HIV Associated Burkitt’s Lymphoma

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Abstract
Burkitt’s lymphoma (BL) is a highly aggressive B-cell non-Hodgkin Lymphoma (NHL) associated with chromosomal translocations resulting in upregulation of the proto-oncogene C-MYC, which drives progression through the cell cycle (1). NHL accounts for approximately one third of AIDS-related malignancies and the frequency of BL is 2.4–20% of HIV-associated NHL (2). The outcome of HIV-associated non-Hodgkin lymphoma (NHL) has improved substantially in the highly active antiretroviral therapy (HAART) era. However, HIV-Burkitt lymphoma (BL), which accounts for up to 20% of HIV-NHL, still has poor outcome with standard chemotherapy. We present here a 26 years old female who presented with congestive cardiac failure and sudden onset paraparesis and was finally diagnosed to have right atrial mass and had extradural lesion extending from L2 to S1 which turned out to be High grade NHL - Burkitt’s Lymphoma.

Introduction
Burkitt’s lymphoma is an uncommon form of non-Hodgkin lymphoma in adults, with an incidence of approximately 1200 patients per year in the United States. Immunodeficiency associated Burkitt’s lymphoma is more commonly seen with human immunodeficiency virus (HIV) infection than other forms of immunodeficiency (3). In patients with Burkitt’s lymphoma, central nervous system involvement is a frequent complication which is difficult to treat and associated with poor prognosis. Here we present a case of HIV associated Burkitt’s Lymphoma who presented with right atrial mass and cauda equina syndrome.

Case Report
26 year old female, married since 8 years, was admitted with complaints of breathlessness, swelling over both lower limbs and distension of abdomen since 8 days and weakness of both lower limbs since 2 days. Patient was apparently alright 8 days back when she started getting breathlessness which was initially exertional. Patient was admitted to a private hospital where she was diagnosed to have HIV infection. Patient received symptomatic treatment, however breathlessness increased over next 8 days and the patient was referred to our hospital for further management.

At presentation in our hospital, patient was breathless even at rest (NYHA grade IV dyspnoea). Breathlessness was associated with swelling over both lower limbs and distension of abdomen. The patient also had weakness of both lower limbs since 2 days which was acute in onset more in right lower limb than left lower limb and was associated with backache and urinary retention. Within next 2 days, the patient developed complete loss of power, loss of sensation and inability to move both lower limbs. This was accompanied by development of swelling over right mandibular region.

There was no history of chest pain, orthopnoea, paroxysmal nocturnal dyspnoea, cough, trauma, weakness in upper limbs. Family and personal history was not contributory.

On general examination patient was conscious and oriented, afebrile, pulse was 130/min, blood pressure was- 110/70 mmHg. Jugular venous pressure was raised. Bilateral pitting pedal edema was present. However there was no pallor, icterus, lymphadenopathy, clubbing or cyanosis.

On local examination there was a 5 x 2 cm sized hard swelling in right mandibular region which was fixed to underlying mandible. On systemic examination, heart
Figs. 1 and 2: Showing atrial mass filling the right atrium with mild to moderate pericardial effusion.

Figs. 3, 4 and 5: Showing well-defined extradural soft tissue intensity lesion within spinal canal extending from L2 to S1 vertebral body levels with mass effect.
sounds were normal. Respiratory system examination revealed bilateral basal crepts. Abdomen was soft, distended with right hypochondriac tenderness and minimal free fluid in abdomen.

On central nervous system examination, patient was conscious and oriented. Higher functions and cranial nerves were normal. There was hypotonia in both lower limbs. Power was Grade V in both upper limbs but Grade II in right lower limb and Grade IV in left lower limb. Reflexes were normal in both upper limbs, however both knee jerk and ankle jerks were depressed in both lower limbs. Plantars were not elicitable bilaterally. Sensory examination was normal on both sides. However there was spinal tenderness at L2-L3 vertebra. Within 2 days, the weakness increased and the patient developed paraplegia with complete loss of sensations in both lower limbs with a sensory level at L2. Power in both lower limbs became grade 0 with bilateral lower limb areflexia. Plantars were not elicitable.

At this stage provisional diagnosis was kept as Acute sensory-motor paraplegia due to extradural compression at L2 with right heart failure. Patient was further investigated. Patient had haemoglobin 10.9 g/dl, haematocrit-30.8, WBC count 7500/cmm, plt count 341000, random blood sugar level was 90 mg%, creatinine was 1 mg/dl, sr sodium-145 mEq, sr potassium -4.2 mEq. Patient was confirmed as HIV-1 Positive on ELISA with a CD4 count of 465. HIV viral load was not done. USG Abdomen showed moderate free fluid in abdomen, mild pericardial effusion with bilateral pleural effusion. 2D Echocardiography showed mild to moderate pericardial effusion and a large irregular mass 2.7 x 2.8 cm in size was seen in right atrium, occupying 70% of right atrium and obstructing the tricuspid valve (? Myxoma ? Thrombus), dilated inferior vena cava with normal left ventricular size and function (Figures 1 and 2).

MRI lumbosacral spine (plain + contrast) showed a well defined extradural soft tissue intensity lesion within spinal canal extending from L2 to S1 vertebral body levels with mass effect, suggestive of either a)
neurogenic tumour – peripheral nerve sheath tumour
b) Infective granulation tissue/fungal aetiology which was less likely due to involvement of commonly adjoining vertebral bodies and absence of marked oedema (Figures 3, 4 and 5).

