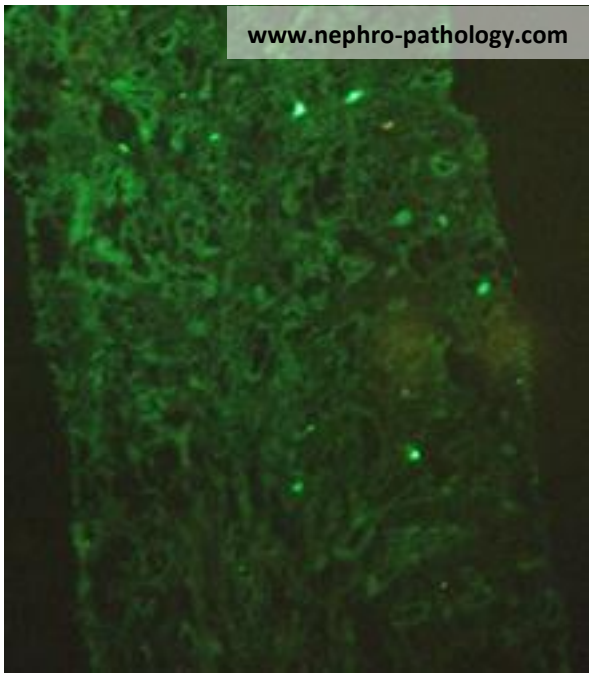


Microscopic examination showed features of tubular injury, chronic tubulointerstitial nephritis and few atypical appearing casts in tubular lumina. The casts had a pale appearance on H&E stained sections and showed “brittle” appearance with few “fracture planes”. Focally prominent epithelial cell reaction was noted in relation to the tubular ca





Kappa Light chains



Lambda Light chains

Glomeruli were unremarkable. There was no evidence of segmental tuft sclerosis, crescent formation, necrotizing / thrombotic lesions or Congophilic glomerular deposits. DIF studies did not show significant glomerular staining. There was intense (3+) linear staining for kappa light chains along the tubular basement membranes with negativity for lambda light chains,

indicating kappa light chain restriction. Atypical intratubular casts also showed a similar immunostaining pattern.

DIAGNOSIS:

Renal monoclonal immunoglobulin deposit disease: Light Chain Deposition Disease (LCDD- kappa light chain restriction), coexisting with myeloma cast nephropathy (MCN) also showing evidence of kappa light chain restriction in the atypical intratubular casts.

DISCUSSION:

Nonamyloidogenic renal monoclonal Ig deposition disease (MIDD) includes the entities of light-chain DD (LCDD), light and heavy-chain DD (LHCDD), and heavy-chain DD (HCDD). Among these conditions, LCDD is the most prevalent and may occur as a "pure" LCDD or can co-exist with myeloma cast nephropathy (MCN). In one series, LCDD constituted 19% of 118 renal biopsies from patients with multiple myeloma (1). Reports of LHCDD and HCDD are rare, with less than 50 well documented cases reported in the literature (2-6).

Histological findings in most cases are characterized by a nodular sclerosing glomerulopathy, and are associated with variable proteinuria, renal insufficiency, and dysproteinemias. Interestingly, at the time of renal biopsy, up to 30% of patients with renal MIDD have no detectable monoclonal protein in serum or urine (7) and in significant number of cases, renal biopsy diagnosis of MIDD precedes any other clinical evidence of dysproteinemias . In a large series of 34 patients with MIDD (23 pure MIDD and 11 MIDD with MCN), only 11 of 34 patients had an "M spike" tested and identified on SPEP and/or UPEP before biopsy. After renal biopsy diagnosis of pure MIDD, an M

spike was identified on SPEP in 48% and on UPEP in 52%. In the same study, in 3 of 23 patients with pure MIDD (13%), both SPEP and UPEP (and immunofixation) were negative. A positive SPEP was present in 80% of patients with LHCDD, compared with 25% of patients with LCDD and 67% of patients with HCDD (8). In another recent large series of 64 patients with, 51 had LCDD, 7 had HCDD, and 6 had LHCDD. Five patients (not included in the analysis) had a concurrent myeloma cast nephropathy. Clinical evidence of dysproteinemia was present in 62 patients (97%), including multiple myeloma in 38 (59%). M-spike was detected on serum protein electrophoresis in 47 (73%). Serum free light chain ratio was abnormal in all 51 patients tested (9).

Kappa is the predominant light chain deposited within renal basement membranes in LCDD, as identified in 91% of our cases, and is similar to the reported incidences of 73 to 91% in various series (10-13). This is in contrast to the increased λ-to-κ ratio seen in amyloidosis and correlates with the reported predominance of Vk4 and Vl6 as precursor proteins in LCDD and amyloidosis, respectively (14,15). Among cases of HCDD, gamma (γ) is the predominant class of heavy chain.

Although a nodular sclerosing glomerulopathy is the most common finding on light microscopy in MIDD, its incidence ranges from 31 to 74% (8,9, 10-13). Lack of this pattern (as seen in the present case) is particularly evident in cases of co-existing LCDD & MCN, possibly because of their early presentation due to MCN-induced acute renal failure, providing insufficient time for the development of nodular sclerosing lesions. Alternatively, the pathogenic light-chain proteins in this entity may be less sclerogenic, as suggested by their impaired ability to upregulate mesangial synthesis of Transforming growth factor beta: TGFb (16). Clinically, patients with LCDD and MCN are older, have greater degree of renal impairment at presentation and have

poorer outcome compared to those with a pure MIDD, highlighting the importance of recognizing this combination on pathological examination of renal biopsy.

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