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Original Article

Bowel Lymphoma in Children: Management and Outcome

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Abstract

Background: Primary bowel lymphoma is an uncommon neoplasm in children and not well documented in literature with regard to its outcome and management. **Materials and Methods:** A case record review of children with bowel lymphoma was undertaken in a tertiary care institute, from 2010 to 2016 and the relevant data were recorded. **Results:** 21 children were managed with bowel lymphoma over a period of 7 years. Pain abdomen was the most common presenting symptom (19/21). Ileum was the site of involvement in most children (17/21). Localised disease was seen in 13/21 while 8 had diffuse involvement. Predominantly (13/21) children presented at an advanced stage (III/IV). Surgical intervention was needed in 14/21 while 7/21 were managed only with chemotherapy. Majority (15/21) had Burkitt's lymphoma on histology. 13 of 21 (61.9%) have completed chemotherapy and on regular follow up. Among 8 who died, 6 were directly related to disease progression despite aggressive management. **Conclusion:** Bowel lymphoma in children is distinctly different in the site of presentation from that of the adults. Advanced stage at presentation portends poor prognosis. Bowel lymphoma is to be considered in case of recurrent intussusception in children.

Keywords: *Bowel lymphoma, Burkitt's lymphoma, childhood malignancies, non-Hodgkin's lymphoma*

Introduction

The pediatric population constitutes 32.4% of the total population of India and malignancy is an emerging major childhood killer.[1] Primary tumors of the gastrointestinal (GI) tract are rare in children and represent <5% of all pediatric neoplasms.[2] The scarcity of the disease and variable clinical presentation preclude early diagnosis when the likelihood of cure exists.

Among GI malignancies, non-Hodgkin's lymphoma (NHL), especially Burkitt's lymphoma (BL) is the predominant variety.[3] In children, Paediatric gastrointestinal tract lymphoma (PGTLs) tend to occur in the small and large intestines, as opposed to the stomach in adults.[3]

Although lymphoma is the most common pediatric GI malignancy, there are not many studies available in the literature. The study documents the experience of pediatric bowel lymphomas in a tertiary care institute.

Objective

1. To evaluate the clinical presentation of pediatric GI lymphoma
2. To determine the prognosis and prognostic factors of pediatric GI lymphoma.

Materials and Methods

It is a retrospective plus prospective study of GI lymphomas in pediatric age group presented to Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, over a period of 7 years (2010–2016). Patient demography, history, examination, investigations, treatment, and follow-up were recorded.

Dawson *et al.*'s[4] criteria were used to differentiate primary from secondary bowel lymphoma. The tumor was considered primary when there is no superficial adenopathy at diagnosis, no mediastinal adenopathy at chest radiography, normal blood cell counts, no involvement of liver and spleen, and involvement of only regional lymph nodes at laparotomy.

St Jude's Staging system[5] was used to stage the disease.

Investigations to complete the workup included ultrasonogram, computed tomography [Figure 1], biopsy of mass, bone scan, and bone marrow biopsy.

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LMB-96 chemotherapy protocol [Figure 2] was used for treating patients. Progressive disease patients received additional rituximab, ifosfamide, carboplatin, etoposide regimen. Surgery was reserved for residual tumor and complications of mass.

Numerical data were expressed in mean ± standard deviation and range. Fisher's exact *t*-test was used to find a difference between two groups and Chi-square test was used to find a difference between three or more groups. $P < 0.05$ was considered statistically significant.

Results

A total of 21 patients were found during the study period. Mean age was 6.05 ± 3.34 years with 14 (66.67%) patients aged ≤5 years. The smallest patient was aged 3 years while the eldest was 14 years. Males were more commonly affected (7:1). Pain abdomen was the most common presentation (90.5%), followed by distension of abdomen (85.7%) [Table 1].

In the study, 7 (33.3%) patients presented with radiological intussusception while 2 (9.5%) had actual intussusception [Figure 3] whereas 4 (19%) patients had target sign on imaging suggestive of intussusception. One (4.7%) patient had a history of surgery for intussusception.

Most common site of involvement was terminal ileum (81%) [Table 2]. Thirteen (61.9%) patients had localized disease while 8 (38.1%) patients had diffuse disease at presentation. Eight (38.1%) cases belonged to Stage II of St. Jude's system of classification, 7 (33.3%) belonged to Stage III, and 6 (28.6%) belonged to Stage IV. Eighteen (85.7%) patients had primary GI lymphoma whereas 3 (14.3%) had secondary GI lymphoma.

