GASTROINTESTINAL NON-HODGKIN'S LYMPHOMA CLINICO-PATHOLOGIC STUDY

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ABSTRACT

Objectives:
The aim of this study is to determine the clinicopathologic features of primary gastrointestinal non-Hodgkin's lymphoma (GI NHL) at King Abdulaziz University Hospital-Jeddah, and to compare our results to those reported in the literatures.

Patients and Methods:
Twenty three adult patients with primary GI NHL diagnosed over 5-years period (2000-2005) were retrospectively studied clinically and histopathologically. They were classified using the REAL/WHO histopathologic classification.

Results:
Of the 23 patients with primary GI NHL, 14 (60.9%) were Saudi, with male to female ratio of 1.3:1. The mean age of the male patients was 61. 3 years ranging from (42-83) years with a SD ± 13.09 while for females was 64 years, age range (50-75) with a SD± 9.14 . Abdominal pain was the most common presenting symptoms (78.3%) and the most common primary site was the stomach (73.9%) followed by the small bowel (13 %). The most frequent histologic subtype was the diffuse large-B cell lymphoma accounting for (60.9%) of all cases, followed by marginal-zone cell lymphoma (MALT type) which was Helicobacter pylori associated in (39.1%). A large proportion of patients with primary GI NHL had early disease (Stage IE: 20%, Stage IIIE 58.6%). In regards to treat-
Epidemiologic studies support a strong association between MALT type NHL and Chronic Helicobacter pylori infection (8). The most dramatic evidence supporting a pathogenetic role for H. pylori in MALT type NHL is remission of the tumor following eradication of H. pylori with antibiotic therapy (9).

The aim of the current study is to analyse the clinicopathologic features of primary GI NHL at King Abdulaziz University Hospital (KAUH), Jeddah. Our results will be compared to those reported in the literatures.

MATERIALS AND METHODS

Patient population:

A total of 23 cases of adult patients with primary GI NHL diagnosed at KAUH during (2000-2005) were studied retrospectively. Medical records of all patients were reviewed, clinical and pathological informations were recorded in a structured questionnaire form. Primary GI NHL were defined according to Lewin et al (5). The laboratory and radiological work-up included complete blood count, creatinine, liver enzymes, lactate dehydrogenase normal range (200-450 IU/L), uric acid, chest X-ray, computed tomography of chest and abdomen, bone marrow biopsy and endoscopic evaluation with multiple biopsies of the upper and lower GI tract.

Histology and Immunohistochemistry:

Tissue sections were obtained from formalin-fixed paraffin blocks and stained with hematoxylin and eosin. Special stain such as Periodic Acid-Schiff (PAS) and reticulin stain were used in selected cases whenever indicated. Each biopsy was investigated immunohistochemically by staining for Leucocyte Common Antigen (LCA), CD20, CD79, CD3 and CD45. Additionally, Helicobacter pylori was demonstrated using either fast cresyl violet or Giemsa stain.

Clinical Staging and Histopathologic Classification:

Patients were staged according to the Ann Arbor Classification in its modification by Musshoff (10). Histopathologic classification was done using the current REAL/WHO classification (11).

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revealed that mass or filling defect was seen in 80% of cases, followed by ulcerated lesions and diffuse thickening of the mucosa in (15%), (5%) respectively. According to a modified staging classification, a larger proportion of patients with GI lymphoma had early disease (Stage IE: 20%, Stage IIIE 58.6%) while stage IIIE and IVE accounted for 4%, 17.4% respectively.

