IMMUNOTACTOID GLOMEROLUPATHY: A CASE OF MONOCLONAL GAMMAPATHY OF RENAL SIGNIFICANCE

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Background:

Immunotactoid glomerulopathy (ITG) is a rare glomerular disease characterized by highly organized crystallin structure of immune deposits Congo Red (CR) negative in the absence of systemic disease. The typical manifestations include proteinuria often associated with nephrotic syndrome and hematuria. Specific therapeutic approaches have not been established. Recurrent disease has been reported in renal allografts. These patients have a greater predisposition to an underlying lymphoplasmacytic disorder.

Table 1. Clinical data at presentation and during follow-up

	April 2008	May 2011	December 2013
Creatinine (mg/dl)	1.3	1.6	1.3
Creatinine Clearance (ml/min)	85	45	80
Proteinuria (gr/24h)	2.5	2-2.5	1.4
Monoclonal Component	IgGκ	IgGκ	IgGκ
FLCκ (mg/L)	44.7	25.6	8
FLCλ (mg/L)	22.9	12	5
Bence Jonces	negative	negative	negative
Cryoglobulin	negative	negative	negative
Renal Biopsy	IT/CG ?(*)	ITG	
BMB(**) (%plasmacell)	Not Performed	40%	20%
Treatment:	RAS inhibitors (°)	VTD(°°) 5 cycles	ASCT(°°°)

(*) ITG: Immunotactoid Glomerulopathy; CG: Cryoglobulinemic Glomerulonephritis;
(**) BMB: Bone Osteomedullary Biopsy;
(°) Renin –Angiotensin System Inhibitors;
(°°)VTG:Velcade+Thalidomide+Dexamethasone;
(°°°) ASCT:Autologous Stem Cell Transplantation

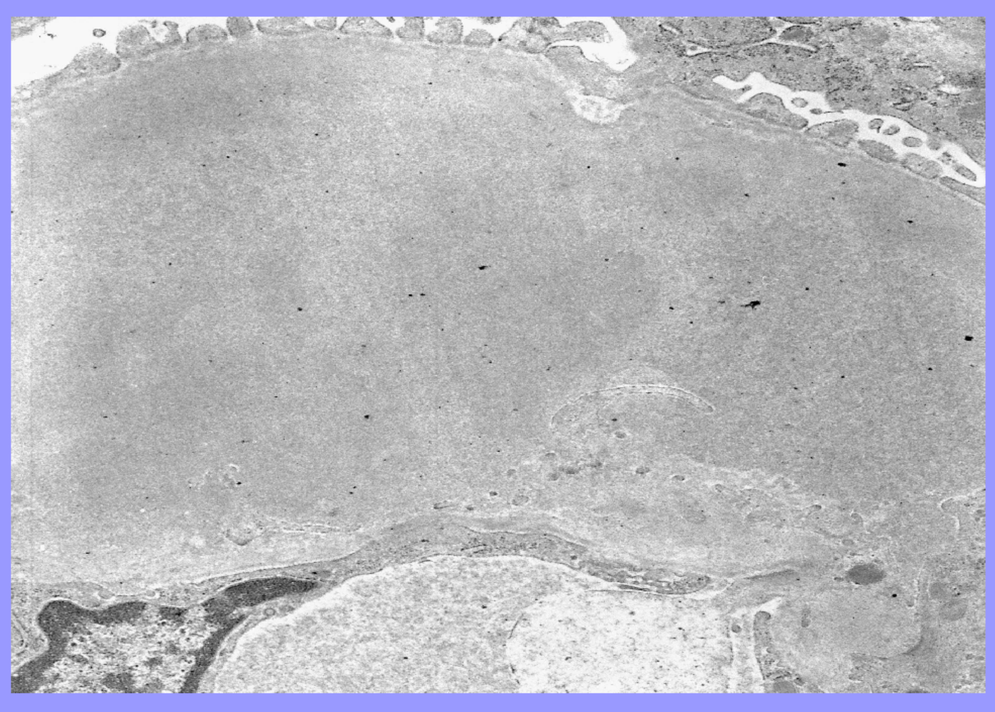

Figure 1. deposits of varying density of microtubules on a background of unorganized electron-dense material (UrPb 7000x)

Case Report:

A 58 year-old man with a history of hypertension, dyslipidemia and obesity was referred to our attention for non nephrotic proteinuria (about 2 gr/24 h) and renal failure (sCr 1.3 mg/dl,CrCl 85 ml/min). Relevant laboratory findings included a monoclonal component (MC) IgGk(0.7 g/dL), free light chain(FLC)k 44.7mg/L,FLC λ 22.9 mg/L,with Bence Jones negative (BJ). There was no evidence for autoimmune or cryoglobulinemic disease. A renal biopsy was performed and showed nine glomeruli, one completely sclerosed. The remaining glomeruli revealed increased mesangial cellularity with large PAS positive deposits. Immunofluorescence (IF) microscopy could not be performed due to the lack of renal cortical tissue. Ultrastructural examination revealed massive mesangial and subendothelial CR negative deposits of organized microtubules with focal crystalline aspect. Diagnosis remained uncertain between a highly suggestive form of occult cryoglobulinemic glomeulopathy and ITG. The patient was discharged with a RAS blocking agent and systematically monitored for renal function, proteinuria and serum cryoglobulin which, despite all our investigations, never turned up positive. A bone marrow biopsy (BMB) was not performed. After three years, the patient was hospitalized due to the progression of renal failure (sCr 1.6 mg/dl,CrCl 45 ml/min) and persistent of non nephrotic proteinuria. In the attempt to reach a definitive diagnosis a renal biopsy was repeated a second time confirming on light microscopy the presence of mesangial and subendothelial deposits which on IF stained for IgG, IgM, C3 and k light chain. Electron microscopy revealed a various density of microtubules measuring approximately 20 nm in thickness on a background of unorganized electron-dense material. The MC was 0.93g/dL FLC k 25.6 mg/L, FLCλ 12 mg/L with BJ negative. To investigate the role of MC on renal injury, a BOM was performed showing 40% proliferation of plasma cells producing IgG monotypic for k light chain. Serum IgGk MC was very likely to be responsible for the observed renal deposits. Diagnosis of ITG was then established and the patient was treated with bortezomib and dexamethasone according to a be-weekly schedule plus Thalidomide 100 mg every day. After 5 cycles the patient showed a very good hematological (MC 0,76 g/dl with FLCk 8 mg/L and FLCλ 5 mg/L) and renal response (sCr 1.3 mg/dl, CrCl 83 ml/min) with proteinuria reduced by almost 50%. The patient underwent bone marrow transplant but unfortunately died immediately after the surgery due to infective complications

Conclusions:

We reported here the case of a difficult and late diagnosis of ITG in a patient with multiple myeloma.
- Renal ultrastructural and IF findings were essential in establishing the diagnosis.
- Reduction of MC and renal function improvement after treatment strongly supports the pathogenetic role of the MC in renal injury.
- This case points up the importance to always investigate any presence of serum/urine monoclonal component, regardless if small, for its possible "renal significance''

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L) Renal pathology. L3) Renal histopathology.
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