

Burkitt's Lymphoma in a Post-renal Transplant Recipient: A Rare and Aggressive Malignancy

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ABSTRACT

Burkitt lymphoma is a highly aggressive form of non-Hodgkin B-cell lymphoma known for its rapid proliferation. It commonly involves areas such as the jaw, abdominal region, or Central Nervous System (CNS). This type of lymphoma is often associated with infections like Epstein-Barr Virus (EBV) and Human Immunodeficiency Virus (HIV). Additionally, it frequently features chromosomal translocations that affect the MYC oncogene. The case involves a 34-year-old man with diabetes who has been undergoing immunosuppressive treatment for 10 years following a kidney transplant. He presented with complaints of lower abdominal swelling, nausea, vomiting, and backache for the past 15 days, along with signs suggestive of intestinal obstruction for the last five days. Comprehensive history-taking, clinical examination, and diagnostic investigations indicated an intestinal obstruction caused by a mobile intra-abdominal mass located in the suprapubic region. An ultrasound-guided Tru-Cut biopsy of the intra-abdominal mass identified it as Non-Hodgkin Lymphoma (NHL), most likely Burkitt Lymphoma (BL), which was subsequently confirmed through Immunohistochemistry (IHC). The patient was managed with Rituximab (a monoclonal antibody), and his immunosuppressive therapy was continued. However, he showed a poor response to treatment after four weeks, prompting a revision of the regimen to the Cyclophosphamide, Vincristine, Doxorubicin, and High-Dose Methotrexate/Etoposide, Ifosfamide, and Cytarabine (CODOX-M/IVAC) chemotherapy protocol. The aim of this paper presentation is to highlight the rarity of the disease and the management of a patient on immunosuppressant therapy following an organ transplant.

Keywords: Histopathology examination, Immunohistochemistry, Non-hodgkins lymphoma

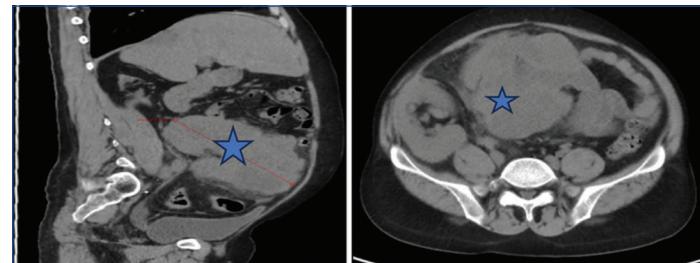
CASE REPORT

A 34-year-old male renal transplant recipient had been on immunosuppressive therapy with tacrolimus, mycophenolate mofetil, and prednisolone for 10 years and developed diabetes four years ago. He presented with nausea, vomiting, low backache, and a lower abdominal mass for 15 days, along with abdominal pain and obstipation for five days prior to admission. Clinical examination revealed a pale individual with a lower abdominal mass measuring 17×15 cm, which was mobile, non-tender, solid, and had well-defined margins [Table/Fig-1]. The patient was managed as a case of intestinal obstruction, likely secondary to a neoplastic mass.



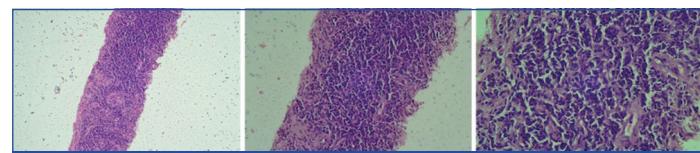
Table/Fig-1: Patient photograph left lateral view showing abdominal distension, globular, more on the infra-umbilical region.

Blood investigations showed anaemia (haemoglobin=9.8 g/dL), leukocytosis (13,000/µL), hyperuricaemia (54 mg/dL), and elevated creatinine (1.1 mg/dL). An abdominal ultrasound revealed a solid lesion measuring approximately 17×15×12 cm in the infra-umbilical region, compressing the bowel and causing intestinal obstruction. Contrast-Enhanced Computed Tomography (CECT) of the abdomen and pelvis confirmed the lesion's location and the presence of small bowel obstruction [Table/Fig-2]. An ultrasound-guided tru-cut biopsy was performed.



