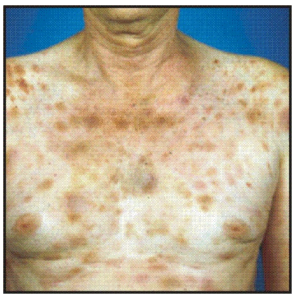
ORIGINAL PROF-872

EXTRA NODAL LYMPHOMA



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ABSTRACT ... dratiq7@yahoo.com **Objectives:** To study the different clinical presentations and treatment options of extra nodal lymphoma. **Design:** Prospective **Setting & Period:** Surgical Unit, Bhawal Victoria Hospital, Bahawalpur from May 01,2000 to April 30,2004. **Material & Methods:** Patients of either sex & age diagnosed as case of extra nodal lymphoma were included in the study. The clinical record of the patients included biodata, symptoms & signs, biopsy report, biochemical & radiology report, treatment (surgery, chemotherapy, radiotherapy) given and follow up. **Results:** In this study we had 13 patients. Out of these 4(31%) were female and 9(69%) were male. Extra nodal sites included GIT (54%), testis (15%) spinal cord (15%) & skin (15%). The prognosis in most of the cases was not so good. **Conclusion:** Due to this extensive presence of lymphatic tissue, lymphoma can develop in and spread to, almost any part of the body, For the treatment purpose staging of the disease is very important like any cancer, the earlier the lymphoma is diagnosed, the easier it is to treat.

Key Words: Lymphoma, Extra nodal Lymphoma, Non hodgkin lymphoma.

INTRODUCTION

Lymphoma is one of the common neoplasms affecting the entire lymphatic system including the spleen, thymus and liver. Extra nodal lymphoma means that primary area of presentation of lymphoma is not the lymph node. Extra nodal lymphoma can be further categorized as primary or secondary, with secondary indicating that the lymphoma first presented itself in an extra nodal site[1-3].

Lymphomas result when DNA damages or change occurs to immune cell (a lymphocyte) that alters the behavior of the cells. The damage to DNA results in the abnormal production of proteins that prevents the cells from dying when they should, or cases sustained rapid cell division that produces more of its kind. These malignant cells then may accumulate to form tumors that may enlarge the lymph nodes or spread to other areas of lymphatic system, such as the spleen or bone marrow[2,3].

Lymphoma can also spread to or first appear outside the lymphatic system and is called extra nodal disease. The underlying pathology (the type of cell its stage of maturation, its genetic characteristic's, etc.) further classifies the extra nodal lymphoma. These properties may be more relevant to the likely behavior of the lymphoma and the best types of treatments[2,4-7]. Extra nodal forms of lymphoma are less common and account for less than 15% of lymphoma. The gastrointestinal tract is the most common extra-nodal site for lymphomas. It may also involve non lymphoid tissues such as testis, bones, eyes, brain, heart, white blood cells (leukaemic),skin and kidneys etc[8,9].

They World Health Organization has staged lymphoma by the extent of the disease[2,3,9]

Stage I. Limited to one node or organ.
Stage II. Involvement of many nodes in a region.
Stage III. General node involvement.
Stage IV. Liver or spleen with or without stage III.
Stage V. Metastasis to bone marrow with or without stages I-IV.

Signs & Symptoms of Lymphoma will vary depending on the location of the tumors. The clinical presentation could be of mobile abdominal mass, of sub acute intestinal obstruction, bleeding per rectum, itching, nodules on the skin, testicular swelling and paraplegia etc[4,5,10-13]. Diagnosis is made with a biopsy of the involved tissue for the histo-pathology. Staging of lymphoma involves haematology, blood chemistries, bone marrow aspirates, radiographs, ultrasound and CT scan[2,3,9].

Therapy for extra nodal lymphoma usually requires surgery, chemotherapy and, or radiation with follow up diagnostic checking for recurrence. Success is dependent on the location of extra nodal lymphoma. The treatment differs depending upon condition of patient, stage and histology of the tissue. Considering these factors, best option is chosen for individual patient. For example, if there is residual or recurrent disease after surgery, radiotherapy is given to minimize the chances of recurrence[2,3,7-9].

Poor survival factors include: age > 60 years, advanced stage disease, poor performance status, an elevated LDH, involvement of more than two extra nodal sites, splenomegaly, peripheral blood involvement, anemia and elevated b2 microglobulin. The international Lymphoma Prognostic Index, which includes several of these features, has been found to be of prognostic value[9,14,15]. Conventional chemotherapy treatment with cyclophosphamide, vincristine, prednisone (CVP) or with the addition of doxorubicin (CHOP) results in and overall response rate of approximately 85% and a complete response rate of 45%. Unfortunately, conventional chemotherapy does not result in durable responses and is thus not considered curative[6,14]. The median progression-free survival is 20 months with an overall median survival of 36 months.

