

PRIMARY NON-HODGKIN'S LYMPHOMAS OF GASTRO-INTESTINAL TRACT – A CLINICO-PATHOLOGICAL STUDY

A. H. NAGI*, M. AYYUB AND L. A. AL MENAWY

Department of Pathology, Lahore Medical and Dental College, Lahore - Pakistan

Department of Gastroenterology and Pathology, Abdul Aziz Hospital and Oncology Center, Jeddah, KSA

This study aims to retrospectively review the pattern of patients with various gastro-intestinal lymphomas seen in King Abdul Aziz Hospital, Jeddah, Saudi Arabia from June 1990 to June 2002 with a view to determine and analyse various clinical and pathological aspects of this disease. All cases of Primary non-Hodgkin's lymphoma of gastro-intestinal tract received and diagnosed in Histopathology department of King Abdul Aziz Hospital, Jeddah, between June 1990 and June 2002 were retrospectively reviewed and the data was analysed to determine age, gender, ethnicity, clinical presentation, anatomical localization, histological type and Helicobacter pylori status. A total of 47 patients were retrieved for this study, with 85.10% being Saudi nationals. The male to female ratio was 1 : 0.74%. The mean age was 52.44 years. The peak age of onset was in the 6th decade. About 45% of our patients had gastric lymphoma, whereas 20.53% had small bowel lymphoma. Among the total number of patients, 46.81% men had MALT type lymphomas. Helicobacter pylori were positive in all patients with gastric lymphoma. Gastrointestinal lymphomas are frequently seen in patients in Saudi Arabia, with MALT gastric lymphoma being the commonest tumour. The strong association between H. Pylori and gastric lymphoma as an important aetiological factor is emphasized.

Extranodal marginal zone B-cell symptoms of mucosa associated lymphoid tissue (MALT) type is seen in many extranodal sites¹. However the gastro-intestinal tract (G.I.T) is the most frequent site of extra-nodal non Hodgkin's lymphomas (NHLs) accounting for 30-40% of all extra-nodal sites.² Primary NHLs of the GIT are relatively rare, constituting only 1-4% of malignancies arising from stomach, intestine and colon.³ However secondary GIT involvement is relatively common ranging from 10-60% depending on the stage of primary lymphomas.⁴ Despite being rare, these Primary NHLs of GIT are becoming increasingly important, as the management approach differs significantly from other GIT malignancies. Primary NHLs of GIT especially involving the small bowel are relatively common in Middle East and Mediterranean region.⁵ A National Cancer Registry (NCR) was set up in Saudi Arabia in January 1994 and Cancer was categorized as a mandatory notifiable disease. Since then all cancer cases diagnosed anywhere in the Kingdom are expected to be registered with NCR. According to the 2nd report published by NCR in 1999, NHLs account for 7.4% of all cancer cases in Saudi Arabia with an overall age stan-

dardized incidence rate (ASR) of 5.2/100,000 population.⁶ King Abdulaziz Hospital is one of the main public hospitals in Jeddah, Saudi Arabia. The oncology center in this hospital is the only facility in The Ministry of Health (MOH) hospitals in Jeddah with the provision of all modalities of treatment for various malignancies. Consequently most of the patients with malignancies are referred to this hospital for further management.

This presentation is aimed to retrospectively study the pattern of patients with Primary NHLs of GIT seen in this hospital from June 1990 until June 2002, with a view to determine various clinical and histopathological features of this malignancy, as seen in this hospital. We have also compared our results with those previously published from Saudi Arabia and elsewhere.

MATERIALS AND METHODS

All cases of NHLs diagnosed in the department of pathology King Abdulaziz Hospital, Jeddah between January 1990 until June 2002 were retrospectively reviewed. Patients with Primary NHLs of GIT were separated from the main group of patients with NHLs. This group with primary NHLs of GIT were studied in detail to determine their age, gender and clinical presentations as given in pathology data sheets.

