Abdominal Burkitt's lymphoma in Children

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Abstract

Background: Burkitt's lymphoma is a high grade B-cell neoplasm, which is a kind of small non-cleaved cell lymphoma**.** It is presumably the fastest growing human malignancy, and the patients are prone to develop tumor-lysis syndrome. Here we present findings on our patients with Burkitt lymphoma**.**

Materials and Methods: This descriptive retrospective study included 46 children with abdominal Burkitt's lymphoma who were treated during 15 years from June 1998 to Dec 2013 at Mofid Children's Hospital.

Results: Offourty six patients 32 (70%) were boys and 14 (30%) were girls with ages ranging from 2 to 14 years. Surgical exploration was carried out in all cases, the lesions were located in the small intestine (N=17), large intestine (N=15), ileocecal region (N=12), and stomach (N=2). We performed a complete mass resection in 16 cases, debulking in 10 and lymph node/mass biopsy in 20 cases. Pathologic examination revealed Burkitt's lymphoma for all patients. The majority were stageIIE and stage IIIE (24 and 19 respectively). Post-operative complications were seen in five cases with the most common being persistent ileus. All patients received a sort of systemic chemotherapy. The mean follow up duration was 6 years. Death occurred in 7(15%) of our patients, due to tumor lysis syndrome and acute renal failure.

Conclusion: The extent ofdisease at presentation is the most important prognostic factor in abdominal Burkitt's lymphoma. Children with BL are at a high risk of tumor lysis syndrome before or during chemotherapy. Surgery still plays an important role in this pathology, and chemotherapy offers an excellent chance for long term disease free survival.

Key words: Burkitt's lymphoma, Treatment, Children.

Introduction

Lymphoma is the third most common childhood malignancy which accounts for approximately 7% of pediatric oncology patients. Non-hodgkin lymphoma (NHL) is commonly classified into three categories: (1) B-cell (NHL include Burkitt's and Burkitt-like lymphoma, and diffuse large B-cell lymphoma), (2) lymphoblastic lymphoma (primarily precursor T-cell Lymphoma and less frequently precursor B-cell lymphoma) and (3) Anaplastic large cell lymphoma (T-cell or nul cell lymphoma).[1,2,3]Burkitt's lymphoma (BL) is highly aggressive, rapidly growing B-cell neoplasm mainly affecting children and young adults, that are characterized by dysregulation of the C-myc oncogene.[4]

BL is a high grade B-cell neoplasm under the umbrella of non-Hodgkin's lymphoma. There exist three major clinical types: Endemic form which is a common childhood malignancy strongly associated with the Epstein-Barr virus (EBV), The non-endemic (sporadic) form which is rare and the immunodeficiency-related BL, almost often seen in AIDS patients; the sporadic form typically presents as extra nodal disease.[5] BL is a progressive disease primarily treated with intensive chemotherapy therefore the presence of sepsis or any other condition, that delays chemotherapy, will have a bad effect on the prognosis. Thus, it is of importance to diagnose the disease before complications occur and initiate treatment immediately.[5] There are two potentially life-threatening conditions that are often seen in children with NHL: (1) Pressure effect on vital organs such as mediastinal tumor which

could result in major airway obstruction, this condition is more prevalent in lymphoblastic lymphoma, and (2)Tumor lysis syndrome, most often seen in lymphoblastic and Burkitt or Burkitt-like NHL.[1] In this article, we will focus on the management of patients with Burkitt's lymphoma.

Material and methods

In a descriptive retrospective study, 46 children with intra-abdominal Burkitt's lymphoma whom have been operated on, in Mofid children's Hospital from June 1998 to Dec 2013 were evaluated. A complete preoperative work-up was done in all cases which included complete blood count, urinalysis, biochemical analysis, and imaging studies, Bone marrow and cerebrospinal fluid (CSF) examinations were also added except in urgent cases.

Localized disease was defined as limited to one anatomic area and adjacent mesenteric lymph nodes, and disseminated disease was defined as a tumor which extended beyond the primary site or when metastasis existed. All patients underwent laparotomy and the surgical procedure was classified as total excision, debulking or incisional biopsy. Laparotomy was performed in all patients.

16 cases underwent emergency surgery because of acute abdomen, and others were referred with the symptoms of abdominal mass, pain, anorexia, and weight loss. After completing laboratory and radiological studies, all of them underwent elective surgery with the pre-diagnosis of abdominal malignant tumor. All had chemotherapy consisting of a combination of cyclophosphamide, vincristine, prednisolone, prednisone, and adriamycine post-operatively, which was repeated every 4 weeks. All were checked by abdominal and thoracic Ct-scan and CSF analysis during and post-chemotherapy periods if needed. Collected data from the patient's medical records were analyzed and variables such as age, gender, diagnostic tools, tumor localization, surgical and medical treatment and outcome were evaluated.

