Surgical Biopsy in Cervical Lymphadenopathy

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ABSTRACT

Background: Cervical lymph nodes are the most frequently enlarged and biopsied of all the peripheral lymph nodes and in most of the cases the enlargement results from benign infectious causes, however, the presence of cervical lymphadenopathy (LAP) requires accurate diagnosis to exclude more serious causes. The aim of this study was to analyze cases of Iraqi patients presenting with cervical LAP who underwent surgical lymph node biopsy to establish accurate diagnosis.

Materials and Methods: This retrospective study included 25 patients who presented with cervical LAP for whom surgical biopsy was performed to establish a definitive diagnosis. The investigated data included the demographic and clinical parameters in addition to the final histopathological diagnosis.

Results: Twenty five patients were included in this study with a mean age of 33.8 years and female predominance; benign diseases were diagnosed in 56% of the cases whereas the remaining 44% were diagnosed with malignant diseases. Tuberculous lymphadenitis was the most common cause.

Conclusion: This study emphasizes the importance of surgical lymph node biopsy in establishing a definitive diagnosis in patients presenting with cervical LAP.

Keywords: Surgical biopsy, cervical LAP, definitive diagnosis. **(J Bagh Coll Dentistry 2016; 28(4):111-114)**

INTRODUCTION

Lymphadenopathy (LAP), a medical description of swollen lymph nodes [(1)], is a symptom that manifests in patients of all ages [(2)] and may be caused by a wide variety of infectious, hematological, neoplastic and connective tissue disorders [(3)]. LAP can be localized or generalized and it is also classified as acute, subacute and chronic, the latter constitutes any LAP that does not resolve by 6 weeks [(4)]. Of all the peripheral lymph nodes, the cervical ones are the most frequently enlarged and biopsied and in most of the cases the enlargement results from benign infectious causes, however, the presence of cervical LAP requires accurate diagnosis to exclude more serious causes. The optimal work-up for cervical LAP includes thorough history taking, physical examination, blood tests and imaging [(5)]. Ultrasonography (US), computed tomography (CT) and magnetic resonance imaging (MRI) are helpful in evaluating the size, site, contents and the vascular pattern of the lymph nodes [(6,7)] but the definitive diagnosis usually requires fine needle aspiration cytology (FNAC) and/or lymph node excisional biopsy which is considered a vital part of the management [(8)].

The aim of this study was to analyze cases of Iraqi patients presenting with cervical LAP who underwent surgical lymph node biopsy to establish accurate diagnosis.

MATERIALS AND METHODS

This retrospective study included patients who presented with cervical LAP of more than 1 month duration and underwent surgical lymph node biopsy at the Oral and Maxillofacial surgery units of Al-Yarmouk teaching hospital and Ghazy Al-Hariri hospital for surgical specialties during the period extending from January 2009 to January 2015.

A thorough personal and family history was taken from all the patients followed by intraoral and extra-oral clinical examination to exclude any source of infection. The examination of the neck included the site, size, laterality, tenderness and the texture of the lymph nodes. In addition to the clinical examination and blood investigations, US and/or CT were taken for all the patients to provide information about the size and the extent of the enlarged lymph node, in some cases FNAC was performed.

Patients presenting with an acute upper respiratory tract infections, febrile illness, and history of head and neck malignancy or lymphoma were excluded from this study. All the surgical procedures were performed under general anesthesia after obtaining informed consents from the patients; the most accessible enlarged lymph node was excised through extra-oral approach and sent for histopathological examination. The investigated data included the demographic and clinical parameters in addition to the final histopathological diagnosis.

Descriptive statistics included percentages and means of patients' age and gender, durations of onset of LAP and final diagnoses. Inferential statistical analysis included Student T-test for 2

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independent means, analysis of variance (ANOVA) and Tukey HSD tests for the mean age of patients with different reported etiologies in addition to Chi square test, the difference was considered significant at $p \leq 0.05$.

