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Case Report

BILATERAL PRIMARY RENAL BURKITT LYMPHOMA PRESENTING AS NEPHROTIC SYNDROME WITH TUMOUR LYSIS SYNDROME

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Abstract :

We report a case of seven year female child presented with nephrotic syndrome along with tumour lysis syndrome. There are some case reports worldwide with the resembling presentation but the diagnosis remains controversial in majority of them. We report the presentation of this case as misdiagnosis, hence a mistreatment and further difficulty in interpretation of stage of the disease due to administration of steroids. The patient was diagnosed as bilateral primary renal Burkitt lymphoma after a delay of 2 months after her presentation to hospital for her symptoms. She had persistent renal dysfunction and was started on chemotherapy but had poor outcome. It may suggest the individualisation of the patient for treatment because such patient may not tolerate the established protocols of chemotherapy for this disease, due to established renal dysfunction. We propose a modification of previously proposed criteria by Malbrain for diagnosis of primary renal lymphoma (PRL) and suggest a better term 'probable primary renal lymphoma' (PPRL) because the diagnosis of PRL is of controversy as well as exclusion. We delineate the criteria for PPRL.

Keywords: Renal Burkitt Lymphoma **,**

CASE REPORT

A seven year old girl with 13.5 kilogram weight presented with breathlessness since 2 days. She had history of low grade fever, progressive distension of abdomen, night sweats and not eating well since one month. She had no history of bleeding, rash, oliguria. Since one week she had few episodes of vomiting, swelling over feet and puffiness of face. There was no palpable lymphadenopathy. She had no past or family history of any medical illness. On general examination she had pallor. There was no icterus, cyanosis or clubbing. She had anasarca. She also had tachycardia, tachypnea & hypertension (blood pressure 142/104 mm of Hg). Cardiovascular examination was normal. Respiration was laboured but breath sounds were normal. On abdominal examination only positive sign was that both kidneys were palpable, ballotable with smooth surface and were non tender.

Her investigations revealed haemoglobin (HB) 5.6 gm/dL, total leukocyte count (TLC) 16000/µL,platelet count (PLC) 134000/µL, serum creatinine (Cr) 6.5 mg/dL, blood urea nitrogen (BUN) 82 mg/dL, total protein (TP) 5 g/dL, serum albumin (ALB) 1.3 g/dL, serum sodium (NA) 134 mmol/L, serum potassium (K) 6.4mmol/L, liver function test (LFT) normal and arterial blood gases (ABG) showed severe metabolic acidosis with respiratory

alkalosis. Uric acid (UA) level was 54 mg/dL. Urine analysis showed microhematuria along with nephrotic range proteinuria. Ultrasonography of neck, thorax, abdomen and pelvis was carried out which showed only abnormality of bilateral mildly enlarged kidneys with slightly altered echotexture.

This patient received blood transfusion, was subjected to peritoneal dialysis and stabilised subsequently. She was treated with steroids (ranging equivalent to 1-2 mg/ kg of prednisolone per day for 2 months) for nephrotic range of proteinuria suspecting childhood nephrotic syndrome (nephrotic range proteinuria, oedema and hypertension) which is usually responsive to steroids. Further she was kept on dialysis with biweekly schedule. Due to persistently high creatinine, low urine output and microhematuria, she had undergone renal biopsy, the report of which was suggestive of malignant round cell tumour. So the severe hyperuricemia and hyperkalemia on presentation was actually tumour lysis syndrome.

Till this moment this patient was being treated at nephrology centre and was labelled as acute uric acid nephropathy. Positron emission tomography (PET scan) was carried out without contrast which showed no active uptake in any part of body. After this report of malignancy she was transferred to oncology setting but after a long duration of time comprising about two months from initial presentation.

