Pattern of extra-nodal non Hodgkin’s malignant lymphoma in Asir Central Hospital, Abha

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Abstract: The aim of this study is to analyze the pattern of non-Hodgkin’s malignant lymphoma in extra-nodal locations among non-Hodgkin’s lymphoma patient from Asir region. Sixty-five histologically confirmed cases of non-Hodgkin’s malignant lymphoma with extranodal disease as primary manifestations were seen at Asir Central Hospital, Abha, between October 1987 and May 1994.

Results: Primary extra-nodal non-Hodgkin’s lymphomas represented 38.7% of the 168 cases of non-Hodgkin’s lymphomas diagnosed in Asir Central Hospital during the last six and a half years. The mean age was 44 years (range 3 to 92 years) and male:female ratio was 1.95:1. Fifty-six patients (86.1%) were Saudis while 9 (13.9%) were non-Saudis. Percentage (crude relative) frequencies of various sites were: gastrointestinal tract (52.8%) and head and neck (26.8%). The ratio of gastric to small intestinal lymphomas was 1.5:1 and only two small intestinal lymphomas showed features of immunoproliferative small intestinal disease. Thyroid lymphomas represented 36.8% of head and neck lymphomas. Histologically, only one case (1.4%) was low grade, 54 cases (72%) were intermediate grade and 17 cases (26.6%) were high grade.

Conclusion: This study shows a high frequency of extra-nodal forms of non-Hodgkin’s lymphoma in this part of the Kingdom with a high proportion affecting the gastrointestinal tract, particularly the stomach. Other features included lack of immunoproliferative small intestinal disease among Saudi patients, high frequency of thyroid lymphomas as compared to nasopharyngeal lymphomas and very low frequency of low grade lymphomas.

Keywords: Extra-nodal, non-Hodgkin’s lymphoma

Non-Hodgkin’s lymphoma (NHL) is one of the most common malignant tumors in Saudi Arabia. It is the second most common type of cancer among patients from the Asir region. Tissues other than lymph nodes may be the apparent primary site of origin of NHL. In three relatively large series from the West and South Asir, the frequency of extranodal disease as primary clinical manifestation of NHL was 37%, 24% and 21%, respectively.

The present report is intended to study the general pattern of extranodal NHL in Asir province of Saudi Arabia and compare it to reports from other countries including Middle Eastern countries.

Materials and methods: A total of 168 cases of NHL were diagnosed at the Histopathology Laboratory of Asir Central Hospital, Abha, between October 1987 and May 1994. The records of all patients were reviewed and only cases with extra-nodal disease as primary manifestation were included in the present study. A case was considered extra-nodal when the disease was clinically confined to extra-nodal site and the immediate lymphatic drainage. Stage III and Stage IV cases were excluded from the study. Involvement of other sites was excluded, mainly on clinical and radiological basis, including ultrasound, computerized tomography and in some cases, magnetic resonance imaging. Invasive methods for staging was carried out in a few cases where there was extra-nodal tissue involvement because it was difficult to determine whether the primary was nodal or extra-nodal.

All specimens were fixed in 10% buffered
formalin pH 7.4; embedded in paraffin and subjected to routine staining. Some cases were also subjected to immunoperoxidase staining for common leukocyte antigen to exclude anaplastic and/or small cell carcinoma. The cases were classified according to the Working Formulation. The data were presented as percentage (crude relative) frequencies and/or absolute numbers.

**Results** Out of a total of 168 cases of NHL, 65 (38.7%) presented in extranodal sites as the primary manifestation of the disease. The male:female ratio was 1.95:1 and the mean age was 44 years. Of these, 56 (86.1%) were Saudi nationals while the remaining 9 cases (13.9%) were non-Saudis. Distribution of the cases according to age and sex is shown in Table 1. There is a peak in the first decade and another peak in the sixth and seventh decades. The cases were classified histologically according to International Formulation as shown in Table 2. All except one case were aggressive NHL, out of which 47 (72.0%) were intermediate grade and 17 (26.6%) high grade. The only case of low grade lymphoma was of follicular type, while the rest were of diffuse type. The most common extra-nodal site in our series was the gastrointestinal tract with 38 cases (52.8%), followed by head and neck with 19 cases (26.4%), and liver with 3 cases (4.2%). Of the gastrointestinal lymphomas, 21 cases (29.2% of the total) were in the stomach while 14 cases (19.4% of the total) were in the small intestine. Of these, only two cases fulfilled the criteria of IPSID. In the head and neck, the thyroid was the main site of involvement with 7 cases (9.7% of the total), followed by the nasopharynx with 4 cases (5.6% of the total) and the oral mucosa with 3 cases (4.2% of the total).
Discussion The present study shows that there is a high incidence of NHL presenting as extra-nodal disease in the south-western part of Saudi Arabia. NHLs are relatively common in the Kingdom,\textsuperscript{1,2} comprising approximately 10% of all malignant neoplasms. In the West, they constitute less than 3% of all malignancies.\textsuperscript{4} Extra-nodal forms (38.7%) were about twice as common in our study as in most of the series from the Western countries and South Asia.\textsuperscript{5} This is in conformity with other studies from the Middle East with 44% extranodal NHL.\textsuperscript{4}

The relative proportion of low grade lymphomas in our series was considerably less than in the United States\textsuperscript{7} where low grade lymphomas represented 49.0%, while the proportion of immediate grade lymphomas was very high. Even the high grade lymphomas (26.6%) were higher than in the United States, where it is seen in 12.0% of all NHL cases. However, in comparison to other studies from the Kingdom,\textsuperscript{9} high grade lymphomas are in this area. The reason for the lower percentage of cases of high grade lymphomas in this region could be attributed to increasing health awareness among the local population and the seeking of medical advice relatively earlier than before.

