RESEARCH ARTICLE

Pattern of Lymph Node Pathology in Western Saudi Arabia

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Abstract

Background: This study aimed to characterize the histopathological pattern of lymph node pathology among Saudi patients and to highlight the age and gender variations of these lesions as base line data. Materials and Methods: We retrospectively analyzed the data from lymph node biopsy specimens received at the Department of Pathology, King Fahad Hospital, Madinah, Saudi Arabia from January 2006 to December 2013. Results: Of the 289 lymph node biopsy specimens received, 154 (53.3%) were from males and 135 (46.7%) from females giving a male: female ratio of 1.14:1. Age of the patients ranged from 2.5 to 96 years with a mean age 33.9 years. The commonest lymph node group affected was the cervical (30.4%) followed by axillary (9.7%) and inguinal (8.7%). Malignant lymphoma [71 Hodgkin's disease (HD), 57 non Hodgkin's lymphoma (NHL)] 128 (44.3%), reactive hyperplasia 68 (23.5%), and tuberculosis 41 (14.2%) were the common causes of lymph node enlargement. While HD, reactive hyperplasia and tuberculosis were commonest in young adult patients (10-29 years old) and rare above the age of 50 years; NHL was the predominant cause of lymph node enlargement above 50 years. Conclusions: Lymph node biopsy plays an important role in establishing the cause of lymphadenopathy. Among the biopsied nodes, lymphomas were the most common (44.3%) followed by non-specific reactive hyperplasia (23.5%) and tuberculous lymphadenitis (14.2%).

Keywords: Lymph node - pathology - madinah - Western Saudi Arabia

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Introduction

Peripheral lymphadenopathy is a common condition in the clinical practice of both the surgeons and physicians including the paediatricians. Easy accessibility of acquiring a sample for cytological or histological examination has made it an important component of practices of the pathologists as well. Even though, Fine needle aspiration cytology (FNAC) has been introduced in the laboratory diagnostics since last two or three decades (Handa et al., 2012); there are still many situation, where excision biopsies is mandatory, especially in suspected cases of lymphoproliferative disorders. Recent literature also cites a study on the role of ultrasound (US) guided core biopsy in the diagnosis and typing of lymphoma in the head and neck region (Burke et al., 2011).

From the histopathological prospective, most of the diagnoses are reactive or non-specific inflammatory conditions, however a significant number of cases are composed of granulomatous inflammations, the most common cause being tuberculosis in the under privileged world (Fazal-I-wahid et al., 2013). Enlarged cervical lymph nodes are a common finding on physical examination in the pediatric population (Rajasekaran and Krakovitz, 2013). Although most cases are due to reactive changes (Biswas et al., 2013); lymphoproliferative disorders are more common in this age group (Jamal et al., 2014); in contrast to the other extreme of age exhibiting metastasis from nearby or distant malignancies (Qadri et al., 2012; Lad et al., 2014).

In the recent literature, there are a number of publications from all over the world on lymph node pathology, in the form of reviews, original articles and case reports. A case report on Kikuchi disease with review of literature (Deaver et al., 2014) and a literature review on enlarged neck lymph nodes in children (Rajasekaran and Krakovitz, 2013) from USA; and experience of US guided core biopsy on head and neck lymphoma (Burke et al., 2011) from UK are examples of studies from the developed western world.

From African continent, we have research work from South Africa (Khuzwayo and Naidu, 2014) and Ethiopia (Muluye et al., 2013); along with three recent studies from Sudan (Ageep, 2012; Bilal and Elshibly, 2012; Ahmed et al., 2013) and a slightly older article from Nigeria (Olu-Eddo and Ohanaka, 2006). From the Asian continent, large bulk of lymph node pathology articles are from Indo-Pak Subcontinent; just to mention a couple of most recent works from India (Roy et al., 2013; Reddy et al., 2014) and similarly from Pakistan (Fatima et al., 2011; Naseem et al., 2011). From the neighbouring countries of Kingdom of Saudi Arabia (KSA), there are two recent

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studies, one from Turkey (Tatar et al., 2011) and one from Iran (Etemad-Moghadam et al., 2010).

