ORIGINAL ARTICLE

Primary Ileocaecal Lymphoma :Clinico-Pathological Features and Results of Treatment

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Abstract

The present study was conducted to establish the clinico-pathological features and response to treatment in primary ileocaecal lymphomas. Fifteen patients with primary ileocaecal lymphoma were analyzed with respect to clinical presentation, histopathological aspects and response to various treatment modalities. Abdominal pain and a palpable abdominal mass were the commonest presenting features. Ten (66.66%) patients had clinical stage IIE disease, four (26.66%) had stage IE, and one patient (6.66%) had stage IV disease. Malignant lymphoma small lymphocytic (MLSL) was present in 40% of patients followed by malignant lymphoma diffuse large cell (MLDLC) in 26.26% and malignant lymphoma diffuse small cleaved cell (MLDSC) in 20% of patients. Malignant lymphoma diffuse mixed (MLDM) and malignant lymphoma lymphoblastic (MLL) was present in 6.66% of patients in each. All the patients underwent laparotomy with 14 undergoing surgical resection which included resection of terminal ileum. In one patient only, a biopsy was taken. Combination chemotherapy (CCT), 4 to 6 cycles of CHOP/CVP was used in all the patients. Three patients with persistent residual disease after surgery and CCT were treated with 35 Grays (Gy) of external beam radiotherapy on a tele-cobalt unit at 80 cms of source to skin distance. Eleven (73%) patients remained disease free at 10 months to 14 years from the start of treatment. The survival trends indicate a poorer outcome for more advanced clinical stage. A well designed prospective and randomized trial based on a large number of patients is essential to work out an optimal management policy in primary ileocaecal lymphoma.

Key Words

Combination chemotherapy, Radiotherapy, Hemicolectomy, Lymphoma.

Introduction

Gastrointestinal tract is the commonest site for extranodal lymphoma (1). About 40% of the extranodal lymphomas are primarily present in the gastrointestinal tract and they account for approximately 1-2% of all gastrointestinal malignancies and less than 10% of all lymphomas (2-4). Lymphoma primarily involving the ileocaecal region is common in India (5,6) and other developing nations, particularly those around the

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Mediterranean sea (7) where it is referred to as the Mediterranean lymphoma or immunoproliferative small intestinal disease (IPSID). We report here our experience with 15 patients of ileocaecal non-Hodgkins lymphoma (NHL) with reference to their clinico-pathological features and response to treatment.

Material and Methods

The records of all patients with non-Hodgkins lymphoma (NHL) managed by the departments of General Surgery, Medical Oncology and Radiation Oncology at Sher-i-Kashmir Institute of Medical Sciences between August 1984 to January 1999 were reviewed and patients with primary gastrointestinal lymphomas (PGIL) were identified. From these records, patients with involvement of ileocaecal subsite were selected for further review and analysis. Dawson's criteria (8) were used to establish the ileocaecal origin of a given lymphoma at the initial presentation. A diagnostic laparotomy was performed in all the patients. The disease was bulky in most cases with masses over 8-15 cms in diameter. Fourteen patients were subjected to right hemicolectomy with resection of terminal ileum and mesentric lymph nodes. A 70 year old male patient with gross liver involvement had only a diagnostic biopsy. Routine staging procedures included complete blood counts, serum biochemistry, serum immunoglobulins, bone marrow aspiration/biopsy, chest roentgenogram, barium enema, abdominal ultrasonography and abdominal computed tomography. Patients were staged using the Ann Arbor staging system (9). Histological review was done according to National Cancer Institute Working formulation (10). All the patients received four cycles of adjuvant combination chemotherapy which included cyclophosphamide 750 mg/m^2 I.V on day 1, adrianmycin 50 mg/m^2 I.V on day 1, vincristine 1.4 mg/m^2 I.V on day 1 and prednisolone 40 mg/m^2 P.O days 1 to 5 (CHOP/CVP). The entire cycle was repeated at 21 days interval. Three patients with subsequent palpable residual disease were treated with two more cycles of combination chemotherapy and external beam radiotherapy (XRT) to the ileocaecal region and the drainage lymph node sites for a total dose of 35 Gy's delivered in 4-5 weeks in 23 fractions of 150 CGy at 5 fractions per week. The patients were treated on a tele-cobalt-60 unit at 80 cms of source to skin distance. The patients were followed at regular intervals of 6-8 weeks to evaluate the response to treatment.

