A Rare presentation of a Lymphoma in a young girl as Acute Kidney Injury and with Neurological Involvement

BALAMURUGAN SWAMINATHAN
Department of Nephrology,
MADRAS MEDICAL COLLEGE AND GOVERNMENT GENERAL HOSPITAL

Abstract:
A 20 yrs old girl presented with high grade intermittent fever, head ache, vomiting and swelling on both sides of neck for 2 weeks. Empirical ATT started. After a week she developed edema legs, oliguria and found to have renal failure. Examination showed Pt was febrile, had anemia, bilateral multiple cervical and axillary lymphadenopathy splenomegaly. Investigation showed Trace proteinuria, no active sediments Hb 10.8gm, Total count 14,000cu.mm, Serum creatinine 4.8mgdl with raised LDH. FNAC of nodes attempted, failed. CXR Mediastinal Widening. USG abd- splenomegaly with Bilateral enlarged kidneys with multiple wedged shape hypochoeic areas present. Two days later she developed BL LMN facial palsy, Bulbar muscle weakness with Quadriparesis. Started on iv methyl prednisolone 1 g for 3 days. Improved.. CSF analysis - numerous lymphocytes with large lymphoid cells (80 percent smudge cells) lymphocytic leukaemia with CNS involvement. CT MRI brain showed lymphomatous infiltration in base of skull and dorsal spine. Rapid regression of lymph nodes, after pulse steroid therapy precluded tissue diagnosis. Kidney biopsy Patchy interstitial lymphoid infiltrates with millacute tubular necrosis. Immunohistochemistry of renal biopsy showed Atypical T-cell lymphoid infiltrate most consistent with T-Lymphoblastic Lymphoma leukemic Infiltrate. Started on chemotherapy with vincristine and dexamethasone. Meanwhile pt developed sudden respiratory difficulty and intubated and on respiratory support. She was treated with intrathecal chemotherapy. Inspite of chemotherapy, her condition deteriorated and succumbed. Diagnosis- Lymphoblastic Lymphoma Stage 4 Acute kidney injury ATN Lymphomatous Infiltration of Kidneys. Disseminated disease with CNS involvement.

Keyword:
Lymphoma, AKI, Lymphomatous infiltration kidneys, CNS
Smudge cell:
Ms. P, 20 yrs old presented with high grade intermittent fever, myalgia and swelling on both sides of the neck for 2 weeks. Empirical ATT was started by a local physician.

Meanwhile she also received over the counter drugs and pain killers/ NSAIDS. She had H/o head ache, vomiting. After a week she developed edema legs, wheeze and given iv dexamethasone. Referred to GGH, Chennai for renal failure with creatinine 3.6mg/dl. On examination patient was febrile, had mild pallor, bilateral multiple small cervical and axillary lymph nodes – of size < 1 cm, not matted. Mild edema legs. Pulse rate – 120/min. BP – 140/100 mm Hg. RR – 14/min. Abdomen : splenomegaly. Provisional diagnosis- Tuberculous lymphadenitis with ATT induced renal failure./? NSAIDS induced AKI/ lymphoma with tumor lysis syndrome. Urine Analysis: Trace proteinuria, no RBCs: PCR - 0.16: Haemoglobin – 10.8 gm/dl; Total count – 14,000/cu.mm: DC P72 L28; ESR 40mm in 1 hour; Platelet – 2.2 lakhs/cu. Mm; Blood Urea – 74mg/dl; Serum creatinine – 4.8mg/dl; Sodium – 136 meq/l; Potassium – 3.9 meq/l; Uric acid – 6.1mg/dl; Calcium – 9 mg/dl; Phosphate – 5.1 mg/dl; Total proteins – 5.8 g/dl; Serum albumin – 3.7 g/dl; Blood Sugar – 90mg/dl; Serum LDH – 1853 U/L; Liver function tests – normal; INR – 1.12; FNAC of nodes attempted, couldn’t get tissue.

CXR : Mediastinal Widening; Ultrasound abd : splenomegaly, no hepatomegaly. RK – 12X4.4 cm Increased echoes, LK – 11.8 X 4.2cm multiple wedged shape hypoechogenic areas present.

