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Nephrotic syndrome in the elderly caused by primary renal non-Hodgkin's lymphoma: Case report

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Abstract

We reported a rare case with nephrotic syndrome (NS) in 84-year-old Vietnamese man due to Non-Hodgkin lymphoma (NHL) without clinical extrarenal manifestations. He was admitted to our hospital because of leg edema. Kidney biopsy was done routinely as our protocol. Minimal change in the glomeruli was observed by light microscopy and no immune complex deposition by IF assay. The tubular and interstitium were not fibrotic but infiltrated by several lymphocytic and plasmocytic cells. The lymphoid cells were positive for CD20 but negative for CD3. He received chemotherapy with low dose Rituximab and achieved complete remission without any significant side effects of chemotherapy. Our patient is the oldest patient among 50 cases with primary renal lymphoma PRL) reported and responses very well to low dose Rituximab without any side effects.

Keywords

nephrotic syndrome; Primary renal lymphoma; Non- Hodgkin lymphoma; kidney biopsy

Introduction

Currently, only 50 cases with primary renal lymphoma (PRL) have been reported in the literature. However, a large proportion of these patients did not use PET scan to rule out infiltration in other extra-organs or lymph nodes [1]. In 2000, Stallone et al reviewed the available literature and reported only 29 cases of PRL fulfilling diagnostic criteria [2]. This case is the first case of PRL in an elderly Vietnamese patient diagnosed exactly with fulfilled criteria and treated successfully by low dose Rituximab.

Case Report

A 84-year-old Vietnamese man was admitted Thong Nhat Hospital, HoChiMinh City in March 20, 2013. His past-history was hypertension, prostatic hypertrophy and no kidney diseases, diabetes. He presented with a 2 week history of edema in legs. No fever, pain and hematuria were noted. His family history was not contributory. At the admission, blood pressure was 130-140/80 mm Hg, body weight was 53 kg, increased 3 kg. Urine volume was normal (1-1.5 L/day). Physical examination revealed no enlarged or palpable mass and lymph nodes. The remaining systemic examination was not significant.

The peripheral blood count was unremarkable. The peripheral blood smear revealed no immature cells. Liver functional tests, bilirubin and electrolytes were normal. Serum tumor markers were negative and showed in table 1. The remaining laboratory tests were all within the normal limits.

Imaging*:* A normal chest X-ray was obtained. The abdominal ultrasound did not reveal any coexisting lesion in the hepato-pancreato-biliary system.

Kidney biopsy was done by BARD Magnum biopsy gun and ultrasound guidance with 18 Gauge automatic needle, one pass on the left side and no complication post procedure. Renal tissue was stained HE, PAS and immunofluorescent with 5 markers (IgA, IgG, IgM, C3 and C1q) and immunohistochemical study.

Pathology report for renal biopsy: Macroscopic findings: two cores of cortico-medullary kidney, 7mm and 10mm in length. Microscopic findings: The fragment includes 7 glomeruli. There was no global glomerular sclerosis. Two glomeruli have mild leukocytes infiltration. The glomerular basement membrane is optically normal. Tubular atrophy and interstitial fibrosis expand in 15% of parenchyma. Presence of a monotonous lymphocyte interstitial infiltration with hypercellularity, and adipose tissue infiltration. The arteries show no abnormality. The neoplasia of monotonous lymphocytes, hypercellularity, scanty cytoplasm, round nuclei, non-cleaved cell, rare mitosis. Tumour cells were strongly CD20 ++ in cytoplasm (Immunoperoxydase). Immunofluorescence: IgA: no glomerular deposits (0/4 glomeruli); IgG: no glomerular deposits (0/4 glomeruli), IgM: some mesangial granular deposits (2/4 glomeruli); C1q: no glomerular deposits (0/4 glomeruli); C3: no glomerular deposits (0/4 glomeruli). *Conclusion*: diffuse B- Cell Lymphoma Non-Hodgkin in the kidney.

Discussion

PRL is defined as lymphoma arising primarily in the renal parenchyma and not resulting from the invasion of an adjacent lymphomatous mass and without evidence of systemic involvement [3,4]. PRL comprises only 0.7% of extranodal lymphomas [1,5]. The incidence of nephrotic syndrome (NS) associated with classical Hodgkin's disease (cHL) is extremely low and estimated at about 0.5 to 1%, therefore, diagnosis of PRL might be mistaken and NS is usually considered as primary cause. The diagnosis often was standed at this step. This patient had been presented NS and also considered as primary NS because there were no any clues for secondary causes and there were no systemic symptoms of NHL. This case is the first case of PRL in Vietnam diagnosed exactly with fulfilled criteria.

The pathogenesis of NHL is poorly understood. It might be related to some factors such as infection, immune diseases, environment pollution such as dioxin, radiation, pesticides…[1,6]. After reviewing carefully his past history, we recorded that he was contacted dioxin in the Vietnam war. However, we had no facilities to confirm this relation.