RESULTS

Twenty five patients presented with cervical LAP, they included 16 females (64%) and 9 males (36%) with a male: female ratio of 1:1.8, the age range at presentation was from 8 to 83 years with a mean of 33.8 years. A mean duration of 6 months of lymph nodes enlargement was reported by the patients. On clinical examination LAP was bilateral in 7 patients (28%) and unilateral in 16 patients (64%), whereas in 2 (8%) patients it was in the midline. Surgical biopsy involved the most accessible lymph nodes; these were submandibular**(Fig 1)** in 13 patients, upper jugular in 9 patients, submental in 2 patients and posterior triangle in 1 patient.

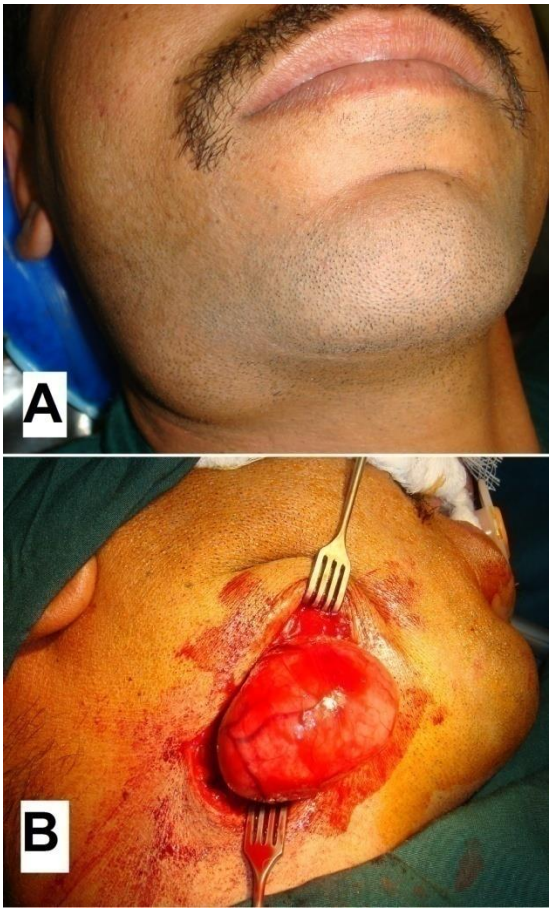

Figure 1: (A) Preoperative view showing enlarged right submandibular lymph node. (B) Intra-operative view showing excision of the enlarged lymph node through submandibular incision.

Fourteen patients (56%) with a mean age of 23.3 years were diagnosed with benign diseases while the remaining 11 patients (44%) with a mean age of 44.8 years had malignant diseases; the main characteristics of the 2 groups are shown in **Table 1.**

Table 1: Summary of the characteristics of LAP in patients diagnosed with benign and malignant diseases

	Benign	Malignant	P value
Mean age	23.3 years	44.8 years	0.0025*
Gender Male Female	 2 patients 12 patients	 7 patients 4 patients	0.0107*
Laterality Unilateral Bilateral	 10 patients 2 patients	 6 patients 5 patients	0.1339

*** = Significant**

The histopathological results revealed 4 etiologies for cervical LAP (**Table 2**), the differences in the mean ages of patients among different etiologies were statistically significant, but to note that patients who presented with LAP due to secondary metastasis were significantly older than patients who were diagnosed with other LAP etiologies who showed non-significant differences.