Results

The patients consisted of 32 (70%) boys, and 14 (30%) girls, with ages ranging from 2 to 14 years. Table 1 shows the presenting symptoms of the patients. Abdominal pain was the most common symptom which was present in 38(83%), followed by abdominal swelling which was present in 30 (65%) patients. In 16 cases the pathology was established preoperatively by endoscopy or ultrasound or CT guided biopsy, while in 30 cases exploration was done based on radiological and clinical data only. The aim of surgery was to establish the diagnosis, evaluate the disease extent and remove the whole lesion if possible or take biopsy. The tumors were located in small intestine (N=17), large intestine (N=15), ileocecal (N=12), and stomach (N=2) andtable 2 shows the site of the disease in all the 46 patients. Complete mass resection was performed in 16 (35%) cases, debulking in 10 (22%), and lymph node/mass biopsy in 20 (43%). Five patients (11%) had extensive intra-abdominal Tumor, and tumors were fixed and had liver, or kidney metastases. Pathology examination revealed Burkitt lymphoma for all patients. The majorities were stage IIE and stage IIIE (24 and 19 respectively); only three patients had stage IVE disease. Post-operative complications occurred in five cases with the most common being persistent ileus,followed by blood loss more than 250cc, wound dehiscence, and subhepatic abscess which required CT guided drainage. All patients received a sort of systemic chemotherapy and the response to chemotherapy was collectively reported as complete remission

in 39 patients (85%), tumor regression in 3 (7%) and disease progression in 6 (13%).

All 16 patients with localized tumor are alive after a mean follow up duration of six years (survival rate=100%). Mortality in the debunking group was 3 (30%) cases due to tumor lysis syndrome and acute renal failure, but the other 7 cases are alive (survival rate=70%).

Of the 20 patients in the biopsy group, 4 were lost to follow up during chemotherapy regimens (tumor lysis 2, CNS involvement 1, post chemotherapy sepsis 1), the remaining 16 are alive with a mean follow up duration of 6 years (survival rate = 80%). Second look operation was performed in patients of our biopsy group due to residual tumors. Survival rate in all 3 groups are shown in table 3.

Table 1: Presenting symptoms in the study group

Symptom	Number	Percent
Abdominal pain	38	85
Abdominal swelling	30	65
Vomiting	16	35
Intestinal obstruction	16	35
Constipation	12	26
Diarrhea	5	11
Melena	5	11
Bleeding per rectum	4	9

Table 2: Shows the site of the disease in our 46 patients.

Site	Number	Percent
Stomach	2	4
Small bowel	17	37
Large bowel RT Colon LF Colon	 13 2	 29 4
Small and large bowel (All in the ileocecal region)	12	26

Table 3: Initial surgical procedure and survival

Abdominal tumor type	Procedure type	Patients No	Mortality	Survival (%)
Localized	Total resection	16	0	100
Disseminated	Debulking	10	3	70
	Biopsy	20	4	80
Total	-	46	7	-

Discussion

Burkitt's lymphoma occurs more frequently in children than in adults with male to female ratio of 2.5:1[6].In our series this ratio was 3:1. The predominant GIT malignant tumor in children is NHL of the distal small bowel and the caecum[7]. The distribution of our cases is consistent with this fact as it was seen in 42 of our 46 cases (91%); this was also reported in other series[8]. In our study we had 2 cases of pediatric gastric lymphoma, which is compatible with other studies. As known, patients with Burkitt's NHL in North Africa and the Middle East (including Iran) appear to have a spectrum of organ involvement that more closely approximate that of sporadic rather than endemic form of the disease, since most patients present with abdominal tumor [9].Large proportion of patients with sporadic form of Burkitt's NHL would present with abdominal pain, as in our study 85% of the patients had abdominal pain. About ¼ of such patients may come with a right iliac fossa mass[10];similarly, a routine pattern of clinical presentation was reported in our series (Table 2). The distribution of cases among different stages in the present study was also similar to most reported series[10].

The survival results of our study support several conclusions determining the appropriate role of surgical intervention in pediatric gastrointestinal NHL.

Although, localized disease, complete resection, earlier stage (stage II) and response to chemotherapy had significantly affected the overall survival, the strongest predictor of disease-free survival was tumor stage at diagnosis, as measured by extent of abdominal disease. This is consistent with other studies clearly showing that the outcome is mostly dependent on the number of malignant cells present at initiation of therapy[5, 8, 11],and can be predicted by measurement of serum LDH, interleukin II and B2 microglobulin levels[9].Since children with partially resected or biopsied tumors are treated identically according to the extent of disease, partial resections neither add to survival, nor prevent the patients from entering the higher risk group. Thus, in patients in whom complete resection is impossible, have no evidence of extra-abdominal extension and laparotomy is needed for diagnosis, surgery should be limited only to the least invasive procedure, such as biopsy or a simple intestinal resection-anastomosis. This is to avoid any major surgical procedure that may lead to higher incidence of postoperative complications and more importantly may lead to delay in initiation of chemotherapy. In a large review, patients with pediatric gastric lymphoma had the same 5-year survival rate irrespective of whether the primary tumor was resected or not [12].Nowadays fine needle aspiration cytology can be helpful in diagnosis of abdominal and retroperitoneal masses in children[13].

Earlier reports about results of treatment showed overall survival results ranging from 60% to 65%[5].The disease free survival in patients with localized disease was reported to be 85% [10].The results of several new protocol in which the principles of risk stratification is being used, show better results with overall disease free survival of approximately 90%; and patients with stage II have 98-100% disease free survival rate versus 76% in those with extensive disease [14, 15]. In our study overall survival results was 85% which considering its small sample size and different applied chemotherapy protocols can be more or less considered close to other reports in this regard. We had 7cases of mortality (3 in the debulking group and 4 cases in the biopsy group) no mortality was seen in localized tumors.

Conclusion

The extent ofdisease at presentation is the most important prognostic factor in abdominal Burkitt lymphoma. Children with Burkitt lymphoma are at high risks of tumor lysis syndrome before or during chemotherapy. Surgery still plays an important role in this pathology, and chemotherapy offers an excellent chance for long term disease free survival.

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