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The evolution of noncrystalline LCPT

Xuanli Tang
Hangzhou TCM Hospital Affiliated to Zhejiang Chinese Medical University, China

First admission (Aug 2018)
A 49-year-old female patient visited our clinic in Aug 2018, because of edema of bilateral lower extremities for half a year. She didn't undergo any treatment and she had no history of hypertension, diabetes, or recent infection, and no other family history of renal disease. Vital signs were normal. Investigations were indicative of nephrotic syndrome (24-hour proteinuria was 7.82 g with 14.8g/L serum albumin), and renal function was normal (serum creatinine: 0.8 mg/dl). Serum immunofixation electrophoresis (IFE) showed IgGκmonoclonal paraprotein and serum light chain ratio was elevated (5.1). Serum immunoglobulins, complements, ANA, ANCA, hepatitis tests were all negative. No abnormal findings were detected through X-ray or renal B-ultrasound. Bone marrow showed 3% mature plasma cells as well as a very small amount of protoplasma cells (0.004%) and immature plasma cells (0.102%).
First Renal Biopsy: on light microscopy, 17 glomeruli showed minimal change. Mild interstitial fibrosis and inflammation were noted, and focal vacuolated tubules were observed. On IF, no meaningful positivity for either immunoglobulin or complements, as well as light chains. On electron microscopy (EM), the glomeruli had no proliferative lesions or electron dense deposits (EDD), except for more than 90% of foot process effacement (FPE). Therefore, podocytopathy (probably MCD) with mild chronic tubular interstitial lesions was diagnosed.
She was treated with methylprednisolone (MP) 48mg/d and her proteinuria decreased gradually, but it increased again without obvious causes half a year later, and a combination of MP and tripterygium wilfordii (TW, a Chinese immunosuppressive medication) was prescribed. The proteinuria couldn't be controlled ever since, and her serum creatinine was raised to 4mg/dl in Sep 2020. Therefore, she was hospitalized again.

Second admission (Sep 2018)
She was admitted because of edema for two years. Table 1 showed laboratory tests of first and second admission.
X-ray and renal B-ultrasound had no abnormality. Bone marrow detected 4% mature and 1% immature plasma cells with kappa light chain restricted.
PET-CT showed generally increased FDG metabolism, which suggested bone destruction by multiple myeloma.
Second renal biopsy: on light microscopy, 3 out of 7 glomeruli had ischemia. Interstitial fibrosis and tubular atrophy were severe, and inflammation was moderate. Tubules without atrophy showed intense granular and vacuolar degeneration. On IF, no meaningful positivity for either immunoglobulin or complements, except slight to strong positivity of κ light chain was observed in proximal tubules (PTs) cytoplasm (double-stained with NEP) and isolated casts. The distribution of kappa was patchy and focal, and only 40% of PTs without KIM-1 positivity were stained with kappa. This phenomenon suggests that light chain reabsorption happens only in well-preserved PTs. On EM,

the glomeruli showed GBM wrinkling and >90% FPE. Neither EDD nor crystal inclusions were found in glomeruli or tubules. IEM showed negative light chain staining in glomeruli, but 3+ κ-only positivity in lysosomes of PTs. Therefore, the pathologic diagnosis was mainly noncrystalline LCPT (kappa type), and then, podocytopathy without LC deposits, and finally, kappa chain restricted casts without classic histological features.

P-IF on first archived renal biopsy: paraffin IF detection of light chains was performed, because the light chain restriction wasn't observed by the frozen tissue detection on first renal biopsy. It showed kappa staining was intense and diffuse in the cytoplasm of PTs, while lambda staining was mild and focal. Glomeruli and casts were all negative of both light chains. KIM-1 showed only 20% of PT positivity, which suggests there are more well-preserved tubules of reabsorbing function at the very beginning of LCPT onset.

Treatment and follow-up: She was treated with PCD (Bortezomib+cyclophosphamide+dexamethasone) regimen, and after nine rounds of treatment, she achieved a very good partial response of kidney disease, and complete hematological response. The follow-up data is shown in Table 2.

Table 1. Laboratory tests of first and second admission of this patient

		First admission	Second admission
Urine test	UP (g/24h)	4+ (7.82)	3+ (12.5)
	Others	URBC+, UGlu-	UACR 4.5g/L, URBC-, WBC+, UGlu-~2+
	UGlu	-	-~2+
Blood test	Hb(g/L)	112	120
	ALB(g/L)	14.8	14.2
	Scr (mg/dl)	0.8	4
	eGFR(ml/min)	53.3	8.6
	Ca (mmol/L)	2.6 after correction	2.6 after correction
	IFE	IgG、κ (serum)	IgG、κ (serum+urine)
	sLC ratio	5.1↑	7.6↑; sFLC ratio 11.1↑
	serum Kappa	194mg/dl	388mg/dl

Table 2. The follow-up data after chemotherapy

	2020.10	2020.11	2020.12	2021.1	2021.7
SCR (mg/l)	40.5	14.7	12.8	13.2	14.8
UP (g/24h)	12.5	2.3	2.04	0.96	1.2
ALB (g/L)	14.2	35	36.7	41.4	42.0
sFLC Ratio	11.09	N/A	0.91	0.91	0.72
uFLC Ratio	16.6	N/A	0.85	0.89	0.65