*Formerly Senior Consultant Histopathology
KAAH and Oncology Centre, Jeddah, KSA

The histopathological types of these tumours were determined in accordance with the classification proposed by Isaacson.⁷ Tumour sections/and biopsies of all specimens were examined for *Helicobacter Pylori* after being stained with haematoxylin and eosin, and Giemsa. In addition most of the biopsies were stained using immunoperoxidase technique for various tumour markers (leucocytes common antigen (LCA), CD30, CD3, and CD20) representing common lymphoma panel. The data was electronically analysed and results compared with those of other studies published previously.

RESULTS

A total of 386 patients were diagnosed as having different types of non-Hodgkin's lymphomas during the study period. Among them 47 patients were found to have primary NHL lymphomas of GIT, without involvement of any other extra-nodal or nodal site. Hence, these patients were included in the study group. In a total of these 47 patients, 27 (57.44%) were males, whereas the remaining 20 (42.56%) were females with a male : female ratio of 1 : 0.74. Forty (85.10%) were Saudi nationals and the other were non-Saudis mainly coming from other Middle Eastern countries. The distribution of patients in various age groups is shown in Table 1. Ten patients (21.28%) were below 40 years of age. The largest number of patients was between the ages of 60 and 70. The clinical presentation of patients with these malignancies is shown in table 2. Majority of patients presented with symptoms of abdominal pain, mass in the abdomen, anorexic, weight loss, diarrhoea, vomiting and GI bleeding in various combinations. The distribution of gastrointestinal lymphomas among various GIT sites is shown in table 3. Majority of patients had

Table 1: Age distribution of gastro intestinal lymphomas.

Age in years	No. of Patients	% of Total
0 – 10	1	2.13
11 – 20	2	4.26
21 – 30	1	2.13
31 – 40	6	12.77
41 – 50	9	19.15
51 – 60	9	19.15
61 – 70	15	31.91
71 – 80	2	4.26
81 – 90	2	4.26
Total	47	

lymphomas arising either from stomach (44.68%) or small bowel (25.53%). There was a significant number of patients having colonic lymphomas (17.02%).

Table 2: Clinical features at presentation of gastrointestinal lymphoma.

Symptoms	No. of Patients	% of Total
Abdominal Pain	28	59.57
Abdominal Mass	22	46.81
Vomiting	8	17.02
Diarrhoea	8	17.02
Anorexia	10	21.28
Weight loss	12	25.53
G. I Bleeding	6	12.77
Peritonitis	8	17.02

Table 3: Sub site distribution of gastro intestinal lymphomas.

Site	No. of Patients	% of Total
Esophagus	1	2.13
Stomach	21	44.68
Duodenum	2	4.25
Ileum	10	21.28
Diffuse		
(Gastro-ileal)	5	10.64
Colon	8	17.02
Total	47	

Table 4: Histological pattern of gastro-intestinal lymphomas.

Histological Type	No. of Patients	% of Total
Small cell-Diffuse	7	14.89
Large Cell-Diffuse	14	29.79
Mixed Small and Large Cell	4	8.51
Malt Type / (B-cell)	22*	46.81
Total	47	

*Small B-cell = 17, Large B-cell = 5

Various histological patterns encountered are presented in table 4. The commonest morphological appearance was of marginal zone B-cell lymphoma of MALT type, seen in 46.8% of cases, out of 22 patients with gastric lymphomas, 16 (72.73%) were of MALT type. *Helicobacter pylori*

status of gastrointestinal lymphoma at various sites is shown in table 5. All patients with gastric lymphomas were positive for *Helicobacter pylori*, whereas small bowel lymphomas had *Helicobacter Pylori* detected in 40-50% of cases.

Table 5: *Helicobacter pylori* status of gastrointestinal lymphomas at various sites.