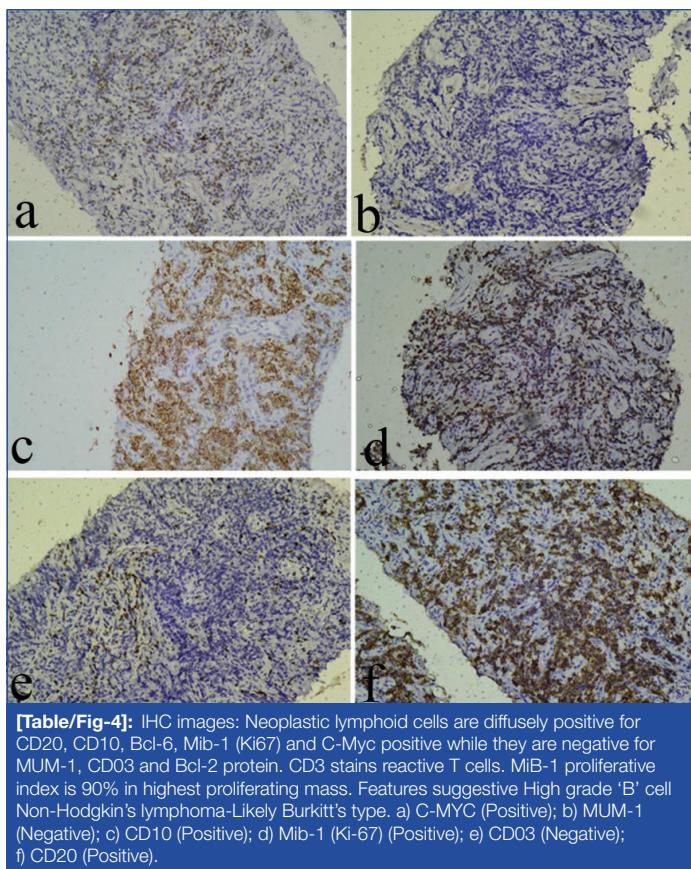
Table/Fig-2: CECT abdomen-pelvis - 17×15×12 cm mass involving bowel loop central and lower abdomen likely neoplastic mass.

Histopathological examination revealed monotonous medium-sized cells with a high nuclear-to-cytoplasmic ratio; the smear showed necrotic debris and a few polymorphs, favoring a diagnosis of Non-Hodgkin Lymphoma (NHL), most likely Burkitt Lymphoma (BL) [Table/Fig-3]. Immunohistochemistry (IHC) showed neoplastic lymphoid cells that were positive for CD20, CD10, Bcl-6, Mib-1 (Ki67), and C-Myc, and negative for MUM-1, CD3, and Bcl-2 [Table/Fig-4a-f]. Based on these findings, a diagnosis of BL was made. Epstein Barr Virus (EBV) Polymerase Chain Reaction (PCR) was negative in the patient.

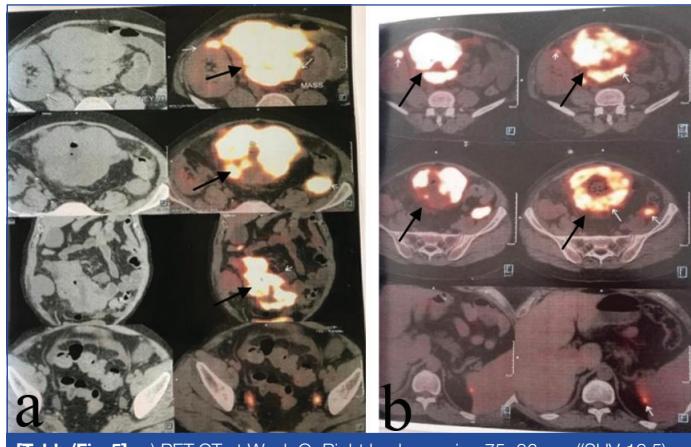


Table/Fig-3: Histopathological Examination (HPE) (left to right : 10x: 20x: 40x) showing monotonous medium sized abnormal cells with high Nuclear: Chromatin ratio, smear showed necrotic debris and few polymorphs favouring the diagnosis NHL, most likely Burkitt's lymphoma.

Fluorodeoxyglucose Positron Emission Tomography (PET)/CT showed uptake in the right lumbar region measuring 75×86 mm {Standardised Uptake Value (SUV) 19.5} and centrally in the pelvis measuring 120×102 mm (SUV 32.01) [Table/Fig-5a,b]. The patient was treated with Rituximab (375 mg/m²), a monoclonal antibody, administered



[Table/Fig-4]: IHC images: Neoplastic lymphoid cells are diffusely positive for CD20, CD10, Bcl-6, Mib-1 (Ki67) and C-Myc positive while they are negative for MUM-1, CD03 and Bcl-2 protein. CD3 stains reactive T cells. Mib-1 proliferative index is 90% in highest proliferating mass. Features suggestive High grade 'B' cell Non-Hodgkin's lymphoma-Likely Burkitt's type. a) C-MYC (Positive); b) MUM-1 (Negative); c) CD10 (Positive); d) Mib-1 (Ki-67) (Positive); e) CD03 (Negative); f) CD20 (Positive).



[Table/Fig-5]: a) PET-CT at Week 0: Right lumbar region 75x86 mm/(SUV-19.5) and pelvis centrally 120x102 mm/(SUV-32.01); b) PET-CT after 4 weeks : Right lumbar 106x73 mm/(SUV-19.2) and pelvis centrally 127x135 mm/(SUV-23.08).

weekly for four weeks [1]. Monitoring included blood sugar levels, renal function tests, hepatic function tests, serum uric acid levels for tumour lysis risk, and serum Lactate Dehydrogenase (LDH) levels.

