ORIGINAL ARTICLE

Clinical Characteristics and Treatment Outcome of Gastrointestinal Non-Hodgkin's Lymphoma

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SUMMARY

Primary gastrointestinal (GIT) lymphoma constitutes only 5 – 10% of all gastrointestinal tumours. The optimal therapy for these lymphomas is poorly defined and still controversial. We present our experience in the treatment and outcome of primary GIT lymphomas in UKM Medical Center, Malaysia. A retrospective review of all patients with primary GIT lymphoma from the year 2002 until 2007 was done. Our series has shown that primary GIT lymphoma is a rare disease as it comprises only 6.5% of all lymphomas treated in this institution. We had a female predominance of this disease with a large majority at an advanced stage of the disease. There was equal distribution involving stomach, small and large intestines. The incidence of primary GIT lymphomas was 6.5% with a female predominance. The majority had advanced diseases (stage III and IV) with equal distribution involving the stomach, small and large intestines. The most common histological variant was diffuse large B cell lymphoma (66%). Most (83%) patients with intestinal lymphoma had surgical resection and adjuvant chemotherapy. All patients with gastric lymphomas had chemotherapy alone. The mortality rate was 22% predominantly in younger patients with aggressive histology subtypes and advanced disease.

KEY WORDS:
Non-Hodgkin's Lymphoma, primary gastrointestinal lymphoma, Extranodal lymphoma

INTRODUCTION

Gastrointestinal (GIT) lymphoma constitutes between 4-20% of all Non Hodgkins Lymphoma (NHL) and 30-45% of all extranodal disease[1]. GIT lymphoma alone constitutes about 5-10% of all gastrointestinal tumours. It usually affects patients within the age of 50-70 years with a male to female ratio of 2:1. The annual incidence is reported to be about 0.8-1.2 / 100,000 adults[2].

Primary GIT lymphoma is regarded as a heterogeneous disease with regard to its presentation and anatomical site of origin. The stomach is the most common site for these lymphomas (55-70%), followed by the small intestine, (20-35%), and the large intestine (5-10%). In addition, diffuse large B-cell lymphomas (DLBCL) and mucosa-associated lymphoid tissue lymphomas (MALT) are the two most frequently encountered histological variants[1].

The optimal treatment for GIT lymphomas is poorly defined due to its low incidence. The role of surgery, chemotherapy and radiotherapy either alone or in combination is still controversial. Most reported series used relapse free survival and overall survival as a gauge for treatment success and the efficacy of surgery is judged based on its effectiveness of local control, associated morbidities and prevention of chemotherapy associated complications[3].

We report our experience of treating patients with GIT lymphomas in UKM Medical Center (UKMMC) over a 5-year period. These patients were jointly managed by the haemotology and general surgical units. We also performed a literature review to identify clinical characteristics and the best treatment strategy for primary gastrointestinal lymphoma.

METHODOLOGY

A retrospective review of all patients with Non-Hodgkin's lymphoma (NHL) from the year 2002 until 2007 was done. Data was collected from patients' records and only those with primary GIT lymphomas were studied. Data analysis included patients' characteristics, tumour histology and the type of treatment. The type of lymphoma was classified according to the WHO classification system. Data were made available from patients concerned either from their most recent examination, time of discharge or time of death. Data analysis was done with SPSS version 11.5.

RESULTS

A total of 138 patients were diagnosed with Non Hodgkin's lymphoma during a 5 year period between 2002 and 2007. Of these, there were nine (6.5%) patients who were identified to have primary GIT involvement during this study period. The patients comprised three male and six female patients involving four Malays and five Chinese (Table I). The mean age of presentation was 55.8 years (range of 31-82 years).

The anatomical site of occurrence in order of frequency were the stomach 33% (three), caecum and small bowel 22% (two each), terminal ileum and descending colon 11% (one each). The mean duration of symptoms prior to consultation was 4.6 months (range of 1 to 24 months). Six patients (66%) had vague abdominal complaint of loss of weight and appetite while gastrointestinal bleeding was evident in 5 patients. Dysphagia occurred in one gastric lymphoma and altered bowel habit occurred in another.

This article was accepted: 29 June 2010
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Table I: Characteristics of patient with primary GI lymphoma

No	Age	Sex	Race	Presentation	Site	Histology	Treatment	Survival (Months)	Outcome
1	82	F	C	Mass per abdomen, LGIB	Caecum	Diffuse large B cell	Right hemicolectomy, adjuvant chemotherapy	18	Alive
2	67	F	C	Mass per abdomen, LOA,LOW	Terminal ileum	Diffuse large B cell	Right hemicolectomy, small bowel resection, adjuvant chemotherapy	12	Alive
3	57	F	C	Altered bowel habits, LOW,LOA	Caecum	T cells	Right hemicolectomy Adjuvant chemotherapy	84	Alive
4	52	F	Mly	Altered bowel habit, symptomatic anaemia	Descending colon	Diffuse large B cell	Chemotherapy	58	Alive
5	38	M	Mly	LGIB,mass per abdomen	Small bowel	Burkitt's lymphoma	Small bowel resection, adjuvant chemotherapy	6	Dead
6	42	M	Mly	LOA,LOW UGIB	Stomach	Diffuse large B cell	Chemotherapy	1	Dead
7	70	F	Mly	LOA,LOW UGIB	Stomach	Diffuse large B cell	Chemotherapy	NA	NA
8	64	F	C	Mass per abdomen, acute intestinal obstruction	Small bowel (jejeunum)	T cells	Surgical resection, adjuvant chemotherapy	NA	NA
9	31	M	C	LOW,LOA, UGIB	Stomach	Diffuse large B cell	Chemotherapy	NA	NA

LOW – loss of weight LOA – loss of appetite Mly – Malay C – Chinese

UGIB / LGIB – upper / lower gastrointestinal bleed NA – information not available

Palpable abdominal mass was found in five (55%) patients. Positive family history of ovarian carcinoma and lymphoma was found in 1 patient. The mean haemoglobin level at presentation was 8.5g/dl (range 7.1-14.7g/dl). Seven patients received an average of 2 units of packed red cells transfusion prior to administration of treatment (range 2-4 pints).