Results

The median age at presentation was 20 years (range 5-70).Twelve patients were male and 3 were female. Various other patient characteristics are summarized in **Table 1**. The symptoms and signs at the initial presentation are shown in **Table 2**. The duration of symptoms prior to the diagnosis was from a few days to a few months (median 2 months). The most common presenting features were abdominal pain and a palpable mass in the right lower abdomen. Nausea, vomiting and weight loss were present in a significant proportion of patients. One patient had clinical features suggestive of acute bowel obstruction. The most common pre-operative diagnosis was appendicular lump in 60% of patients, followed by tubercular lymphadenitis in 27% and a malignant growth of ileocaecal region in 13% of patients. Four patients at pre-operative barium enema revealed a stricture in the terminal ileum. A 70 year old male patient who presented with bleeding per rectum underwent colonoscopy which revealed an ulceroproliferative growth in caecum, however the biopsy was inconclusive. Masses involving the terminal ileum and caecum ranging

from 8-15 cms in diameter were present in all the patients. Biopsy taken at laparotomy provided the diagnostic tissue in all the patients. There was no evidence of d'sease elsewhere in the small intestine. Mesentric lymph nodes were enlarged in 14 patients with a gross diameter ranging from 3-6 cms, however, only in 10 of these patients nodes were found to be infiltrated by lymphomatous deposits. None of the patients had gross involvement of the para-aortic lymph nodes. Small lymphocytic type of malignant lymphoma was the commonest histological subtype (40%) followed by diffuse large cell lymphoma (26.66%) and diffuse small cleaved cell (20%). Low grade lesion was found in 6 (40%) patients, intermediate grade in 8 (53.33%) patients and only 1 (6.66%) patient had a high grade lesion.

Table 1

PATIENT CHARACTERISTICS

Characteristic	No.of patients
Sex	
Male	12 (80%)
Female	03 (20%)
Total	15
Stage	
IE	04 (26.66%)
IIE	10 (66.66%)
IV	01 (6.66%)
Total	15
History (WF)	
MLSL	06 (40%)
MLDLC	04 (26.66%)
MLDSC	03 (20%)
MLDM	01 (6.66%)
MLL	01 (6.66%)
Total	15
Grade (WF)	
Low	06 (40%)
Intermediate	08 (53.33%)
High	01 (6.66%)
Total	15

WF = Working Formulation

Table 2

Symptoms and Signs at initial presentation

Symptom/Sign	No.of patients
Abdominal pain	14 (93%)
Palpable mass	11(73%)
Weight loss	05 (33%)
Nausea & vomiting	04 (27%)
Fever	03 (20%)
Lower gastrointestinal bleed	02 (13%)
Abdominal distention	01 (7%)

Table 3, shows the relation of stage and histology on the disease status and prognosis. Four patients with stage IE disease remain alive with no evidence of disease at 2, 4, 10 and 14 years after the diagnosis and start of the multi-modality treatment. For those with stage IIE disease, 8 of the 10 patients remain disease free 10 months to 2 years from the start of treatment. The other 2 stage IIE patients are alive with residue disease at 1 and 2 years after the start of treatment. One patient with stage IV disease died 6 months after diagnosis because of disseminated disease process. Three of the 6 patients with low grade small lymphocytic lymphomas remain disease free 10 months to 10 years after diagnosis and start of treatment, 2 of these 6 patients are alive with residual abdominal disease 1 and 2 years after the start of treatment, whereas one patient died of disease 6 months after treatment. Three of the 4 patients with diffuse large cell lymphoma remain disease free 2 to 5 years after the start of treatment and one patient is alive with residual disease at 15 months after diagnosis and treatment. All the 3 patients with diffuse small cleaved cell histology are disease free 2 to 14 years after the

start of treatment. Both the patients with diffuse mixed and lymphoblastic histology are disease free at 2 years and 18 months respectively after the treatment.