The diagnosis of PRL becomes more a challenge because there were no systemic manifestations. In this patient, he was presented edema in legs, heavy proteinuria (above 3 g/24 h), low serum albumin (below 30 g/l), and dyslipidemia. He also had renal insufficiency with low creatnin clearance, only 23.4 mL/min and anemia. Therefore, our first clinical impression of this case was chronic kidney disease (CKD). Should we perform kidney biopsy for the NS elderly patient with CKD elderly?. How high is the risk of the invasive procedure ? and what would the benefit of kidney biopsy bring to the treatment ?. Some nephrologists will start steroid therapy as the first choice of treatment and follow up the response. They only do the kidney biopsy for the patients with steroid-resistant NS. Kidney biopsy remains uncommon and have just been performed in some departments of nephrology in specific cases of renal diseases in

large hospitals in Vietnam, and paid by health insurance with limitation of only around 30 USD for a case. Trained nephrologists and renal pathologists are not widely available. Electron microscopy is not available at this moment. In the elderly, kidney biopsy is rarely performed because nephrologists are afraid of complications and the benefits of kiney biopsy results to the clinical management. Our policy is to perform the kidney biopsy for all primary NS in adults before initiation of treatment. He was presented with renal impairement such as NS and unknown renal insufficiency so that kidney biopsy was done. Results of kidney biopsy are presented in Table 2 and figure 1 & 2. The presence of minimal change glomerular lesions and absence of segmental sclerosis by optical microscopy, the absence of cellular glomerular infiltrates or immunoglobulin deposits, presence of IgM deposits in the mesangium. Unfortunately, electron microscopy was not available in this case to confirm the minimal change. This is also our limitation. Immunohistochemical study of renal tissue was performed and the result was showed in figure 3. Masao H et al emphasized the usefulness of an image guided percutaneous biopsy, which detected the lymphoma samples in 11 out of 407 samples (3%) at their institution. The sensitivity and specificity of such renal biopsies are relatively high, reaching 70 to 92% and 100%, respectively [1].

A literature review indicates that there are three diagnostic criteria of PRL: 1) lymphomatous renal in filtration 2) non-obstructive uni- or bilateral kidney enlargement, and 3) no extrarenal localization at the time of diagnosis [1,2,7]. Clinically, the diagnosis of PRL is considered as analogical diagnosis. Our patient was presented fulfilling the diagnostic criteria of PRL: (1) presentation with nephrotic syndrome, renal failure and absence of other causes of renal failure; (2) non-obstructive renal enlargement with no other organ/nodal involvement on abdominal ultrasound and CT scan; (3) no extrarenal localization confirmed by general PET (positron emission tomography) at the time of diagnosis; (4) diagnosis made on renal biopsy.

Interestingly, effective treatment of cHL with chemotherapy was associated with complete resolution of NS. At the end of the follow-up period (36 months) the patient had renal function improved significantly. Complete remission following chemotherapy was presented by the return of urine protein to the normal range of less than 0.3 g/24 h. There were no complications and side effects of chemotherapy recorded during chemotherapy. Although there are not enough data regarding to effectiveness and side effects of Rituximab in the elderly, chemotherapy has demonstrated efficacy in the elderly patients with NHL. Rituximab has been considered as specific therapy with fewer side effects but expensive. A literature review indicates that treatment with Rituximab is generally well tolerated, particularly in terms of adverse haematological effects and opportunistic infections. Infusion-related reactions such as flu-like symptoms may occur in the majority of patients treated with rituximab [7].

Conclusion

This case serves as a reminder to include the differential diagnosis of PRL when an elderly patient presents with NS. Kidney biopsy is the unique way to establish the correct diagnosis. Chemotherapy with low dose of rituximab was effective and safety even in the elderly patients.

Tables

Table 1: Summary of clinical and paraclinical manifestations at the time of hospital admission.