The experts in pathology in our oncology setting reviewed the histopathology specimen. Immunohistochemistry (IHC) showed leukocyte common antigen (LCA) – Positive, CD20 (Pan B) – Negative, CD2 – Negative, MIB1 - Positive (in around 90-95 % cells), CD 79a – Negative. IHC diagnosis was given as high grade lymphoma with likelihood of Burkitt type lymphoma. However, CD20 was negative may be due to poorly processed tissue. At this moment patient's reports revealed HB 9.6 g/dl, TLC12700 /µL, PLC 78000 /µL, Polymorphs 81 %, Lymphocytes 16 %, Monocytes 2 %, Eosinophils 1 %, UA 11.36 mg/dL, NA 139.6 mmol/L, K 5.93 mmol/L, chloride (Cl) 103.1 mmol/L, BUN 39.44 mg/dL, Cr 7.19 mg/dL. Tests for Human immunodeficiency virus, Hepatitis B and Hepatitis C were negative; Serum Calcium (Ca) 8.99 mg/dl, Magnesium (Mg) 3.2 mg/dl, serum lactate dehydrogenase (LDH) 1019 U/L, Blood Sugar (RBS) 83 mg/dL. Except hypoalbuminemia her LFT was normal.

Further, bone marrow examination showed both marrow aspiration and biopsy was normocellular and uninvolved by the malignancy. Repeat ultrasonography of neck , thorax, abdomen and pelvis showed the presence of bilateral mild pleural effusion, enlarged liver (16 cm in span and normal echo pattern), and mild bilateral enlargement of both kidneys (Right kidney- 93X37 mm and left kidney- 91X43 mm). Both kidneys showed raised cortical echogenicity with preserved corticomedullary differentiation suggesting medical renal disease. Mild ascites was seen. Magnetic resonance imaging of brain and cerebrospinal fluid cytology was normal. Repeat PET scan without contrast showed only mild bilateral ametabolic pleural effusion without any active uptake in the whole body. She was now started on steroids as a part of chemotherapy. Her urine output was 200 millilitre/ day. She was on dialysis support.

We planned for her chemotherapy of LMB 96- intermediate risk protocol. Persistent renal dysfunction not responding to steroids, even in the setting of normal PET scan was considered as residual disease and the objective of further treatment was to cure the patient which will reverse her renal function to normal and make her dialysis free [1].

The initial phase of chemotherapy consisting of cytoreductive cyclophosphamide, vincristine and steroid was administered. After 48 hours of receiving cyclophosphamide patient was puffed up and urine output being less than 75 mL/ per day. She was hemodialysed for that. Next day her investigations showed UA 6.22 mg/dL, Cr. 3.42 mg/dL, HB 6.4 g/dL, TLC 1400 /µL, PLC 18000 /µL, polymorphs 40 %, absolute neutrophil count

(ANC) 500/µL. She had few episodes of rice watery stools. Considering neutropenia she was started on antibiotics and filgrastim support.