Two days later she developed B/L LMN facial palsy. Numbness and progressive weakness of all 4 limbs/Bulbar muscle weakness with H/O regurgitation. Neurologist opined as ? ADEM (acute demyelinating encephalomyelitis). Started on iv methyl prednisolone 1g for 3 days. NCS showed features s/o AIDP. Responded dramatically to steroids. Weakness improved, facial palsy improved. Urine output improved, creatinine settled down to 1.8mgs. Underwent LP, a day after IV steroids. Protein – 800mg/dl, Sugar – 68mg/dl, Cell count – 120/cu.mm( 90% lymphocytes) Cytology numerous lymphocytes with large lymphoid cells 80% smudge cells seen. AFB negative.

(Immature leukocytes of any type that have undergone partial breakdown during preparation of a stained smear or tissue section, because of their greater fragility. Smudge cells are seen in largest numbers in lymphocytic leukaemia. Synonym: basket cell, Gumprecht’s shadows, shadow cells , degenerated cells.)
SMUDGE CELL:
Hematologists suspected ACUTE LYMPHOBLASTIC LEUKEMIA ; CBC – TC 18,000. DC - P 78 L18 E2 B2 ; HB – 11 gm / dl, Platelets -1,00,000/cu.mm, Peripheral smear - normal

CT & MRI brain showed lymphomatous infiltration in base of skull and dorsal spine. There was rapid regression of lymph nodes, after pulse steroid therapy. It precluded tissue diagnosis. Even though CSF was suggestive of lymphoma, absence of tissue diagnosis caused delay in initiating chemotherapy. Hence we proceeded with renal biopsy

Renal Biopsy-Linear cores of renal tissue with 5 glomeruli per section. Mildly enlarged and no increase in cellularity capillary walls are thin. Some tubules appeared dilated with attenuation of lining epithelium. Patchy infiltrates of lymphoid cells which are medium sized and show smooth chromatin. Occasional plasma cells & neutrophils are seen.

Impression: Patchy interstitial lymphoid infiltrates with mild acute tubular necrosis.

Bone marrow aspiration - Normocellular with hypercellular fragments megakaryocytes adequate, Lymphocytes 20%, Atypical lymphoid cells 8%.

EIMMUNOHISTOCHEMISTRY OF RENAL BIOPSY- CD3 – POSITIVE (FOCAL); CD43 - POSITIVE (FOCAL); CD20 – POSITIVE (FEW CELLS); CD79a – POSITIVE (FEW CELLS); Ki67 – 40-50%; CD138 – POSITIVE (OCCASIONAL CELLS); Tdt – POSITIVE; CD56 – NEGATIVE; CD99 – POSITIVE

Impression: Renal tissue shows Atypical T-cell lymphoid infiltrate most consistent with T-Lymphoblastic Lymphoma / leukemic Infiltrate

Started on chemotherapy with vincristine and dexamethasone; Meanwhile pt developed sudden respiratory difficulty and shifted to IMCU; Pt was intubated and on respiratory support; She was treated with intrathecal chemotherapy; Inspite of chemotherapy, her condition deteriorated and succumbed.

FINAL DIAGNOSIS- T-Lymphoblastic Lymphoma Stage 4 / Acute kidney injury — ATN / Lymphomatous Infiltration of Kidneys/ Disseminated disease with CNS involvement

Renal involvement in lymphoma
AKI – Caused by volume depletion, sepsis, uric acid nephropathy, tumour lysis syndrome, post-renal obstruction, renal vein thrombosis.
Lymphomatous infiltration of kidney (LIK)
Direct effects-
Obstruction of ureters; Compression, inva-
sion or retroperitoneal fibrosis; Obstruction of
renal artery or vein; Rupture of renal pelvis or ureter

Indirect effects-
Hypercalcemia; Paraproteinemia, Bence-
Jones proteinuria; Nephrotic syndrome-
Minimal change nephropathy, Membranous
nephropathy, MPGN; Amyloidosis; MIDD;
Immunotactoid glomerulopathy; Dissemi-
nated Intravascular Coagulation.

Treatment-related-
Radiation nephri-
tis; Acute Uric acid Nephropa-
thy: Xanthine precipitate or stone.