From KSA, there are a number of recent publications on lymph node pathology in the form of case reports and original articles. Few examples of case reports are by Elyamany et al. (2013), Baslaim et al. (2013) and Al-Maghrabi et al. (2006). Experiences of BCG lymphadenitis (Bukhari et al., 2012), Castleman's disease (Al-Amri et al., 2010) and Kikuchi-Fujimoto disease (Al-Maghrabi and Kanaan, 2005) have been shared by researchers of KSA. A large series of 452 cervical lymph node biopsies from Eastern KSA has also been recently reported (Al-Tawfiq and Raslan, 2012). Finally extensive literature search reveal no recent or remote scholarly study done in the city of Madinah, which a rapidly growing city of the Western Region of KSA. Our work is first of its kind in recent scientific literature both in Madinah and KSA, in which we are reporting the pattern of lymphadenopathy in the local population.

Materials and Methods

All cases of lymph node biopsies received at Department of Pathology, King Fahad Hospital, Madinah, Saudi Arabia from January 2006 to December 2013 were retrospectively reviewed. Conventional haematoxylin and eosin staining was used to analyse the biopsy specimens and additional special staining was done (e.g. Ziehl-Neelsen stain for acid-fast bacilli [AFB] where required. Histopathology slides of cases within the study period were reviewed by the authors (A.A and A.A) to make a consensus diagnosis. Details of patients such as the clinical data (age, sex, and site) and histopathological diagnosis were obtained from histopathology request forms and register. Data were entered and processed using SPSS version 20 (SPSS Inc. Chicago, IL).

Results

Two hundred and eighty-nine peripheral node biopsies were received at the histopathology department of King Fahad Hospital, Madinah, Saudi Arabia from January 2006 to December 2013. There were 154 (53.3%) males and 135 (46.7%) females giving a male: female ratio of 1.14:1.

The age of the studied cases ranged from 2.5 to 96 years with a mean age of 33.9 years. The majority of the cases (n=134; 46.4%) were seen in the age group 10-29 years. The young age group (<10 years) and the elderly age group (≥70 years) constituted 2.4% and 13.5% respectively. The reviewed cases were classically categorized into four main groups; granulomatous diseases (45; 15.6%), neoplastic diseases (153; 52.9%), non-specific lymph node disorders (78; 27%) and miscellaneous group (13; 4.5%) {Table 1}.

The sites where lymph nodes were excised are shown in Table 2. The head and neck region was the most common location, particularly the cervical group of lymph nodes constituting 88 (30.4%) cases. The most frequent lymph node pathology diagnosed was malignant lymphoma [71 HD, 57 NHL] 128 (44.3%), followed by 68 (23.5%) reactive hyperplasia and tuberculosis 41 (14.2%).

Among the lymphomas, HD was more common accounting for 24.6% of lymphadenopathies. The age of the patients ranged from 8 to 90 years with a mean age 31.1 years. Most of the patients (n=46; 64.8%) were between 10-29 years of age (Table 3). The overall male to female ratio was 1.1:1. Histopathologically, nodular sclerosis variant was the commonest type (32 cases, 45%), followed by mixed cellularity (20 cases, 28.2%), lymphocytic rich (10 cases, 14.1%) and classic not otherwise specified (NOS) (9 cases, 12.7%).

Among 57 NHL cases, 29 patients were males (50.8%) and 28 were females (49.2%) and male to female ratio was 1.03:1. The age range was 15-92 years with a mean age of 52.4 years. Most of the patients (n=38; 66.6%) were seen at 50 years and above (Table 3). Among NHL cases, B-cell lymphomas were the predominant type (53 cases) accounting for 93% of all cases. Of the B-cell neoplasms, diffuse large B-cell lymphoma (DLBCL) was the most common subtype (33, 62.3%) cases, followed by follicular

Table 1. Age and Sex Distribution of 289 Patients with Lymph Node Pathology

Histological Diagnosis	No. (%)	M/F	Mean age (years)
Granulomatous diseases	45 (15.6%)	24/21	30.5
Tuberculosis	41 (14.2%)	18/23	28.9
Sarcoidosis	4 (1.4%)	3/1	36.3
Neoplastic diseases	153 (52.9%)	79/74	48.6
Hodgkin's lymphoma	71 (24.6%)	37/34	31.1
Non Hodgkin's lymphoma	57 (19.7%)	29/28	52.4
Atypical lymphiod proliferation	13 (4.5%)	6/7	53
Metastatic cancer	12 (4.2%)	7/5	43.1
Non specific lymph node disorders	78 (27%)	47/31	30.7
Reactive hyperplasia	68 (23.5%)	42/26	30.3
Sinus histiocytosis	6 (2.1%)	4/2	40.5
Chronic non specific lymphadenitis	4 (1.4%)	1/3	23.5
Miscellaneous	13 (4.5%)	8/5	23.3
Kikuchi disease	12 (4.2%)	7/5	24.2
Dermatopathic lymphadenopathy	1 (0.3%)	Male	13