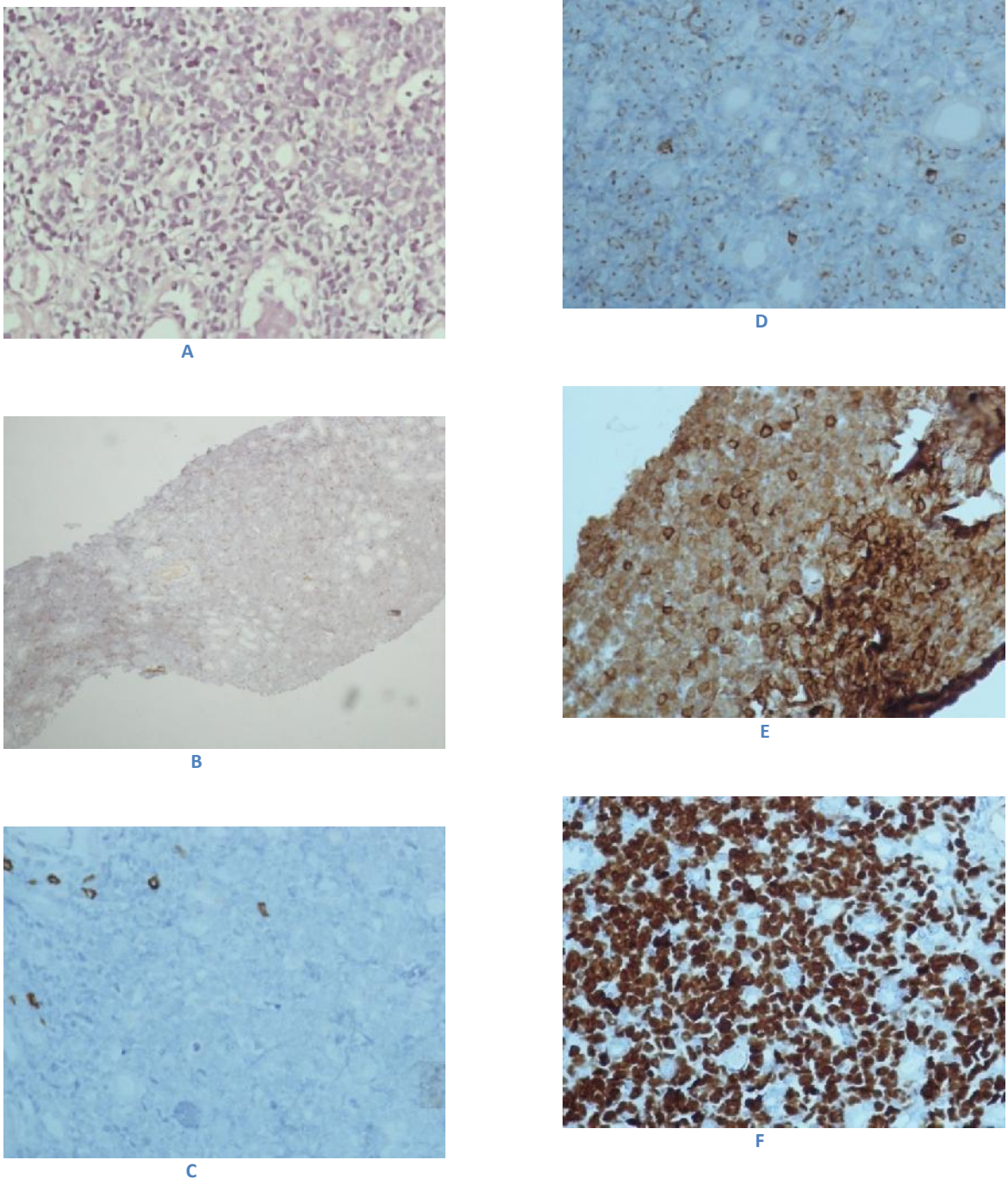

Figure 1. Histopathology (A) and Immunohistochemistry (B-F) of renal biopsy sample. (A) Paraffin section showing diffuse monotonous pattern of growth of medium sized cells with round nuclei, dispersed chromatin and basophilic cytoplasm. (B) CD2 negative (C) CD20 negative (D) CD79a negative (E) LCA positive (F) MIB1 positive in 90-95 % cells

Five days after receiving cyclophosphamide she was subjected for next hemodialysis. Just after dialysis, this patient became breathless, tachypnic, hypotensive, hypoxemic and her sensorium was altered. She was put on antibiotics, ionotrpic support and expired while transferring to intensive care unit.

DISCUSSION

Kandel et al 1987 reported that it is reasonable to assume that renal lymphoma can be a primary lesion; almost all patients with primary renal lymphoma will develop extrarenal lymphomatous disease shortly after diagnosis of their renal tumour; and survival for more than 1 year after diagnosis is rare [1].

The criteria for PRL (Malbrain et al, 1994) are as follows: (1) renal failure as the initial presentation, (2) bilateral enlargement of the kidneys without obstruction and other organ or nodal involvement, (3) diagnosis only made by renal biopsy, (4) absence of other causes of renal failure, and (5) rapid improvement of renal function after radiotherapy or chemotherapy [2].

As per Dawson criteria, lymphoma is said to be primarily extra nodal if 1) absence of palpable superficial lymph nodes on first physical examination; 2) absence of mediastinal lymphadenopathy detected on plain Chest X-ray; 3) dominant lesion at extra nodal sites; 4) involvement of lymph nodes in the vicinity of the primary lesion; and 5) white blood cell (WBC) count within normal range [3].