In regards to treatment, 5 (21.7%) had gastrectomy followed by chemotherapy, 1 (4.3%) received multimodality treatment in the form of gastrectomy and chemotherapy followed by radiotherapy. Fifteen patients (65.2%) had chemotherapy only and the remaining patients two (8.7%) were treated with Helicobacter pylori eradication. The mean follow-up for all cases was 42.2 months. The overall 5 years survival was (47.8%), outcome in patients with primary GI NHL in relation to histology is shown in Table 2.
DISCUSSION

NHL constituted a group of disorders originating from the malignant transformation of lymphocytes and involving either the lymph nodes or extranodal sites. Extranodal lymphomas may comprise 24%-48% of NHL cases and that appears to be an increasing incidence of these lymphoma during the past decades (12). Primary GI NHL is a heterogenous disease with regards to patient's characteristics, stage, histologic subtypes, and treatment results (13). King Abdulaziz University Hospital in Jeddah is considered as a referral center in the Western part of Saudi Arabia with admission facilities for non-Saudi patients. The results from the current study indicate that percentage of non-Saudi patients was (43.5%). Males were more than females with male to female ratio of 1.3:1. This figure is lower than what has been reported from Jordan (14) and the West (2), but is close to the ratio reported from Thailand (15) and China (16).

The peak age of our patients was in the sixth decade, which is older than the age group of a previous study from the Kingdom of Saudi Arabia (17). The GI NHL diagnosis is rarely suspected because of the non-specific presenting symptoms and signs (18). Abdominal pain tends to be the predominant symptom, occurring in up to 93% of patients (19). In our patients with GI NHL abdominal pain was the most common diagnostic symptoms at presentation, followed by abdominal mass in (78.3%) and (21.7%) respectively. The high incidence of gastrointestinal bleeding seen in GI NHL was not a manifesting complaints in our patients population(16).

Primary gastric lymphoma accounts for 3% of gastric neoplasms and 10% of lymphomas. The stomach is the most common extranodal site of lymphoma and is also the most common site of GI NHL (19). Gastric lymphoma can arise from mucosal areas, the so called Marginal zone lymphoma of MALT type. Diffuse large B-cell lymphoma may also arise within the stomach as a primary lesion (previously called "high grade" MALT lymphoma (20). In our patients sites of involvement were the stomach (73.9%), small bowel (13%), colon (8.7%) followed by those in the mesentery in (4.4%). These results were similar to a previous results from KSA (17), Bahrain (21), United Arab Emirates (22), Jordan (14), Thailand (15), China

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association of Marginal zone B-cell lymphoma (MALT type) with H. pylori has been dramatically demonstrated by regression of gastric MALT lymphoma following treatment aimed at eradicating H. pylori (8). Complete histologic regression has been demonstrated in 50 to 80% of carefully selected patients. For instance in patients with localized stage (IE) mucosal disease are candidates for anti-H. pylori therapy. It is estimated that less than 10% of patients with gastric lymphoma are in this category, as the majority have aggressive histology (i.e., diffuse large B-cell lymphoma), extensive mural involvement, or advanced stage (Stage II-IV)29). In the current study (8.7%) only were treated by Helicobacter pylori eradication, the two patients were early stage (IE), remission was achieved and they are still under observation. Combination chemotherapy is usually reserved for patients failing or recurring after other less aggressive therapies, those with advanced stage disease (i.e. Stages IIIE-VI) and those with diffuse large B-cell lymphoma (17). The original concern that chemotherapy in a patient with involvement of the stomach might lead to gastric perforation and/or bleeding has not been confirmed in a number of comparative studies (30,31). In this series (21.7%) had gastrectomy before chemotherapy, and (4.3%) received radiotherapy in addition to surgery and chemotherapy. Majority of our patients (65.2%) were treated by chemotherapy (Anthracyclin containing regimen). Since our study is retrospective, and the numbers of patients are small, conclusion about treatment efficacy should be made with caution.

In Conclusion:

The current study showed that primary GI NHL is commoner among males than females, the peak age is in the sixth decade. Abdominal pain is the most common presenting symptom with not surprising delay in diagnosis, because of the very nonspecific complaints. Gastric NHL accounted for the majority. Diffuse large B-cell lymphoma represents the most common histologic subtype while the extra-nodal marginal zone B-cell lymphoma (MALT type), Helicobacter pylori associated is the next. At presentation 78.6% of the cases had early stages. Anthracyclin containing regimen is the frequently used treatment modality.


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