

## ILEOCAECAL BURKITT'S LYMPHOMA IN A 14 YEAR OLD MALE: A case report and review of literature

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### ABSTRACT

Burkitt's lymphoma is a high grade B cell neoplasm, classified under the category of small non-cleaved cell lymphoma (SCNL). Outside Africa, it accounts for less than 2% of all cases of Non Hodgkin's Lymphoma. It is presumably the fastest growing human malignancy. Cyclophosphamide based combination chemotherapy is the main stay of treatment, and the patients are prone to develop tumor-lysis syndrome. Here we present the interesting case of a 14 year old boy who presented with the clinical picture of subacute intestinal obstruction, underwent iliocaecal resection, and was found to have Burkitt's lymphoma.

**KEY WORDS:** Burkitt's lymphoma, surgical resection, chemotherapy, tumor lysis syndrome.

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### INTRODUCTION

Burkitt's lymphoma (BL) are highly aggressive, rapidly growing B-cell neoplasm mainly affecting children and young adults, that are characterized by dysregulation of the c-myc oncogene.<sup>1,2</sup> It was originally described by Den-

nis Burkitt in equatorial Africa where this tumor accounts for approximately 50% of all childhood cancers.<sup>3,4</sup> It is presumably the fastest growing human malignancy. The rapid growth rate of this tumor makes undue delay in administering proper therapy a substantial hazard. Approximately 50%-80% of adult patients with BL can be cured with intensive chemotherapy regimens and in pediatric populations the cure rate is even higher.<sup>5,6</sup> Relapse cases, occurring always early, still have a very bad prognosis and remain a challenge for the future.<sup>7</sup>

### CASE REPORT

A 14 year old boy presented with the main complaint of pain in the abdomen, mainly in supra-umbilical region of 25 days duration, constipation for the last 20 days, vomiting for the past 2 weeks, loss of appetite for the last 10 days and abdominal distension for the last 5 days and inability to pass stools and flatus for the last 2 days. All these symptoms were progressively increasing in intensity. There was no

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history of fever, significant loss of weight or of altered bowel habits. There was no effect of oral medication on these symptoms.

On examination, the general condition of the patient was fair. There was no pallor, pedal edema or significant LAP. On per abdominal examination, there was no tenderness and no guarding. Per rectal examination was within normal limits. When investigated, the complete hemogram, biochemical profile, chest X-ray and serum LDH were essentially normal. On abdominal USG, there was no free fluid in the abdomen. Few fluid filled bowel loops were seen. CT scan revealed mass lesion in ileocaecum with diffuse thickening of bowel wall. Pre-operative diagnosis of subacute intestinal obstruction was made. At surgical exploration, there was an ileocaecal lump causing near-complete obstruction. Mesenteric LAP was present.

The patient underwent ileocaecal resection, ilioascending end to end anastomosis and local peritoneal lavage. Histopathological examination of the resected ileocaecal segment of gut revealed Non Hodgkin's Lymphoma, high grade Burkitt's type. The isolated lymph nodes were free of tumor infiltration. Bone marrow aspiration and trephine was essentially normal. The patient was put on combination chemotherapy with COP regimen (Inj Cyclophosphamide, Inj Vincristine and Tab Prednisolone) two weeks post-operatively, with frequent monitoring of biochemical parameters of tumor lysis syndrome. He has received three courses so far and is asymptomatic.

## DISCUSSION

Burkitt's lymphoma was originally described by Dennis Burkitt in 1956 in equatorial Africa where this tumor accounts for approximately 50% of all childhood cancers.<sup>3</sup> Outside Africa, it accounts for less than 2% of all cases of Non Hodgkin's Lymphoma.<sup>4</sup> In one Indian series on pattern of solid malignant tumors in children, Pramanik et al<sup>8</sup> studied 263 cases over a 10 year period; of which there were only 2 cases (0.76%) of Burkitt's lymphoma. The WHO clas-

sification subclassified BL, the major component of the small non-cleaved cell lymphoma (SCNL) class, into endemic, sporadic, AIDS-associated and atypical or pleomorphic variants.<sup>9</sup>

Endemic BL occurs largely as a pediatric disease and primarily in Africa, and is almost always associated with Epstein-Barr Virus (EBV) exposure.<sup>10</sup> The subendemic form occurring in children in Brazil is also associated strongly with EBV. The sporadic form occurs in children and adults elsewhere and is less likely (<25%) to be related to EBV. Sporadic BL is clinically similar to but not identical to the endemic form; it is more likely to have leukemic or bone marrow involvement, and less likely to have jaw involvement. Sporadic BL may also occur in patients of any age. BL in India is "intermediate" between the sporadic and endemic types, both in its clinical presentation and its association with EBV, which varies from 25-80%.<sup>11</sup> In all areas, the male to female ratio is 2.5:1. Patients with Human Immunodeficiency Virus (HIV) also appear to be at risk for developing Burkitt's lymphomas. The lifetime risk of developing central nervous system disease is 20%-30% for Burkitt's lymphoma.<sup>6</sup>

The most common site of disease presentation in endemic BL is the face, primarily the mandible and frequently multiple facial bones, which are involved in 55-75% of patients. The next most common area of involvement is the abdomen seen in 30-50% patients. In sporadic BL, the most common site of presentation is the abdomen (ileocaecum, genitourinary organs, spleen, mesentery, peritoneum and abdominal lymph nodes). Approximately 60-70% of sporadic BL patients have advanced disease at diagnosis. Murphy's classification may be used for staging Burkitt's lymphoma.<sup>7</sup>