Table 2. Site of lymph Node Biopsies in 289 Patients

Lymph node site	No.	%
Cervical	88	30.4
Axillary	28	9.7
Inguinal	25	8.7
Mesenteteric	18	6.2
Mediastinal	14	4.8
Submandibular	13	4.5
Unknown	103	35.7
Total	289	100

Table 3. Age Distribution of Patients with Common Lymph Nodes Pathology

Age (years)	Hodgkin's Disease	Non Hodgkin's lymphoma	Reactive hyperplasia	Tuberculosis
<10	1	-	3	2
10-19	25	3	21	9
20-29	21	9	17	19
30-39	6	2	8	7
40-49	6	5	9	-
50-59	5	12	4	2
60-69	2	7	3	2
≥70	5	19	3	-
Total	71 (24.6%)	57 (19.7%)	68 (23.5%)	41 (14.2%)

lymphoma (16 cases, 30.2%) and small lymphocytic lymphoma (4 cases, 7.5%). T-cell NHL comprised of 4 cases (7%) and anaplastic large cell lymphoma (ALCL) was the dominant subtype.

Thirteen cases of atypical lymphoid proliferation and 12 cases of metastatic cancer were diagnosed with a mean age 53 and 43.1 years respectively (Table 1). The most common types of carcinomas were adenocarcinoma, followed by papillary carcinoma and undifferentiated carcinoma.

Seventy eight (27%) patients had non-specific lymph node disorders. These included 68 (23.5%), 6 (2.1%) and 4 (1.4%) cases of reactive hyperplasia, sinus histiocytosis and chronic non specific lymphadenitis. The age of the patients with reactive hyperplasia ranged from 5 to 85 years with a mean age 30.3 years. Most of the patients (n=38; 48.7%) were between 10-29 years of age (Table 3). The male: female ratio was 1.6:1

Granulomatous lesions were seen in 45 (15.6%) cases, and tuberculosis (TB) was by far the most frequent cause accounting for 91.1% (41 cases) of granulomatous lesions. TB was most prevalent in children and young adults with 73.2% of cases in the first three decades of life, with a female: male ratio 1.3:1. Four cases of sarcoidosis were diagnosed. The age of the cases ranged from 18 to 50 years with a mean age 36.3 years. The male: female ratio was 3:1 (Table 1).

Twelve cases of Kikuchi disease were diagnosed constituting 4.2% of all cases. The mean age of patients was 24.2 years, with the youngest patient being 14 years old and the oldest 37 years. The male: female ratio was 1.4:1 (Table 1).

Discussion

We received 289 peripheral node biopsies at the histopathology department of King Fahad Hospital, Madinah, Saudi Arabia from January 2006 to December 2013. There were 154 males and 135 females giving a male: female ratio of 1.14:1. Almost similar male to female ratios were present in the study sample of a recent work from Sudan having 180 females and 147 males, with a male to female ratio of 1.22:1 (Ageep, 2012); and study from Nigeria included 238 males and 189 females, with the ratio of 1.25:1 (Olu-Eddo and Ohanaka, 2006).

The age of the studied cases ranged from 2.5 to 96 years with a mean age 33.9 years. As it is obvious from the figures that our study sample included both pediatric and adult patients, similar was the status in 452 cases study from KSA, described as 122 (27%) children ≤18 years and 81 (18%) patients >60 years (Al-Tawfiq and Raslan, 2012). However, recently Bilal and Elshibly (2012) did a study in Sudanese children having an age range of 1 to 13 years; while from Malaysia, we have a study on adult population ranging from 20 to 50 years (Kim et al., 1999).

Regarding the site, we found cervical group to be most common location sampled, accounting for 88 (30.4%) cases. This observation is consistent with most of the recent studies which have found the cervical group to be the most commonly sampled (Olu-Eddo and Ohanaka , 2006; Naseem et al., 2011; Ageep, 2012); and also consistent with the recent studies that have shared their FNAC experience of peripheral lymphadenopathy (Kochhar et al., 2012; Ahmed et al., 2013; Muluye et al., 2013). This is probably due to these lymph nodes draining the most commonly affected and inflamed region of the body as well as due to easy accessibility of the cervical lymph node for biopsy procedure.