However, after four weeks, there was no significant clinical reduction in the size of the mass lesion. A repeat PET-CT scan showed no notable decrease in the size of the lesions [Table/Fig-4b]. Due to the poor response to Rituximab, the patient was switched to the CODOX-M/IVAC regimen for six cycles, to which he responded well. This resulted in a significant reduction in the size of the lesion and an improvement in symptoms. The patient is currently under regular follow-up and is being closely monitored.

DISCUSSION

BL is a rare but highly aggressive subtype of mature B-cell NHL. The earliest description of BL likely came from Albert Cook, a missionary doctor in Uganda. In his detailed clinical notes, he documented a child with a large jaw tumour—an illustration strongly suggesting a case of BL [2].

First described in equatorial Africa by surgeon Denis Burkitt in 1958, endemic BL was the first cancer linked to a virus (Epstein-Barr

virus, or EBV) and the first associated with a chromosomal translocation (IGH:MYC) [3]. Research on BL led to the discovery of the first recurrent chromosomal aberration, t(8;14), highlighting the roles of MYC and EBV in its development. While most patients respond well to chemotherapy, relapsed or refractory cases often have a poor prognosis [4].

The current standard treatment for BL in children generally involves either a regimen similar to that used for Acute Lymphocytic Leukaemia (ALL) or a shorter course of intensive multi-agent chemotherapy accompanied by prophylaxis for the Central Nervous System (CNS). These treatments have proven effective, with many paediatric patients achieving a cure and long-term survival rates ranging from 60% to 90%. In contrast, results for adults are more inconsistent and largely depend on the specific patient groups included in the limited available studies [5].

BL in adults is still considered highly treatable, and recent trends indicate that outcomes for older patients have improved. However, there is a lack of comprehensive data regarding treatment for individuals over the age of 40 years. A pooled analysis suggests that older patients may experience worse outcomes than their younger counterparts; yet, it's worth noting that at least half of these patients achieve a cure. In adults, BL is usually linked to immunocompromised states, especially HIV infection or immunosuppressive therapy [5].

NHL is the most common haematological malignancy worldwide, with an incidence rate of 0.62%. BL accounts for 2% of these cases. The incidence in India is 2.7%, with a mortality rate of 2.4% [6]. The World Health Organisation (WHO) classification of BL divides it into endemic, sporadic, and immunosuppression-related types. The usual presentation of the endemic type is with facial or jaw involvement, while sporadic cases typically present with Gastrointestinal (GIT) involvement, and immunosuppressed cases may involve the GIT, bone marrow, and/or CNS. B symptoms are uncommon, seen in only about 30% of cases. Typically, immunosuppressed adults present with rapidly developing disease involving the abdomen and B symptoms. Extranodal disease is common, especially in the bone marrow (35%) and the CNS (15%). Early diagnosis and staging of the disease improve the prognosis [7].

BL is a fast-growing B-cell tumour with nearly 100% proliferation, creating a "starry-sky" appearance under the microscope due to macrophages clearing apoptotic cells. The tumour cells are medium-sized with basophilic, vacuolated cytoplasm and round nuclei. They typically express CD10, BCL6, CD20, CD79a, and CD45. Around 25-40% of sporadic and HIV-related cases show the presence of EBV. A hallmark MYC gene translocation, usually t(8;14), drives uncontrolled cell growth, with occasional involvement of chromosomes 2 or 22 [8].

BL is an uncommon subtype of Post-Transplant Lymphoproliferative Disorder (PTLD), making up less than 3% of cases. It typically presents around five years post-transplant in adults. EBV positivity is more frequent in Burkitt-PTLD than in sporadic or immunodeficiency-related Burkitt lymphoma. Sequential therapy is often effective, reducing the need for aggressive chemotherapy in these patients [9]. Outcomes for relapsed or refractory BL are generally poor. A retrospective study showed a 3-year Overall Survival (OS) rate of 37% in patients who responded to chemotherapy, but only 7% in those with chemo-resistant disease after autologous stem cell transplant [10].

BL presenting as an intra-abdominal mass was reported in two cases by Cubranic A et al., demonstrating that BL can occur in older age groups over 70 years with atypical gastrointestinal locations such as the hepatic flexure and stomach. Both cases involved HIV-negative and EBV-negative individuals, emphasising that age and tumour site alone do not exclude BL from differential diagnoses. Accurate differentiation between BL and diffuse large B-cell lymphoma remains challenging but is essential, requiring comprehensive analysis to guide appropriate treatment strategies [11].

BL rarely arises from the appendix and ovaries, presenting as acute appendicitis and infertility, followed by a rapidly growing abdominal tumour. One such case was reported in a six-year-old girl by Mimery AH et al., [12].

CONCLUSION(S)

This case underscores a rare presentation of BL as intestinal obstruction in a post-renal transplant patient. Although latent EBV infection is commonly seen in transplant recipients, it was negative in our patient. Initial treatment with rituximab alone showed a limited response; however, sequential chemotherapy led to significant symptom improvement and a noticeable reduction in the mass size.

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