The pathogenesis of primary renal lymphoma (PRL) is poorly understood. One view is that a chronic infection in the kidney recruits lymphoid cells into the renal parenchyma, during which an oncogenic event takes place (Duannay, 1940). Another explanation is that lymphomas arise in the renal capsule, which is rich in lymphatics, and invade the renal parenchyma secondarily (Salem et al., 1993). Another possible origin of primary renal lymphoma is a lymphomatous process in the perirenal adipose tissue with secondary involvement of the kidney (Betta et al, 1986) [4].

The presentations of the patients reported are in adults are mostly after surgery for solitary renal mass. Other patients presented as rheumatic disease, postrenal transplant lymphoma, abdominal pain, B symptoms, adjacent lymphadenopathy, glomerulonephritis, solitary metastasis. In adults mostly single kidney was involved and in children there was bilateral renal involvement. Investigators reported many classes of non-Hodgkin lymphoma which include large, small, intermediate and mixed cell types with high, intermediate or low grade histology. The neoplastic lymphoid cells may express both B and T immunoblastic phenotypes; primary renal Hodgkin lymphoma has also been reported. Renal biopsy is important in assessing the diagnosis of PRL as well as of acute renal failure for bilateral lymphomatous infiltration of the kidneys. Up to now, there is no standard treatment modality for this entity since the small number of cases reported. Multidrug chemotherapy is mandatory for high grade lymphoma and when the disease is diagnosed preoperatively. High dose chemotherapy in the future may offer a curative approach in primary bilateral renal disease and without end-stage renal disease. Survival is extremely poor since 75% of patients die less than 1 year after operation. Prognosis may be improved by early detection of disease and by performing systemic chemotherapy [5].

In our patient, obstructive nephropathy was promptly excluded by ultrasonography. The presence of extensive hyperuricemia (serum uric acid >20 mg/dl) and uric acid crystals rises another differential of uric acid nephropathy. There is possibility of compression of renal arteries by lymphoma and it may cause hypertension but in our case the disease was not documented on PET scan. The presence of hypertension, nephrotic range proteinuria and oedema lead to a diagnosis of nephrotic syndrome. Eventually, the presence of enlarged

kidneys and Histopathological evidence of Burkitt lymphoma clearly fixed the final diagnosis of primary renal lymphoma as the cause of renal failure. The prognosis in these patients is usually poor with most patients dying within 9 months of presentation. Our patient had death within 4 months of presentation. Malbrain criteria needs slight modification as it is not fully satisfied in every reported case. Some reported cases do not show renal failure. Not all patients had good response to therapy. The renal dysfunction once occurred may not recover necessarily if there is some permanent damage to kidney due to severe hyperuricemia in tumour lysis.

Thus we come to a conclusion that PRL is a diagnosis of controversy and exclusion. So we suggest the better term 'possible primary renal lymphoma (PPRL)' and the criteria for it can be proposed as (1) unilateral or bilateral involvement of the kidneys, (2) diagnosis made by renal biopsy, (3) absence of other causes of renal failure if patient presents with renal failure, (4) absence of palpable superficial lymph nodes on first physical examination, (5) absence of mediastinal lymphadenopathy, (6) dominant lesion at kidney, (7) involvement of lymph nodes in the vicinity of the kidney; and (8) white blood cell (WBC) count within normal range.

CONCLUSION

Any patient who presents with nephrotic syndrome with tumour lysis syndrome should be vigilantly exercised with the workup to rule out malignancy. A very high level of uric acid should point towards severe tumour lysis and should arise the suspicion of Burkitt lymphoma. The treatment of Burkitt lymphoma and non-malignant nephrotic syndrome is totally different; hence the treatment plan should be decided as much as early. The misdiagnosis and treatment in wrong direction may become a cause for poor outcome. The determination of residual disease in presence of persistent renal dysfunction and PET negative cases needs more exploration. The criteria proposed previously by malbrain needs a modification and hence we proposed a modification of those criteria.

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