Table 1: Clinical presentation of pediatric gastrointestinal lymphoma

Presentation	*n* (%)
Pain abdomen	19 (90.5)
Distension	18 (85.7)
Vomiting	11 (52.4)
Mass per abdomen	14 (66.7)
Intussusception	3 (14.3)
Blood in stools	2 (9.5)
Constipation	1 (4.7)
Intestinal obstruction	10 (47.6)

Table 2: Site of involvement

Site of involvement	*n* (%)
Terminal ileum	17 (81)
DJ junction	1 (4.7)
Jejunoileal	2 (9.5)
Ileocolic	5 (23.8)

DJ – Duodenojejunal

Seven (33.3%) patients were managed with chemotherapy alone while 14 (66.7%) required some surgical intervention at least. Surgical intervention included resection and anastomosis (9 patients - 42.9%) [Figure 4], diversion (3 patients - 14.2%), laparotomy and biopsy

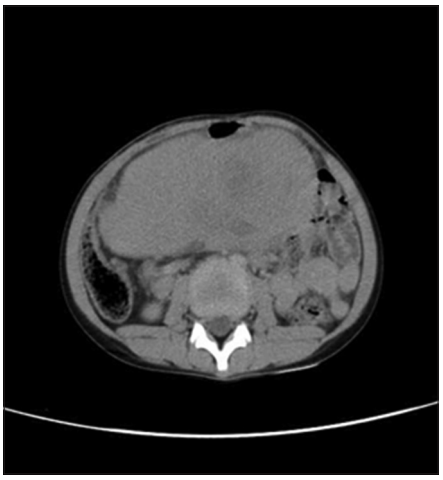

Figure 1: CECT Abdomen showing a small bowel mass

Group	Prephase	Induction phase		Consolidation phase		Maintenance
A		COPAD-1	COPAD-2			
B	COP	COPADM-1	COPADM-2	CYM-1	CYM-2	COPADM-3
C	COP	COPADM-1	COPADM-2	CYVE-1	CYVE-2	m_1 m_2 m_3 m_4
				↑ MTX if CNS +ve		

Fig.1: LMB 96 protocol schedule

Patients were stratified into 3 risk groups: A, B, and C, depending on stage, resection status, percentage of blasts in BM, and CNS involvement. Group A: Resected stage I and abdominal stage II. Group B: Patients not eligible for inclusion in group A or C. Group C: Patient with CNS involvement and more than 70% of blast in bone marrow. In the LMB 96 protocol, cranial irradiation was skipped and replaced with high-dose methotrexate (MTX) between consolidation phases in patients with CNS-positive disease.

COP- Cyclophosphamide, Vincristine & Prednisolone; COPAD- COP + Adriamycin; COPADM- COPAD + high dose methotrexate; CYM- Cytarabine + high dose methotrexate(MTX); CYVE- Cytarabine + Etoposide; m- maintenance (COPADM)

Figure 2: LMB-96 chemotherapy protocol

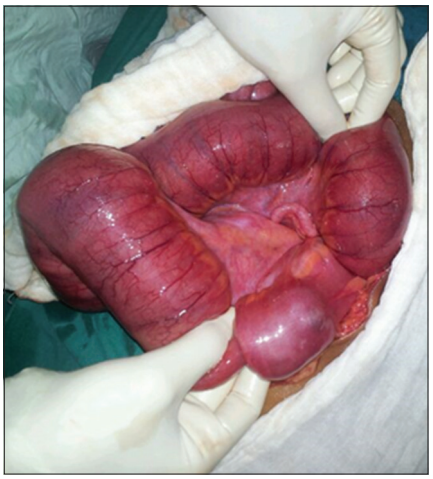

Figure 3: Lymphoma presenting as intussusception

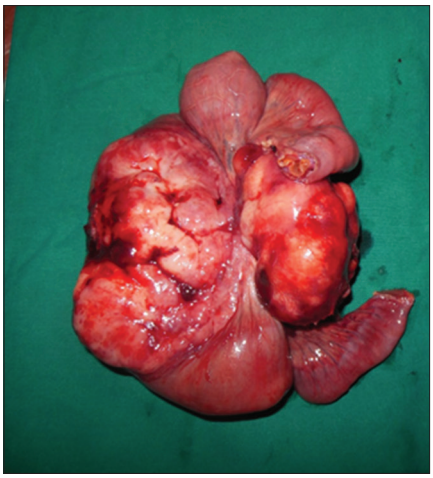

Figure 4: Resected small bowel mass lymphoma

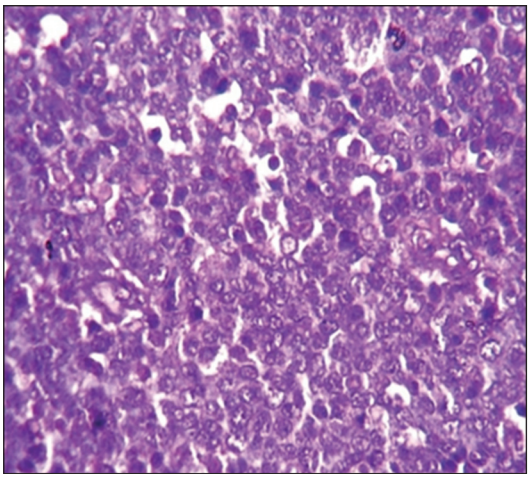

Figure 5: H & E, x100 Burkitt's lymphoma with starry sky appearance

(1 patient - 4.7%), and laparotomy and reduction of intussusception (1 patient - 4.7%).