Table 3

Impact of Stage and Histology on disease

	No. of patients	NED	RD	DWD
Stage				
IE	4	4	–	–
IIE	10	7	3	–
IV	1	–	–	1
Total	**15**	**11(73.33%)**	**3(20%)**	**1(6.66%)**
Histology (WF)				
MLSL	6	3	2	1
MLDLC	4	3	1	–
MLDSC	3	3	–	–
MLDM	1	1	–	–
MLL	1	1	–	–
Total	**15**	**11(73.33%)**	**3(20%)**	**1(6.66%)**

NED = No evidence of disease
RD = Residual disease
DWD = Dead with disease
WF = Working formulation

Discussion

The present study summarizes our experience in management of primary ileocaecal non-Hodgkins lymphoma. On account of rarity of this disease involving the ileocaecal region, the total number of patients is small which makes it difficult to arrive at conclusions regarding the optimal management policy. In the western countries stomach is the most common site involved by primary non-Hodgkin's lymphoma accounting for 60-70% of the cases (11). In the Indian studies by Reddy *et. al.* and Talvalkar an incidence of 42% and 55% respectively have been reported from ileum and ileocaecal regions (5-6). In the present study the 15 cases of ileocaecal lymphoma accounted for 25% of the total number of 60 patients with primary gastrointestinal lymphoma and was the commonest subsite involved followed by ileum (22%), duodenum (20%), stomach (14%), rectosigmoid (9%), colon (6%), jejunum (2%) and uncertain site of origin (2%).

The commonest presenting symptom was abdominal pain and the commonest sign was a palpable lower abdominal mass. None of our patients gave a history suggestive of coeliac disease which is often associated with small bowel lymphomas (12). The clinical presentation compared favourably with the studies of Singh *et. al.* (13) and also those of Mead, *et. al.* (12). None of the patients had peripheral lymphadenopathy which is comparable to observations of Lewin *et. al.* (14) but in contrast to those of Hande *et. al.* (15) at the National Cancer Institute who found peripheral lymphadenopathy in 16 of 18 patients with diffuse histiocytic lymphoma of GI tract. At laparotomy most of our patients had bulky disease with masses ranging from 8 to 15 cms in diameter. In 6 patients macroscopic residual disease was left behind after surgery. The majority (53%) of patients were classified as intermediate grade and the rest as low grade (40%) and high grade (7%). This is in marked contrast to the study by Arseneau *et. al.* (16), who published cases of ileocaecal NHL which were mostly of high grade. Paucity of cases in the present study makes analysis of various prognostic factors impossible. The survival trends indicate a poorer outcome with more advanced clinical stage, **Table 3**. The impact of histological subtype on prognosis is unclear due to small number of patients. Ambiguity surrounds the role of abdominal radiotherapy as only 3 patients received 35 Gy of external beam radiotherapy to abdomen, although one of these patients survived 14 years after completion of treatment.

The overall outcome of patients with primary NHL involving the lleocaecal region is favourable, with 73% alive and disease free at 10 months to 14 year from diagnosis and start of treatment. In view of significant macroscopic and possible microscopic residual disease there is a strong rationale for adjuvant treatment comprising 4 to 6 cycles of combination chemotherapy (CHOP/CVP) with abdominal radiotherapy to persistent residual abdominal disease. Properly designed prospective randomized trials based on a large number of patients are essential to define the relative roles of surgery, chemotherapy and radiotherapy in the optimal management of ileocaecal lymphomas.

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