Lymphomatous infiltration of kidney (LIK)
Kidneys are more common site for metas-
tatic lymphomatous infiltration (more often
with Non hodgkin’s lymphoma) The involve-
ment is diffuse, bilateral and symmettri-
cal. Renal involvement has been reported in
6–60% of cases at autopsy. Often asymptomatic, patient may present
with flank pain, haematuria palpable mass
and renal failure or Hypertension, resulting
from renal ischaemia from compression by
the tumour. Acute kidney injury due to LIK is
uncommon. Urinalysis - mild proteinuria, few
RBCs and occasional hyaline and granular
casts. Ultrasonogram of kidneys shows
hypoechogenic areas with enlarged kid-
neys. CT picture shows irregularities within
renal parenchyma, non enhanced with con-
trast study. MRI and PET can be useful.
Richmond et al (Am J Med 1962)- LIK is the
most common extra-nodal site for metas-
tatic lymphoma and has been observed in
34% of 696 autopsies. 0.5% of those with
renal involvement had developed AKI. Dense
Tumor infiltration of renal parenchyma cause
compression of tubular lumen and intrarenal
obstruction. Tubules are compressed, epithelial
cells flattened, tubular basement mem-
brane flattened. Reversible ATN has
also been described. Glomeruli are
morphologically normal.
LIK are high grade in nature. LIK should
be suspected in any patient presenting
with an unexplained AKI and enlarged
kidneys. Renal biopsy is an important
tool to confirm the diagnosis. M etas-
tatic lymphoma in kidney indicates ad-
vanced disease and overall prognosis is
poor.

Acute tumor lysis syndrome - most
frequently encountered in patients with
a large tumor burden (often due to rap-
idly proliferating lymphoma or leukemia)
in whom aggressive radiation or chemo-
therapy has been recently initiated & in
the setting of particularly extensive dis-
ease with rapid cell lysis, resulting in
profound hyperkalemia, hyperphos-
phatemia, and hypocalcemia (due to
precipitation of calcium phosphate) may
be observed. This is termed acute tu-
mor lysis syndrome.

Acute uric acid nephropathy
If rapid lysis of tumor cells occurs, mas-
see quantities of uric acid precursors
are released. This induces a marked
increase in synthesis of uric acid and
thus acute-hyperuricemia. The sub-
sequent renal uricosuric response may be
of sufficient magnitude to exceed solu-
ability limits for uric acid in the distal
nephron, particularly in the presence of
dehydration or metabolic acidosis. The
resultant intrarenal obstruction pro-
duces a characteristic pattern of acute
renal failure. The kidneys are enlarged,
very bright on ultrasonography, the re-
duced urine volume contains massive
amounts of uric acid crystals. The
plasma urate exceeds even
1000 µmol/l. In patients with tumour
breakdown the plasma and urinary phosphate concentrations are also very high.

**Treatment** - Prophylaxis during treatment of malignancies, with an adequate volume repletion and a diuresis established before treatment begins. Addition of either or both alkalinization and allopurinol (which again should be started before treatment) although theoretically attractive do not seem to make much difference. In addition, use of allopurinol runs the risk of inducing acute xanthine nephropathy since xanthine is even more insoluble than uric acid and its solubility does not increase on increasing the urine pH. In the majority of treated patients the urinary concentration of xanthine exceeded its limit of solubility. Injections of encapsulated uricase or a recombinant PEG-uricase with a longer biological half-life (rasburicase) is available. Dialysis will often be required to tide the patients over their renal failure, and should be done by haemodialysis.

**Glomerulopathy as a complication of lymphoma or leukaemia:**
Hodgkin's Lymphoma was most commonly associated with minimal change nephropathy while Non-Hodgkin's Lymphoma with crescentic nephritis and mesangiocapillary glomerulonephritis, and chronic lymphocytic leukaemia with mesangiocapillary glomerulonephritis has been suggested that there is an alteration in T-cell function with increased secretion of lymphokines or of abnormal lymphokines producing increased vascular permeability and proteinuria. An alternative hypothesis implicates a tumour related virus or an unrelated intercurrent viral infection as the cause of the glomerular lesion.

**References:**