Histopathology [Figure 5] revealed 15 (71.4%) BL and 6 (28.6%) diffuse large B-cell lymphoma.

Thirteen (61.9%) patients completed chemotherapy and on follow-up ranging from 1 to 6 years with no evidence of recurrence. One patient is currently undergoing chemotherapy. There were 8 mortalities (38.1%) in our study. All succumbed during chemotherapy; 6 patients due to progressive disease, one due to uncontrolled sepsis, and the other due to a complication of central venous access.

Stage of the disease (*P* - 0.0068) and diffuse disease at presentation (*P* - 0.0176) were found to be associated significantly with increased mortality whereas age, sex, site of involvement, primary/secondary disease, surgical intervention, and histopathology did not show statistically different outcome [Table 3].

Table 3: Prognostic factors of bowel lymphoma

Parameter	*n*	Death	Percentage	Fisher's exact test (*P*)
Age (years)				
≤5	14	7	50	0.173581
>5	7	1	14.28	
Male	18	8	44.44	0.257143
Female	3	0	0	
Stage II	8	0	0	0.006841
Stage III and IV	13	8	61.54	
Localized	13	2	15.38	0.017573
Diffuse	8	6	75.00	
Primary	18	6	33.33	1.000000
Secondary	3	2	66.67	
Small bowel	15	5	33.33	χ^2=1.7769
Large bowel	1	1	100.00	*P*=0.411288
Both	5	2	50.00	
Resection and anastomosis	9	2	22.22	χ^2=3.5979
Diversion	3	1	33.33	*P*=0.308287
Biopsy	1	1	100.00	
No surgery	7	4	57.14	
BL	15	6	40.00	1.000000
DLBCL	6	2	33.33	

DLBCL – Diffuse large B-cell lymphoma; BL – Burkitt's lymphoma

Discussion

Pediatric gastrointestinal tract lymphoma (PGTL) is rare yet the most common bowel malignancy in childhood.[6] It constituted only 54 (1.2%) of 4547 pediatric malignancy cases registered between 1952 and 1996.[7] The mean age of our study is similar to peak age for NHL of GI tract in children mentioned in the literature, i.e., 5–15 years.[7] The male to female ratio of childhood GI NHL[2] is reported to be from 7:1 to 1.8:1 which is similar to our study.

Small and large intestines are the most commonly involved sites in pediatric age group unlike adult patients in whom stomach is the most common site (50%–60%).[6] Most of the pediatric patients present with lymphoma involving distal small bowel (50%–93%) but can occur anywhere in the GI tract.[8] Our study shows terminal ileum (81%) is the most common site of involvement.

The most common presenting symptom is reported to be abdominal pain, followed by mass per abdomen[2] and our study follows this order. Nearly, half of children with GI NHL have tumor infiltrates confined to GI tract with possible regional lymph node involvement.[2] Our study showed localized disease in 61.8% cases.

The ultimate treatment approach in GI lymphoma remains debatable. Recent studies have proposed the use of chemotherapy alone as an effective treatment option in primary GI lymphoma in all stages.[9] Surgery is reserved for complications such as obstruction, perforation, and bleeding. Despite disagreements regarding treatment, the disease stage at presentation and extent of involvement remain the most important criteria determining survival.[2,6] Our study showed that advanced Stage (III and IV) at presentation and diffuse disease at presentation carry increased mortality.

The overall 5- and 10-year survival rates of pediatric GI lymphoma cases treated with combined surgery, chemotherapy, and radiation remain 52% and 44%, respectively.[8] Our study showed 61.9% patients are free of disease and on follow-up.

Differential diagnosis includes enteritis, inflammatory bowel disease, leiomyoma, leiomyosarcoma, or gastrointestinal stromal tumor.

Our study has an interesting finding that lymphoma can either mimic or present with intussusception. About 50% of the study group had radiological intussusception.

Conclusion

Bowel lymphoma in children preferentially involves ileum. Chemotherapy is the mainstay of treatment in bowel lymphoma. Diffuse disease and advanced Stage (III and IV) at presentation are poor prognostic factors, associated with high risk of mortality. In children presenting with recurrent intussusception and beyond the typical age group of idiopathic intussusception (3 years), lymphoma is to be ruled out.

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Conflicts of interest

There are no conflicts of interest.

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