Manifestions	Laboratory tests
Nephrotic syndrome (NS)	Proteinuria: 9.775 g/24h; Serum albumin 16.4g/L; Total protein: 66.2 g/L; Total cholesterole: 4.99 mmol/L; HDL- Chloesterole: 0.96 mmol/L; LDL- Chloesterole: 3.6 mmol/L; Triglyceride: 0.87 mmol/L.
Renal insufficiency	Serum ure and creatinin were 8.8 and 147 µmol/L, respectively. Creatinin clearance was 23.4 mL/min. Plasma sodium, potassium, and calcium were in normal range. Hb: 9.42 g/dL
Renal ultrasound	Both kidneys were in normal size, echogenicity, no stone, bilateral renal cysts.
Abdominal ultrasound	Bilateral pleural effusion, some small cysts in spleen, liver, prostatic hypertrophy
Cardiovascular system	Normal
Thyroid	Thyroid function test was in normal range. T3: 0.78 (ng/mL); T4: 1.13 (ng/mL); TSH: 5.305 (ng/mL)
Blood sugar	Fasting blood sugar: 4.1 mmol/L
Serum tumor markers	CEA: 4.18ng/mL, Cypra 21.1: 4.2ng/mL, PSA: 6.18ng/mL, αFP: 2.28 UI/mL, CA 19.9: 5.82 UI/mL
Serum β2 microglobulin	> 4000 µg/l (increased)
Blood sediment	1st hour: 100 mm, 2nd hour: 120 mm (increased)
Biopsy for bone marrow	Normal
Hepatitis and HIV test	Serum HBsAg, anti HCV, and anti- HIV were negative
PET-CT scan	Thyroid nodules on both lobes without hypermetabolic. Bilateral pleural effusion. Emphysema both lungs and mild pulmonary fibrosis at the left lung base. Bilateral renal cysts. There was a fluid density mass measuring approximately 7.3cm in diameter, sited between spleen and left kidney, which was not sure that cystic lesion belong to spleen or to kidney. Mild prostatic hypertrophy. There were some lymph nodes located next to celiac trunk and aorta (above and below the left renal vein), which measured from 1.0 to 1.5cm in diameter. There is mildly increased radiotracer uptake within these lymph nodes. Further evaluation with other images to understand the nature of them is recomended.

Table 2: Renal function, proteinuria pre and post treatment with Rituximab.

Time (month/ year)	Serum ure (mmol/L)	Serum creatinin (µmol/L)	Serum total protein (g/dL)	Serum albumin g/dL	Proteinuria (dipstick)	Proteinuria (g/24h)	Medication
9/2013	8.8	147	66.2	16.4	3+	9.775	Pre- treatment
12/2013	8.7	199	75.5	35.2	(-)	0.02	Mabthera 500mg
3/2014	8.1	161	77.3	39.9	(-)	0.07	Mabthera 500mg
6/2014	7.8	153	69.7	35.5	(-)	0.09	Mabthera 500mg
9/2014	9.0	152	70.4	33.8	(-) 1.0g/L	0.097	Reditux 500mg
12/2014	10.6	137	67.2	32.0	(-)	0.16	Reditux 500mg
3/2015	12.8	123	56.6	23.7	(-)	6.12	Mabthera 500mg
1/2016	6.2	151	68.5	34.4	(-)	0.16	Mabthera 500mg
2/2016	7.8	142	-	-	(-)	0.22	Mabthera 500mg
3/2016	6.9	126	70.9	34.0	(-)	0.9	Mabthera 500mg
6/2016	8	108	69.6	37.4	(-)	0.1	Off Rituximab

Figures

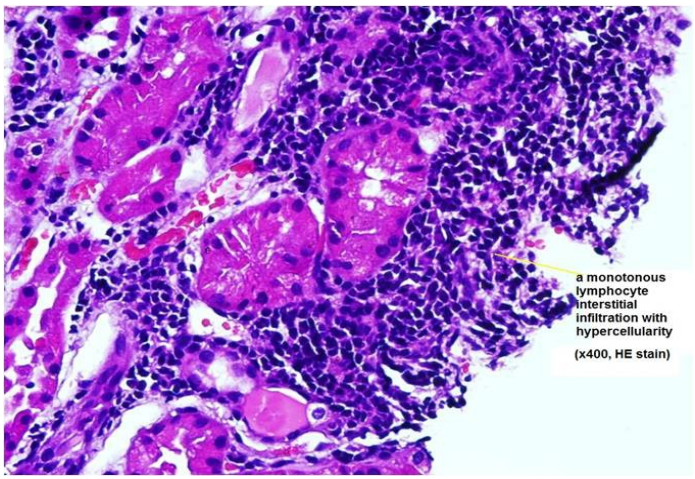

Figure 1: A monotonous lymphocyte interstitial infiltration with hypercellularity (x400. HE stain)

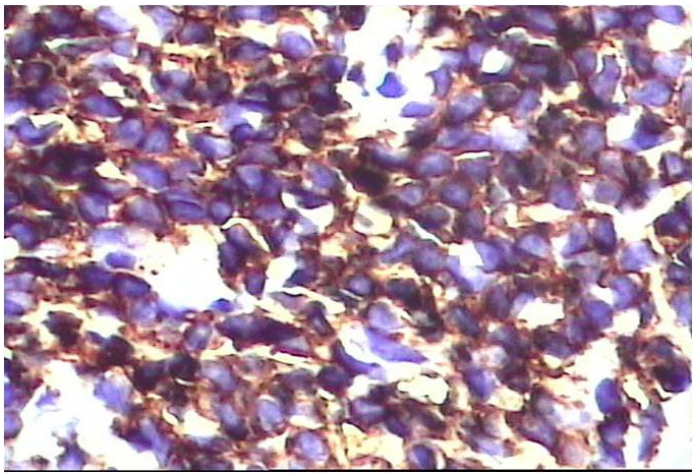

Figure 2: Tumour cells were strongly CD20 ++ in cytoplasm (Immunoperoxydase, x400).

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