AIMS & OBJECTIVES

The purpose of study was to study the different clinical presentation and treatment options of extra nodal lymphoma.

MATERIAL & METHODS

The study was conducted at surgical units, Bahawal Victoria Hospital. Bahawalpur from 01-5-2000 to 30-4-2004. A total of 13 patients who presented with extra nodal lymphoma, irrespective of age and sex were included in the study. Patients with primary lymph node involvement were excluded.

The clinical records of the patients was made on a performa. It included bio-data, symptoms & signs, biopsy report, biochemical & radiological report, treatment (surgery, chemotherapy, radiotherapy) given and follow up. A diagnosis is made with a biopsy of the involved tissue for histo-pathology. Staging (i.e. the extent of disease) involves hematology, blood chemistries, bone marrow aspirates, radiographs, ultrasound and CT scan. Therapy for extra nodal lymphoma usually requires surgery, chemotherapy and or radiation with follow up diagnostic checking for recurrence. Computer

programme SPSS was used for analysis.

RESULTS

Total thirteen patients presented with extra nodal lymphoma during the period of 01-05-2000 to 30-04-2004. Out of these 4(32%) were female and 9(68%) were male. The age ranges from 14 years to 65 years with the maximum patients 8(72%) falling in the age group 40-65 years. Different sites involved in the body with extra nodal lymphoma in our study are shown in the Table-I. Different clinical presentation of these patients are as shown in Table II.

In our study seven patients (54%) presented with extra nodal lymphoma of gastro-intestinal tract. Abdominal mass was the most common presentation in these patients. Four patients presented with mobile abdominal mass. Mass led to episodes of sub acute intestinal obstruction, some times there was distension of abdomen and some times patient passed flatus and feaces. At the time of obstruction patient used to feel colicky abdominal pains. One patient each presented with peritonitis, bleeding per rectum & recto-vaginal fistula.

Skin nodules were the next common presentation in our study. Two patients (15.3%) presented with skin nodules on the chest, abdomen & on the back, ranging from 2-4cm in size. There was also H/O fever and itching on the abdomen and chest.

Table-I Different sites involved in extra nodal lymphoma

Site	Male	Female	%age
Transverse colon	1	1	15.3
Ascending colon	Nil	1	7.2
Ileum	1	1	15.3
Rectum	1	1	15.3
Testis	2	Nil	15.3
Spinal cord	2	Nil	15.3
Skin	2	Nil	15.3

Table-II Clinical presentations of patients with extra nodal lymphoma

Presentations	No. of patients	%age
Mass abdomen	4	32.5
Peritonitis	1	7.2
Bleeding per rectum	1	7.2
Recto vaginal fistula	1	7.2
Skin nodules	2	15.3
Paraplegia	2	15.3
Testicular Swelling	2	15.3

Table-III Treatment of patients with extra nodal lymphoma

Site of growth	No. of patients	Operation	Chemotherapy Radiotherapy
Colon	3	Colectomy	Chemotherapy
Ileum	2	Resections & anastomosis	Chemotherapy
Rectum	2	Colostomy & Biopsy	Chemotherapy
Skin nodules	2	Biopsy	Chemotherapy & Radiotherapy
Spinal cord	2	Excision of growth	Chemotherapy & Radiotherapy
Testis	2	Orchiectomy	Chemotherapy

Table-IV Biopsy Results of different extra nodal lymphoma			
Site of growth	**No. of patients**	**Operation**	**Biopsy Report**
Colon	3	Colectomy	Diffuse lymphocytic
Ileum	2	Resection &anastomosis	Small lymphocytic
Rectum	2	Colostomy & Biopsy	Diffuse large cell
Skin nodules	2	Biopsy	Primary Cutaneous lymphoma
Spinal cord	2	Excision of growth	Small lymphocytic
Testis	2	Orchiectomy	Diffuse large cell

Two patients (15.3%) presented with testicular swelling. Its consistency was firm to hard, swelling was smooth and cord contents were normal in size. Two patients (15.3%) presented with backache and weakness of legs. There were no sensations below the umbilicus in one patient. Power in legs was grade. 1/5. CT scan showed para vertebral mass. All patients underwent surgical treatment and then followed by chemotherapy & radiotherapy (Table-III) biopsy report of patients of extra nodal of lymphoma of various sites are shown in Table-IV.

DISCUSSION

"Lymphomas do not only & only arise in lymph nodes. Many arise in non-lymphoid sites such as the skin and gastrointestinal tract. The gastrointestinal tract is the most common extra-nodal site for follicular lymphomas, the most common nodal based type of lymphoma."[1,3,9,14].