The Burkitt cells have ample "squared-off" cytoplasm, a high mitotic rate, and a starry-sky pattern reflecting ingested apoptotic tumor cells within macrophages.<sup>2,5</sup> Virtually all BLs are B-lineage neoplasms, expressing surface immunoglobulins. They usually carry the IgM and/or IgD heavy chain and are usually CD10 (CALLA) positive consistent with neoplasm of

relative immature B cells. Unlike lymphoblastic neoplasms, they are negative for terminal deoxyribonucleotide transferase (Tdt). Almost all cases of endemic Burkitt's lymphoma carry a translocation involving chromosome 8: t(8;14) is present in about 80% of cases, t(8;22) in 15% of cases (all with lambda light chain expression), and t(2;8) in 5% of cases (all with kappa light chain expression).<sup>12,13</sup> The chromosomal abnormalities tend to juxtapose c-myc (normally on chromosome 8) with an immunoglobulin promoter. The resulting aberrant c-myc over expression may allow virtually 100% of lymphoma cells to be in the cycle.

Once the diagnosis of BL is established, treatment should be started relatively promptly as the tumor is very rapidly growing. The role of surgery in intra-abdominal Burkitt's lymphoma remains controversial. When the tumor is localized, total resection results in a good outcome. However, in the presence of extensive intra-abdominal diseases, the operation should be limited to biopsy only.<sup>14</sup> Surgery should be considered only for limited but bulky, mobile and easily resectable disease. CT scan may help to predict whether or not disease can be resected adequately. Disease confined to the ovary, omentum, or small bowel may be resected more easily than retroperitoneal disease. Radiotherapy given in daily fractions is not of great efficacy as a primary treatment for BL, as the tumor cells are rapidly growing and may escape from the conventional fractionated radiotherapy protocol. Indications of radiotherapy include bulky CNS disease, bulky masses causing spinal cord compression, SVC obstruction, tracheal obstruction, and pharyngeal obstruction.

Chemotherapy is the mainstay of treatment, regardless of the age.<sup>1</sup> It should be started 10-14 days after surgery in patients without substantial residual disease and in whom serum LDH has returned to normal and is not rising; in the remaining patients chemotherapy should be started immediately after surgery. Clinical trials have demonstrated that short duration, multi-agent, dose-intensive chemotherapy regimens combined with aggressive central

nervous system therapy results in 70% to 80% long-term survival rates in children and young adults, whereas long-term disease-free survival rates in older adults remains suboptimal at 15% to 25%.<sup>7,15</sup> Autologous bone marrow transplantation has proven feasible in many patient populations with BL/BLL and may lead to cure in selected patients.<sup>15</sup>

Cyclophosphamide, vincristine, doxorubicin, high-dose methotrexate (CODOX-M)/ifosfamide, etoposide and high-dose cytarabine (IVAC) is a highly effective alternating non-cross-resistant regimen developed by Magrath et al<sup>16</sup> at the US National Cancer Institute. United Kingdom Lymphoma Group (UKLG LY06) tested this protocol in 60 patients, from 16 to 60 years of age with locally diagnosed, non-HIV-related, non-organ-transplant-related BL. Overall, 2-year event-free survival (EFS) was 64.6% (95% CI 50.4% to 78.9%) and 2-year overall survival (OS) was 72.8% (95% CI 59.4% to 86.3%). For low risk patients, 2-year EFS was 83.3% and OS was 81.5%. For high risk patients, 2-year EFS was 59.5% and OS was 69.9%.<sup>17</sup> According to The French Society of Paediatric Oncology (SFOP), based on the use of the international LMB96 protocol, the event free survival of all stage IV Burkitt's lymphoma is higher than 85%, and approaches 80% in the cases with central nervous system involvement and 90% in the cases without CNS involvement.<sup>7</sup> Encouraging results of Rituximab, a chimeric monoclonal antibody against the CD20 antigen, given along with intensive combination chemotherapy in refractory cases, have been reported.<sup>18</sup>

Poor prognostic factors at the time of disease presentation include advanced stage, high serum LDH (>1000 IU/L), bone marrow involvement, leukemic presentation, meningeal involvement, high uric acid level, and high antibody titre to EBV early antigen.<sup>5</sup> Tumor mass contributes to poor prognosis not only because of tumor resistance, but also because of the substantial risk of tumor lysis syndrome; characterized by hyperkalemia, hypocalcemia, hyperphosphatemia, lactic acidosis, hyperuricemia and azotemia.<sup>6</sup> It may result in renal

failure and acute death. Attempts to minimize this risk include vigorous hydration and use of allopurinol, with frequent monitoring of metabolic parameters. The administration of recombinant urate oxidase (rasburicase) also has been shown to provide effective prophylaxis against hyperuricemia in pediatric and adult patients with hematologic malignancies. HIV positive patients used to have poorer survival secondary to infectious complication and comorbid disease. With the discovery of highly active antiretroviral therapy, the ability to treat and control Burkitt's lymphoma in patients with HIV has improved.<sup>6</sup> Relapse, if it occurs, usually manifests within the first year. BL is usually cured if relapse doesn't occur within two years.

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