Site	No. of Patients	No. of Patients	% of Total
Esophagus	1	0	0
Stomach	21	21	100
Duodenum	2	1	50
Ileum	10	1	10
Gastroileal	5	2	40
Colon	8	1	12.5
Total	47	26	55.32

DISCUSSION

The Gastrointestinal tract is the most frequent location for Primary extra-nodal non-Hodgkin's lymphomas.^{1,19} However Primary NHLs of GIT accounts for only 1-4% of GI malignancies.³ Despite being rare these malignancies are important, because of interesting disease association and distinct management programs. This group of diseases also has an interesting epidemiological distribution. Small bowel lymphomas are less common in western countries, whereas the situation is reverse in Middle East because of high prevalence of IPSID (Immuno-proliferative small intestinal disease).⁵ There are only a few studies on primary GIT lymphomas from Kingdom of Saudi Arabia. A National Cancer Registry (NCR) was established in Saudi Arabia in 1994 with the aim of registering all cancer cases in the Kingdom with NCR. According to 2nd cancer incidence report, published by NCR, ASR for NHLs was 5.2/100,000 with NHLs being the second commonest malignancy in female and 4th common tumour in males. However NCR did not reveal the pattern of Primary GIT lymphomas in KSA. Our study represents the pattern of Primary NHLs of GIT seen in King Abdulaziz Hospital and Oncology Center, Jeddah, which is a tertiary care facility in Western region of KSA. In this study, male to female ratio was 1 : 0.74. The mean age at diagnosis was 52.44 years. Among the total 21.28% of patients were below forty years of age. The peak age at presentation was in the 6th decade, whereas second highest peaks were seen in the 4th and 5th decades. These results are different from the data published from Western studies where the peak age incidence appear to be in 7th decade.^{8,17} The majority of our patients (85.10%) were

Saudi nationals whereas the rest came from other Middle Eastern countries. Most of the patients presented with symptoms of abdominal pain, abdominal mass, anorexia, weight loss, diarrhea, vomiting and GI bleeding in various combination. A few patients presented with signs of peritonitis and intestinal obstruction and the diagnosis was confirmed after laparotomy. It is interesting that none of our patients had a documented history of autoimmune diseases, HIV or Coeliac disease or have been on immuno suppressive drugs. These conditions are well established pre-disposing factors for the development of GI lymphomas. Anatomical localization in our study suggested that majority of patients had gastric lymphomas (44.68%). Small bowel (lymphomas) was the next common site (25.53%). A significant number of patients had colonic involvement (17.02%). The most common histological pattern of these tumours was MALT type of lymphomas (46.81%); whereas the commonest location of MALT type of lymphoma in our patients was stomach (72.73%). This finding is comparable to most western studies.^{14,17,18} The other group was of diffuse large cell type seen in 29.79% of cases. IPSID type of small bowel lymphoma was not seen in any of our patient. This finding was in sharp contrast to the previous studies from this area,¹³ where IPSID type of lymphoma is thought to occur much more frequently than MALT type of lymphomas.^{5,13} It was believed that poor socio-economic conditions predispose to this malignancy. The changing pattern is perhaps due to improved economic situation and emergence of western life style of people of this area in the past few decades.

Helicobacter pylori were detected in histological sections of all patients with gastric lymphoma, but only in 40-50% of patients with small bowel lymphoma. There is a strong epidemiological evidence, suggesting that *H. Pylori* infection is associated with MALT lymphoma. The incidence of gastric marginal zone B-cell MALT lymphomas is higher in geographical areas with a high prevalence of *H. Pylori*. The other strong evidence for the pathogenical role of *H. pylori* comes from the resolution of biopsy proven low grade MALT lymphoma after eradication of *H. Pylori* with antibiotic treatment.^{15,16} The true prevalence of *H. Pylori* in Saudi Arabia is not known, but a higher incidence of gastric B-cell MALT lymphoma in our series points to high endemicity of this organism.

As a **Conclusion** gastro-intestinal lymphoma is not an uncommon disease in this part of the world. Some important differences exist between the pattern seen in our series and that reported previously from Middle East, notably the absence of IPSID type of small bowel lymphoma. We stress

the strong association of H. Pylori and B-cell MALT lymphoma seen in our patients. We hope that by improving socioeconomic conditions in this part of the world, the prevalence of H. Pylori will be reduced and will also minimize the incidence of gastric marginal zone B-cell MALT lymphomas.

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