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Primary Burkitt's Lymphoma of Kidney: A Rare Entity.

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Abstract:
Burkitt's Lymphoma is an aggressive form of Non-Hodgkin's Lymphoma, with higher incidence in children comprising 30% of pediatric lymphoma. The hallmark of which is a translocation involving c-MYC gene on chromosome 8. Burkitt's Lymphoma comprises of 6.35% of all lymphoma cases in Pakistan, with male predominance. Lymphoma rarely presents as a primary pathology of acute kidney injury. Burkitt's lymphoma in adult population is uncommon and few cases have been reported where Burkitt's lymphoma presents as a cause of acute kidney injury. There are three epidemiological subtypes Endemic (African), sporadic (non-endemic) and immunodeficiency related. Sporadic cases dominate amongst others in Pakistan.

Key Words: Burkitt's, Lymphoma, non Hodgkin's, Hodgkin, kidney, infiltration, acute kidney injury, hemodialysis.

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Introduction:
Burkitt's Lymphoma is a highly aggressive malignancy with 40% overall cases reported in children and less than 5% in adults. It is commonly diagnosed by stage III and IV with extra nodal invasion mostly involving CNS and bone marrow.[1] It is rare to present with acute kidney injury with primary lymphoma. Secondary causes are more frequently reported with acute kidney injury (AKI) secondary to tumor lysis syndrome, urinary obstruction and urate nephropathy.[2] Here we present a case of a middle-aged male who presented with acute kidney injury requiring hemodialysis.

Case Presentation:
A 42 years old man presented with incidental finding of raised serum creatinine associated with recently discovered uncontrolled hypertension and nausea for the past 1 month. He was previously treated for hepatitis C with Sofosbuvir and Ribavarin 1 year earlier with a latest negative PCR 6 months ago. Patient was taking NSAIDS since last three months for back ache, on average 5 tablets a week.

His renal function tests were deranged with a jump in serum creatinine from 0.93 to 6.1mg/dl over 4 months. Urine analysis was negative for proteinuria and bland sediment. Autoimmune profile including ANCA was advised along with spot urine protein to creatinine ratio. Autoimmune profile was negative as shown in table 1. Complete blood counts showed a Haemoglobin of 14.9 mg/dl, white cell count of 9900/ml and platelets 263000/ml. LDH was significantly high at 983 units/L. Ultrasound revealed large sized kidneys measuring 14.1x 7.8x 2.2 cm on the right side and left was 14.4x 8.8 x 2.5cm. Based on history and initial assessment

the differential included NSAID induced AKI and RPGN (rapidly progressive glomerulonephritis) or an infiltrative disease based on large size kidneys. Patient' s serum creatinine and serum urea increased exponentially, and hemodialysis was initiated, Table 2. After 3 sessions of hemodialysis kidney biopsy was performed. No procedure related complication was noted. His histopathology report showed microscopic picture of Burkitt' s Lymphoma; sheets of monomorphic, large sized anaplastic cells with abundant basophilic cytoplasm, round nuclei with coarse chromatin. Immunohistochemical staining reported positive for CD10, CD20, CD3, Ki67 (95%), and C-myc (70% tumour cells), Figure 1.

PET scan was performed for extent of the disease and revealed, metabolically active disease involving both kidneys, stomach, sub centimeter cervical lymph nodes, nasopharynx, osseous and bone marrow sites. Since the main uptake was in the kidneys, it was labeled as primary lymphoma of the kidney.

Patient was referred to oncologist and received chemotherapy resulting in rapid decrease in serum creatinine and discontinuation of dialysis one week later. A follow up ultrasound 4 weeks later revealed reduction of kidney size from 14 cm to 12.5 cm. A further follow up at 8weeks reveled stable creatinine at 1.4mg/dl.

Table 1: Autoimmune profile in our patient presenting with acute kidney injury.

Autoimmune profile		
Parameters	Values	Normal Values
c-ANCA	1.9 u/ml	Less than 10u/ml
p-ANCA	0.9IU/ml	Less than 5 IU/ml
C3	115.5	66-185 mg/dl
C4	26.3	15-52 mg/dl
ANA	Negative	>1:80

Table 2: Serial serum creatinine levels in our patient with acute kidney injury.

Date	1/8/2020	13/12/20	20/12/20	21/12/20	22/12/20	03/03/2021
Serum Creatinine (mg/dl)	0.93	6.1	7.5	7.7	8	1.4
Serum Urea (mg/dl)		111	93	97	113	30

Discussion:

WHO classifies Non-Hodgkin' s Lymphoma into three subcategories; endemic, sporadic, and immunodeficiency related [3]. Non-Hodgkin' s Lymphoma are about 1 – 2% of all lymphomas in adults and 30 – 40% of childhood non-Hodgkin lymphomas in Europe and North America are sporadic-type Burkitt' s lymphoma.[4]

Primary renal lymphoma (PRL) is defined as a non-Hodgkin lymphoma (NHL) restricted to kidneys without extensive nodal disease [5]. It is a rare entity present in less than 1% of population. Despite being a non-endemic area for NHL, Pakistan is still ranked higher amongst other non-endemic countries [6]. According to a local single center cancer registry NHL is listed as the 4th top most malignancy in all age-groups and both sexes combined [7], on the basis of gender, NHL was the third most common malignancy in males and sixth in females. In this registry, most cases were from Punjab province (77.56%), followed by KPK (13.60%). There are higher cases reported in north of Pakistan as compared to south [8]. According to a study conducted in Karachi from 1995 to 1997, Burkitt' s lymphoma (33%) was the most prevalent among the histological subtypes of NHL [9].