Because of their unusual behavior, they present a major challenge even to the experienced clinicians. Similarly the histology of some lymphomas is similar to other cancers like in seminoma & lymphoma of testis, can be a challenge for hitopathologist. By applying organized approach to diagnosis, staging and treatment good results can be achieved. Increased understanding of clinical, hematologic, immunophenotypic and molecular aspect of small lymphocytic disorders has allowed for more accurate delineation of several lymphoma entities. Excellent care can be offered by aggressive & multi disciplinary approach for the management of these patients. To be specific to each type and site of lymphoma, optimizes patients outcome[2,3,7,9].

In our study extra nodal lymphoma of gastro intestinal tract was the common presentation (seven patients) similar as in literature[1,16-18]. According to the literature lymphoma of the colon is a rare malignancy[8,17,19,20] but in this study colon (three patients) is the most common site involved.

This finding is in contrast to the literature. In two patients rectum was involved & in two patients ileum was involved. Patients presented with mass upper abdomen (which was mobile), symptoms of sub acute intestinal obstruction, mass right iliac fossa, bleeding per rectum, peritonitis & recto vaginal fistula. These coincide with the literature[2,5,20]. These patients were operated and then chemotherapy and radiotherapy was given similar to literature[2,3,6,8,10].

Testicular lymphoma was diagnosed in two patients in our study. One presented with painless and other presented with painful testicular swelling[12,21]. It is disease of old age. In our study a young patient of 20 years presented with testicular lymphoma. This finding is in contrast to literature[22].

Swelling was hard in consistency. Ultrasonography showed mass with variable texture. Right orchiectomy was done followed by chemotherapy. This treatment coincide with the literature[21,22]. The natural history of

lymphoma has several special aspects that must be considered when planning treatment. These include a tendency to develop disease in the opposite testicle and, at least in cases presenting with stage-III or IV disease, an increased risk of CNS involvement[21].

There are two special aspects of managing testicular lymphoma. The first concern is the tendency of testicular lymphoma to involve the opposite testicle. If the patient receives systemic chemotherapy only, the risk of relapse in the opposite testis is at least 25%. The addition of 10 to 15 fractions of irradiation to the entire scrotum (to a total dose of 2,500 cGy) virtually eliminates this risk.

Such irradiation causes azospermic infertility and brief acute toxicity including cutaneous anoscrotal inflammation that lasts 2 to 3 weeks. However, low normal testosterone levels are maintained, and impotence is not caused by this irradiation. The second concern in these patients with stage III or VI disease, is the greater risk of CNS involvement. All such patients should be considered for intrathecal chemoprophilexis[12,13,21,22].

Two patients presented with lymphoma of the skin. The clinical presentation was itching, fever, painful skin nodules ranging from 2-4 cm in size which were present on abdomen, chest and on back. Para-aortic lymph nodes were also enlarged. Biopsy of nodule taken which turned out to be primary cutaneous lymphoma. Chemotherapy and radiotherapy were given in addition to symptomatic treatment[2,3,8].

Two patients presented with weakness of legs. On CT scan there was mass in the para vertebral region, patients operated, growth excised, there was recurrence after five months. Radiotherapy and chemotherapy were also given[4,23]. Neurological syndromes complicating lymphoma fall into three main groups:-

1. Acute or subacute spinal cord compression

2. Cranial nerve involvement

3. Meningeal invasion

Intra cerebral deposits are rare.

Spinal cord involvement is the commonest neurological abnormality associated with the reticuloses and compression of the cord occur mostly in the thoracic and lumbar regions. Epidural lymphoma is rarely a manifestation of localized extra nodal disease and usually represents a generalized and progressive disease. Neurological problems usually results from direct compression of the spinal cord or its nerve roots, but vertebral destruction and collapse or interruption of the blood supply to the cord may be involved[2,4,9,11,24].

In this study, the prognosis in the most of the cases was not so good as described in the literature. The reason probably was that, most of the cases presented late when the disease was advanced. The other contributory factor is as the disease advances, the immunity of the body decrease. Moreover chemotherapy and radiotherapy also decrease the immunity of the body[2,3,6,8,9,17].

CONCLUSION

Lymphoma is the disease of lymphatic tissue. This lymphoid tissue is present throughout the body. Due to this extensive presence of lymphatic tissue, lymphoma can develop in and spread to, almost any part of the body, including the spinal cord and brain[1,2,3,8,9,13].

For the treatment purposes staging of the disease is very important like any cancer, the earlier the lymphoma is diagnosed, the easier it is to treat[6,7,25]. From this study, it is concluded that some patients are being wrongly treated long before actual diagnoses are made. For example in this study one patient presented with mass right iliac fossa. This patient was treated by giving Anti tuberculous therapy the mass regressed initially but again appeared. For the prevention of this type of mistake, it is better to make the definite diagnosis first and then start the treatment.

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