The lesion was extending into either sided neural foramina, more on right side and extending deep to psoas muscle causing anterior displacement of nerve roots in filum terminale with thecal sac.

Patient was operated under general anaesthesia. Laminectomy and debulking of extradural tumour from L2 to S1 was done. The lesion was extradural, soft and fragile in consistency, not very vascular (Figures 6 and 7).

Histopathology of the excised tumour revealed High grade Non Hodgkin’s lymphoma – Burkitt’s type. Immunohistochemistry showed strong positivity for CD 20 with MiB index : > 95% (Figures 8, 9, 10 and 11).

Local ultrasonography of right mandibular mass showed heterogeneous lesion in right lower part of face mostly arising from masseter with a possibility of neoplastic aetiology. Hence a CT scan of neck was performed which showed bulky swollen right masseter, temporalis, medial and lateral pterygoids with inhomogeneous enhancement with erosions among adjacent ramus of mandible suggestive of myositis with mandibular osteomyelitis (Figures 12 and 13).

Thus we had a patient of PLHIV (person living with HIV) with cauda equina syndrome due to Burkitt’s lymphoma (Stage IV) and right atrial mass, most likely intra-atrial lymphoma.

Patient was started on highly active antiretroviral therapy(Zidovudine+Nevirapine+ Lamivudine) and later was administered chemotherapy according to BFM B NHL 86 protocol (adult) (German Berlin-Frankfurt-Munster Protocol) after histopathological confirmation. However, unfortunately patient succumbed during the course of chemotherapy.

Discussion

Burkitt’s lymphoma (BL) is named after Denis Parson Burkitt who first wrote about this kind of tumour in children and young adults in Africa. Three main clinical variants: a) Endemic variant seen in Africa b) Sporadic variant and c) Immunodeficiency associated.

a) Endemic type occurs in equatorial Africa and is most common malignancy of children in this area. Ebstein Barr Virus (EBV) infection is seen in 95% cases. It involves jaw or other facial bones, distal
ileum, caecum. b) Sporadic type is seen in Europe and United state. It is mainly a disease of children. Most common site of involvement is abdomen especially the ileoceleal area. EBV positivity is seen in 15-30% cases. c) Immunodeficiency-associated Burkitt’s lymphoma is mainly seen in HIV infected patient. It is 1000 times more common than general population. 2% of AIDS patients develop Burkitt’s lymphoma. It constitutes 30-40% of NHL in HIV positive patients. EBV positivity is seen in 30-40% cases. Majority have Stage IV disease at the time of diagnosis. It may show plasmacytoid differentiation which is unique to AIDS patients. Patients are generally younger, have higher mean CD4 counts of more than 200. Diagnosis of Burkitt’s in HIV positive patients often represents the first AIDS defining criterion in these patients. The closest differential diagnosis is diffuse large B-cell lymphoma. Patients can tolerate the standard chemotherapeutic regimens and have better outcomes if given with HAART.

The differential diagnosis of right atrial mass in a young HIV positive patient includes:
1) Primary cardiac lymphoma
2) Kaposi’s sarcoma
3) Metastatic Non-Hodgkin’s lymphoma
4) Thrombus
5) Myxoma
6) Hodgkin lymphoma
7) Sarcomas
8) Burkitt’s lymphoma

Burkitt’s lymphoma is associated with chromosomal translocation of the c-myc gene 1) [t(8;14)] involves c-myc and IgH- most common 2) [t(2;8)] involves IgK and c-myc 3) [t(8;22)] involves c-myc and IgL.

Non Hodgkin’s lymphoma (NHL) involves spine in two ways. One is primary involvement of only spinal epidural space with no other systemic involvement. This entity is known as primary spinal epidural NHL. Second is involvement of epidural space in a setting of disseminated NHL. NHL has spinal localisation in 0.1-6.5% of cases. NHL presenting for first time as spinal cord compression is rare and occurs in less than 5% of cases. Petit et al. reported 13 cases of NHL presenting as spinal cord compression. One patient had AIDS associated Burkitt’s lymphoma. Kumar S et al. have reported a similar case of Non Hodgkin’s lymphoma in HIV positive patient presenting with spinal cord compression which turned out to be anaplastic large cell lymphoma.

**Treatment**

The tumour has high growth fraction with shortest doubling time (approximately 25 hours). It is highly curable. 80–90% of those with localised disease and 50% of those with more widespread disease are cured. Late relapses are hardly seen. Following chemotherapeutic regimens can be used and choice of regimen depends on the institution.

1) Hyper-CVAD alternating with Methotrexate and cytarabine with addition of Rituximab.
2) CODOX-M/IVAc Regimen (Magrath protocol) with or without Rituximab.
3) Dose-adjusted EPOCH with Rituximab.

**Prognosis**

Prognosis for children is generally good. Tumour responds well to chemotherapy. 80% of children with early-stage disease are cured. Prognosis in adults is predicted by IPI index. a) IPI score 0-1: Overall survival- 73%; Disease Free survival – 70%. b) IPI score 5: Overall survival – 26%; Disease Free Survival – 40%.

Factors with poor prognosis are a) age > 60 yrs b) Stage III or IV disease c) spread to more than one extranodal site d) High levels of LDH e) poor general health. Poor prognostic factors in AIDS patients are CD4 count < 200, opportunistic infection, bone marrow involvement, extranodal spread, age > 35 yrs and poor general health. Average survival is 6 months. Early diagnosis and prompt treatment help improve the survival rate.

**Acknowledgement**

Dr. Sujit Joshi (Consultant Histopathologist)

**References**