Surgery was performed in five patients of whom four patients, presented with a palpable mass, with constitutional symptoms while one patient was operated for an acute intestinal obstruction from small bowel tumour. Two cases operated on were for lower gastrointestinal bleed (LGIB) from caecal tumours. Emergency surgery was performed in three patients, for bleeding and obstuction. All of these patients had adjuvant chemotherapy. The remaining three patients with gastric lymphoma had only chemotherapy without surgery as they did not have significant bleeding or obstructive symptoms. One patient with tumour in the descending colon was treated with chemotherapy alone and responded well. No patient received radiotherapy. The commonest histopathological variant was diffuse large B cells (66%) followed by T cell (22%) and Burkitt's cell lymphoma (11%) (Table I).

Currently, four patients (44%) are alive and under follow up in our institution. Two patients died from neutropenic sepsis and progression of disease. Time of death from diagnosis ranged between 1 to 6 months. The status of three patients were unknown as they have defaulted follow-up and are un-contactable.

DISCUSSION

The mean age of our patients (55.6 years) is rather similar to previous reports[2,4,5,6]. In terms of the presenting symptoms. These results differ slightly from previous reports in which abdominal pain was the main complaint, followed by weight loss and altered bowel habit[2-5]. However the majority of our patients presented with advanced disease (81.8% stage III or IV). This is higher than other reported studies in which advanced disease ranged from 29% - 64%[2,4,5].

Our series also revealed that diffuse large B cell (DLBCL) was the commonest histopathology variant of the non-Hodgkin's lymphoma. DLBCL has always formed the majority of the histological variant detected. It has been reported that patients with intestinal B-cell lymphoma usually present at lower lymphoma stages, had less intestinal perforation, required fewer emergency operations and received chemotherapy more frequently. They also respond well to chemotherapy even in the absence of surgical tumour resection[4]. In contrast, only one patient in our series with B-cell lymphoma presented in the early stage. The remaining six patients were in stage III or IV upon diagnosis.

The standard treatment of primary GIT lymphoma involves a multidisciplinary approach, using the combination of surgery with adjuvant chemotherapy and /or radiotherapy. Surgical excision of the tumour remains the main treatment for intestinal lymphoma. It provides important prognostic information through definitive staging, offering a chance for cure with or without adjuvant therapy and helps prevent complications such as haemorrhage, obstruction and perforation[5]. Adjuvant radiotherapy has only been used sparingly in the treatment of primary colorectal lymphomas and may have a role for loco-regional control, such as after an incomplete resection of a large tumour[5]. Our patients received multi-agent chemotherapy utilizing cyclophosphamide, vincristine, doxorubicin and prednisolone (CHOP) or acute leukemic Berlin-Frankfurt-

Munich (BFM) protocol. Addition of rituximab to the CHOP regime may be employed and has shown to improve overall survival by 15-20% in B cell non Hodgkin's lymphoma[7].

Steven Cai *et al* found that 30% of patients with colorectal lymphoma required an urgent or emergent surgical intervention for similar reasons stated above[8]. He also found that patients who underwent surgery electively as the first treatment were more likely to be rendered disease free (62%) when compared to those who underwent chemotherapy as an initial treatment (47%). It is probable that the patients selected for elective surgery may have more localized disease amenable to surgical resection. However patients who required emergency surgery had similar outcomes to those receiving chemotherapy first (50% vs. 47% disease free survival)[8].

Surgery is still controversial as first line therapy in early stages of gastric lymphoma and is not part of the therapeutic regime[6]. Previous analyses have failed to identify an advantage associated with surgery for patients with stage I or II gastric large cell lymphoma. The 5-year relapse-free survival rate was 86% and 77.9% for patients treated with chemotherapy versus surgery followed by adjuvant chemotherapy respectively, with overall survival rates of 72.6% and 77.8%, respectively. Retrospective analysis from The Royal Marsden Hospital (London, UK) failed to show survival advantages of chemotherapy compared to surgery and chemotherapy in a series of patients with diffuse large B-cell lymphoma[9].

Survival rates for lymphoma at the stomach or small intestine are generally better compared with primary colorectal carcinoma. Using combined surgery and adjuvant chemotherapy, overall five year survival rates ranged from 30% to 55%[8]. Better five year survival rates are seen in gastric lymphomas as compared to intestinal lymphoma (76-81% versus 50-56%)[10].

The main prognostic factors were primary tumour site and extent of disease[6]. Mihaljevic *et al* also found longer survival in patients over 55 years of age. This may be explained by the more aggressive lymphomas found in younger patients, which is the reason for the unfavorable course of the disease[1].

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