The reviewed cases were classically categorized into four main groups; most common being neoplastic diseases, followed by non-specific lymph node disorders and granulomatous diseases. Our results are consistent with that of a research from South India (Roy et al., 2013) reporting the same disease breakdown i.e. neoplastic lesions being most common, comprising 53% (535 cases), followed by non-specific reactive lymphoid hyperplasia and tuberculous lymphadenitis. While from Sudan, a study in the pediatric population, 95% lymph nodes were benign (including 10% tuberculous lymphadenitis) and 5% were malignant (Bilal and Elshibly, 2012); whereas in the adult population, Ageep (2012) report most common cause of peripheral lymphadenopathy to be tuberculosis (39.5%), followed by metastatic diseases (24.7%). In a large study of 1785 patients from Pakistan, tuberculous lymphadenitis was the most prevalent, followed by lymphomas (Naseem et al., 2011). Finally in a 452 cases series from Eastern KSA, non-specific reactive diseases were found to be the commonest, followed by granulomatous disease; (Al-Tawfiq and Raslan, 2012).

The most frequent lymph node pathology diagnosed in our series was malignant lymphoma; with HD being the most common accounting for 46.4% of the neoplastic cases. The mean age was 31.1 years. There was slight male preponderance (male to female ratio 1.1:1). Histopathologically, nodular sclerosis variant was the commonest type, followed by mixed cellularity type. A prospective, hospital-based study from India report, that NHL was more frequently diagnosed than HD which had a median age of onset to be 28.1 and high male to female ratio (3.8:1). Mixed cellularity type was more common according to their experience (Chakrabarti et al., 2010). Their results was substantiated by another Indian study done recently that NHL was more commonly diagnosed than HD (Roy et al., 2013). Whereas in keeping with our observations are the findings of a large Pakistani study of 1785 patients, which reports HD to be more commonly diagnosed than NHL; and also more frequently in males (Naseem et al., 2011). In a large series including 658 cases of HD from Pakistan, the age range was reported to be 1 to 84 years with a male to female ratio of 3.3:1. Similar to the Indian study, mixed cellularity was the most frequently diagnosed subtype of HD (Siddiqui et al., 2006). A recent study from Pakistan has compared the histological appearances of Hodgkin's disease in Pakistani and Saudi patients; and report lack of bimodal age pattern and diagnosis at a younger age. It was found to be more common in males. An important difference was noted which is also consistent with our observation, that nodular sclerosis HD was commonest subtype among Saudis; whereas mixed cellularity HD was more common among Pakistani patients (Nagi et al., 2008).

In our study, amongst 57 cases of NHL, 29 patients

were males and 28 were females; with a male to female ratio of 1.03:1 and a mean age of 52.4 years. Diffuse large B-cell lymphoma (DLBCL) was the most common subtype, followed by follicular lymphoma. In an Indian prospective study, containing 76 NHL cases; the median age of onset was 39.9 years and male to female ratio was 3.8:1. The commonest histological subtype of NHL was reported as diffuse mixed variant (Chakrabarti et al., 2010). In a 20-year retrospective demographic study of 381 NHL cases from Iran; the mean age of NHL was found to be 39.3 years (Etemad-Moghadam et al., 2010). In a large series of 1785 cases from Pakistan, researchers found NHL in only 27 cases; which were more common in the males; and more prevalent in the second and third decades of their lives. In their series, diffuse small cell NHL was the most commonly reported histopathological subtypes (Naseem et al., 2011). In another large scale retrospective review of 557 DLBCL cases from Pakistan, the median age was was reported to be 48.7 years; and male to female ratio of 2:1 (Lal et al., 2008). In contrast to our observations, another study from KSA (city of Qassim) having 385 cases of malignant lymphoma; reports 251 (65.2%) cases of NHL, with a male to female ratio of 1.6:1 and age range of 6 months to 103 years. Diffuse large B cell lymphoma (DLBCL) was the most common type of NHL. Follicular lymphoma (FL) and small lymphocytic lymphoma (SLL) were less common (Akhtar et al., 2009). Similarly a research work from northern Iraq reports predominantly NHL (76%), in their 270 cases series of malignant lymphomas. The most common NHL was Diffuse large B-cell lymphoma (DLBCL) which comprised 52.2% of NHL, followed by Burkitt's lymphoma. While follicular lymphomas (FL) were infrequent (Yaqo et al., 2011). In a clinicopathologic evaluation of DLBCL by immunohistochemistry, a group of scientists from Pakistan conclude that there are high numbers of 'Non-Germinal Cell B type' DLBCL in their study population (Naz et al., . The most common types of carcinomas were adenocarcinoma, followed by papillary carcinoma and undifferentiated carcinoma. Roy et al. (2013) from India found metastasis in 8.5% of their 1010 case series. The majority of cases were found within the age group 40-70 years. Adenocarcinoma was also found to be the commonest metastatic tumor in their experience. In the recent Sudanese study of adult patients, metastatic disease was found in as high as 24.7% cases in patients above 50 years age (Ageep, 2012). Similar high percentage (25.7%) of metastatic disease was seen in a Malaysian study. They also report adenocarcinoma to be the most frequently diagnosed metastasis (Kim et al., 1999). In contrast to all these observations, a Thai study on 72 patients of metastatic disease report papillary carcinoma to be the commonest (41%), followed by lung, bile duct and breast; probably due to their study of cervical lymph nodes exclusively (Taweevisit et al., 2008).