The pattern of distribution of the extra-nodal forms of NHL is typical of the pattern in the Middle East\textsuperscript{8} with some important differences. Most of our cases were in the stomach (29.2\% of all cases, 55.3\% of all gastrointestinal lymphomas). This pattern of gastrointestinal lymphomas was similar to the pattern observed in Middle Europe and North America.\textsuperscript{10,11} On the other hand, primary small intestinal lymphomas have been observed to be the most common form of extra-nodal NHL in other studies from the Middle East,\textsuperscript{8} accounting for 50\% of all extranodal and 75\% of gastrointestinal lymphomas in adults. Small intestinal lymphomas in this study accounted for 19.4\% of all extra-nodal lymphomas and 36.8\% of gastrointestinal lymphomas. Other studies from the Middle East\textsuperscript{8} have linked the high incidence of small intestinal lymphomas to IPSID, geographically confined to Middle Eastern, Mediterranean countries and South Africa. These studies showed 42.7\% of small intestinal NHLs were associated with IPSID. Even though the Asir region is geographically in the Middle East, we observed IPSID in only 2 patients, who were not of Saudi origin. These two patients came from the Mediterranean region. This lack of IPSID in Asir region could be attributed to different socioeconomic patterns and lower incidence of gastroenteritis and pseudolymphomas in this part of the Kingdom, factors that have been associated with IPSID.\textsuperscript{8} Other, as yet unknown factors may also have a role to play.

In a previous study by Brugere et al.,\textsuperscript{12} head and neck was the most common primary site of extra-nodal NHL. Thirty two point nine percent of cases of head and neck lymphomas in this series were in the tonsils, 16.4\% in the nose and sinuses, 16.1\% in the nasopharynx and 6.0\% at the base of the tongue. None of the cases in the latter study were in the thyroid. In contrast, the thyroid was the commonest site in head and neck in the present series with 36.8\% (9.7\% of total cases) followed by nasopharynx with 21.1\% (5.6\% of total cases), oral mucosa with 15.8\% (4.2\% of total cases) and tonsils with 10.5\% (2.8\% of total cases). Thyroid lymphomas have been reported in only 2.5\% of cases in North America\textsuperscript{14} and 2.2\% of cases in Japan.\textsuperscript{15} Female preponderance was marked in thyroid lymphomas in our study with a male:female ratio of 1:6. Female preponderance of thyroid NHLs has been attributed to origin from active lymphoid cells in chronic lymphocytic thyroiditis, a disease that occurs in elderly women.\textsuperscript{16} However, why thyroid is the most common site in the head and neck in this region is not clear.

Etiopathogenesis of malignant lymphomas is not well understood and a variety of factors have been held responsible. Epstein Barr virus, Human T cell leukemia virus type I (HTLV-1), fertilizers, pesticides and other chemicals have also been implicated. HTLV-1 has been associated with an increased incidence of a particularly aggressive form of NHL. The practice of intermarriage within the families could also be an additional factor in this part of the world. However, more detailed studies are still required to delineate causal factors for extranodal NHL in this part of the Kingdom.

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References
ملخص البحث

دراسة نمط حدوث الأورام الإندودية خارج العقد اللمفي في 56 مريضًا من منطقة عسير وذلك في الفترة من شهر (تشرين الأول) 1987 م إلى شهر (آيار) 1994 م.

النتائج:

قد كونت الأورام اللقفيَّة الإندودية خارج العقد اللمفي نسبة 7.38٪ من مجموع حالة أورام لقفيَّة ش誌خت بالفحص السريري. كان متوسط عمر المرضى 44 سنة (3 إلى 92) وكانت نسبة الذكور إلى الإناث 1:1.1 وكانت نسبة المرضى السعوديين 1/86٪ ونسبة السكان من غير السعوديين 1/31٪. وكانت نسبة إصابه المعدة والعمرية أكثر الأماكن إصابه بنسبة 1/57٪. وكانت نسبة حالات الإصابة إصابة الغدة الدرقية 1/36٪ من حالات المرضى في منطقة الرأس والرقبة. ولهذا أظهر الفحص السريري أن هناك حالة واحدة فقط كانت ذات درجة متقدمة في غدة ثقيلا 1/32. وحالة و17 حالة 1/26٪ كانت ذات درجة عالياً.

الاستنتاج:

أظهرت هذه النتائج أن الأورام اللقفيَّة خارج العقد موجودة بنسبة عالية نسبياً في منطقة عسير، حيث من خلال الفحص السريري، وظائف عظام الأرجل وإصابة العقدة الدرقية. ومن نتائج الدراسة أيضاً ارتفاع نسبة إصابة العقدة الدرقية إذا ما قدرت بالحقل، وأيضًا ندرة الحالات ذات الدرجة المتقدمة من الأورام.

مفتاح الكلمات: خارج العقد اللمفي، أورام، أورام، غير، عين، هيرسكي.