Primary renal lymphoma presents with normal to large sized kidneys and is diagnosed on renal biopsy.[10] Primary involvement of the kidneys is rare with few cases reported worldwide. According to a case report conducted, renal infiltration is seen with two common types of patterns; interstitial and intraglomerular. Interstitial involvement causes enlargement of kidneys with increase in lymphomatous cells within the interstitium and subsequent pressure over the parenchyma. Our patient had most likely primary renal lymphoma with secondary metastasis as there were no clinically palpable lymph nodes or evident on radiological evaluation. PET scan showed uptake in some sub centimeter lymph node, bone marrow, and in the stomach. Our patient did not have proteinuria suggesting sparing of the glomeruli also seen in the kidney biopsy.

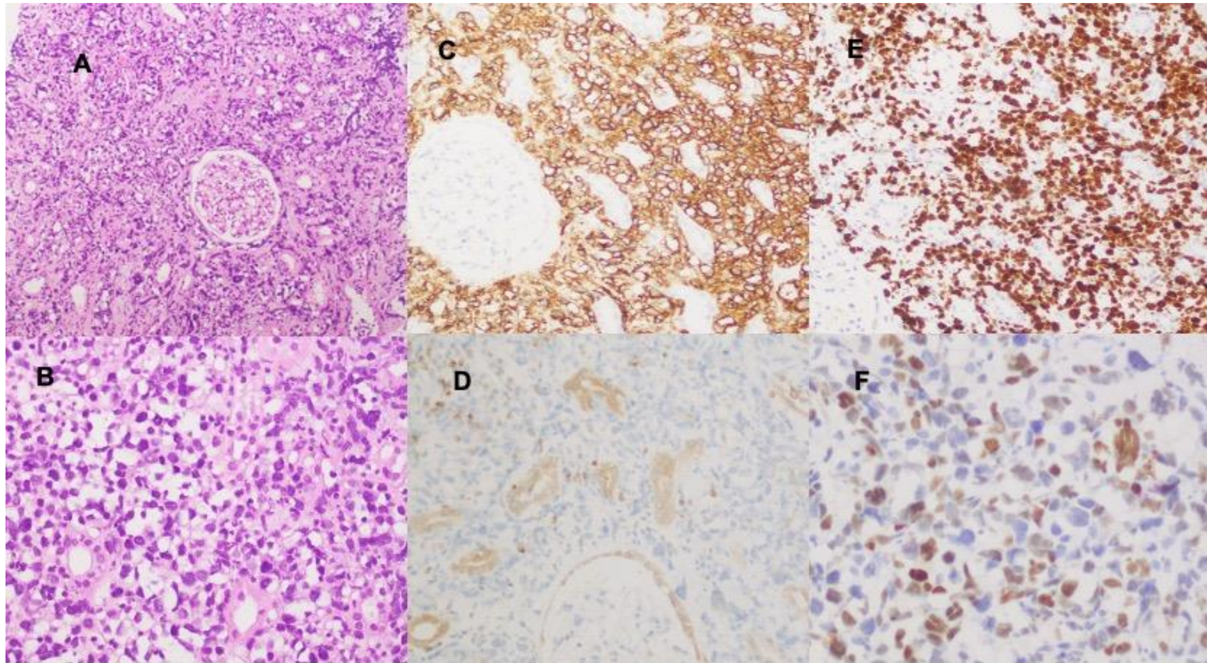

Figure 1: Kidney biopsy showing lymphomatous infiltration of interstitium with positive immunostaining and sparing of glomerulus. **A)** H & E Stain. Low power view 10X of kidney biopsy revealing busy interstitium with lots of large size cells. **B)** High Power view of H & E stain showing sheets of monomorphic, large sized anaplastic cells with abundant basophilic cytoplasm, round nuclei with coarse chromatin **C)** CD 20 Immune staining of infiltrated lymphomatous cells. **D)** BCL -2 stain was negative **E)** Strong Ki-67 immunostaining 95% positive suggesting non B cell lymphoma. **F)** Significant Myc immune stain positive 70%.

Burkitt's Lymphoma is a poorly differentiated lymphocytic lymphoma, with a MYC translocation at 8q24.[11] This translocation of the transcription factor leads to unregulated cellular growth and proliferation signals. It consists of monoclonal proliferating B- lymphocytes with round nuclei and coarse chromatin. The most common presentation are face, jaw, central nervous system and gastrointestinal. Endemic form of Burkitt's Lymphoma is most commonly associated with Ebstein Barr virus infection and involves the face and jaw. Sporadic form has gastrointestinal tract as its primary site in 60-80% and presents as nausea, abdominal pain, vomiting and distention.[1] Our patient did not have significant symptoms related to stomach and we can speculate that it was probably a secondary spread as evident on PET scan in our patient. Most common presentation of secondary NHL in kidneys is extra nodal with symptoms ranging from urinary tract obstruction, tumor lysis syndrome and later chemotherapy induced nephrotoxicity.[12] Hodgkin's and non-Hodgkin's lymphoma both have been reported to cause glomerulonephritis (Membranous and Minimal change besides others) as paraneoplastic syndrome.[14]

Early initiation of chemotherapy improves prognosis, as observed in our patient since Burkitt’s Lymphoma is highly sensitive to chemotherapy.[13]

In conclusion, AKI presenting with enlarged kidneys should raise the suspicion of infiltration especially lymphomas requiring urgent kidney biopsy and management. It is essential to have a quick work up since this will ensure early diagnosis, management and recovery of the kidney functions.

Conflict of Interest: Non declared

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