In our present study, seventy eight (27%) patients had non-specific lymph node disorders including reactive hyperplasia, sinus histiocytosis and chronic non-specific lymphadenitis. The age of the patients with reactive hyperplasia ranged from 5 to 85 years. The male: female ratio was 1.6:1. From South India, the findings are quite similar; they found non-neoplastic lesions in 47% cases. Male to female ratio was 1.8:1. Common age group affected was 11-20 years (Roy et al., 2013). Whereas Kim et al., (1999) from Malaysia, found reactive lymph node pathology in 33.1% cases, having a female preponderance (males 19; females 26) and mean age of 27 years. The KSA study reports that the most common histopathological diagnosis was reactive disease (52.2%, n=236), which was followed by granulomatous disease (15.5%, n=70). Reactive disease was more common in children than adults (Al-Tawfiq and Raslan, 2012). Granulomatous lesions were seen in 45 (15.6%) cases, and tuberculosis (TB) was by far the most frequent cause. TB was most prevalent in children and young adults with most of cases in the first three decades of life, having a female: male ratio 1.3:1. This observation of female preponderance in Extra-pulmonary tuberculosis has also been report from most of the recent studies from the world and the region i.e. from Sudan (Ageep, 2012); Afghanistan (Fader et al., 2010); Turkey (Tatar et al., 2011) and Riyadh, KSA (Al-Otaibi and El Hazmi, 2010). In contrast to our observation of reactive lymphadenopathies being more common than tuberculosis, there are two studies from Pakistan reporting tuberculous lymphadenopathy to be more common than reactive (Naseem et al., 2011; Fazal-I-wahid et al., 2013).

In our study, twelve cases of Kikuchi disease were also diagnosed constituting 4.2% of all cases; with age range of 14 to 37 years. The male: female ratio was 1.4:1. In a recent study from Japan, there were however, more females than male diagnosed with this disease; and the age was reported to vary from 5 to 80 years, although most of the patients (62.7%) were younger than 30 years (Asano et al., 2014). Similar was the observation of Indian worker, although in a smaller series; who report that of their 24 cases, 17 were females and 7 were males (Supari and Ananthamurthy, 2014). From KSA, out of a total of 2500 lymph node biopsies, 15 cases were diagnosed as Kikuchi disease. The female to male ratio was 2.7:1. Ages averaged 29 years and ranged from 13 to 46 years (Al-Maghrabi and Kanaan, 2005).

Finally, in our observation, there were 13 cases of atypical lymphoid proliferation, which were not further investigated or followed-up as per our information at the level of pathology department; and similarly the number of cases of sarcoidosis (4 cases) and dermatopathic lymphadenopathy (1 case) were too small for any meaningful discussion.

In conclusion, our observations are similar to that reported by other recent studies in the region and country, with minor variations in the demographic data dependant on the sample selection. This data would provide a baseline to design future research studies for detailed analysis of individual diseases at laboratory, hospital and/or community levels.

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