Table 2: Summary of the etiologies of cervical LAP

Diagnosis	Patients (%)	Mean age/year	One way ANOVA
Tuberculous lymphadenitis	8 (32)	23.4	df= 3 F= 7.86 P= 0.001*
Secondary metastasis	7 (28)	54	
Non-specific inflammatory reaction	6 (24)	23.3	
Hodgkin's Lymphoma	4 (16)	28.5	

*** = Significant**

Females showed higher incidence in cases of tuberculous lymphadenitis and non-specific inflammatory reaction with a male to female ratios of 1:7 and1:5respectively, whereas in cases of secondary metastasis of unknown primary malignancy males showed higher incidence with a ratio of 2.5:1. Lymphoma, on the other hand, showed equal gender distribution

In 11 patients the surgical biopsies were preceded by FNAC, in 6 patients the results of FNAC matched with the final diagnosis yet in the remaining 5 patients the results were inconclusive. Postoperatively, recovery was uneventful for all

the patients and no major complications were recorded. After confirming the diagnosis, patients were referred for further medical evaluation and management according to the involved disciplines.

DISCUSSION

It is estimated that the human body contains about 800 lymph nodes, 300 of them are situated in the neck [9] and cervical LAP, defined as lymph node measuring more than 1 cm in diameter [10], is one of the commonly encountered conditions in the outpatient setting [5]. In many cases the cause of cervical LAP can be disclosed through non-invasive diagnostic measures yet in other cases definitive diagnosis may require surgical biopsy of the lymph nodes [2]. Although it is believed that in general population only 3.2% of cervical LAP cases require surgical biopsy [11], delayed diagnosis of LAP in certain serious conditions like tuberculosis, lymphoma or secondary malignant metastasis may affect the prognosis of the disease adversely [5], and it is in this context that surgical lymph node biopsy is considered the gold standard for establishing a definite diagnosis [8].

This study showed female preponderance in cervical LAP patients which is in line with other Iraqi studies [12, 13], other studies, on the other hand, reported higher incidence of cervical LAP in males [14]. Benign diseases are also higher in incidence than malignant diseases, Al-Alwan et al. in their study in 1996 reported incidences of benign and malignant LAP which are nearly similar to the current study [15]. The results of this study reveal that tuberculous lymphadenitis is the most common cause of cervical LAP, the same finding is also reported by Abdulnabi [12] and by Hamad and Hamza [13], of note that both studies are from southern provinces in Iraq, although the latter study reported a much higher incidence (70%). Tuberculous lymphadenitis is also reported to be a common cause of cervical LAP in other Asian countries where 58% is reported in India [14] and 22.4% is reported in Korea [16], Weiler et al., in their review of 538 tuberculosis patients, reported only 3.9% of cervical tuberculous lymphadenitis [17]. In developing countries tuberculous lymphadenitis is one of the most common causes of cervical LAP with female preponderance whereas it is considered a disease of the foreign-born in developed countries [18].

The pathogenic mechanism of tuberculous lymphadenitis, in most cases, is through reactivation of dormant lymphatic system disease, initially caused by primary pulmonary tuberculosis, resolving later with minimal pulmonary scarring and a positive tuberculin test. A second mechanism is based on lymphatic spread after the organism gains direct entry through the mucous membrane lining of the oral cavity [17]. Surgical lymph node biopsy is superior to FNAC in establishing an accurate diagnosis of tuberculous lymphadenitis, a finding that is reported in many studies [14, 18].

The malignant diseases diagnosed in this study included lymphoma and secondary metastasis of unknown primary tumors with a higher incidence than that reported in other studies [8, 12, 13] and with significantly higher mean age of patients than that in benign diseases. Secondary lymph node metastasis of unknown primary tumor was detected in 28% of the cases in this study. It is believed that about 10 % of patients with secondary metastasis to the cervical lymph nodes have no identifiable primary tumor, this necessitates a thorough clinical examination and imaging using contrast enhanced computed tomography (CT) scan and positron emission tomography (PET) scan and endoscopic search for primary tumors with special attention to sites of the head and the neck where a primary lesion may remain occult, for example, the tonsil, the base of tongue, nasopharynx and pyriform sinuses [19].

Patients with metastatic diseases had significantly higher mean age than all other patients with male predominance which is in line with other studies [12, 20]. FNAC is described as a reliable diagnostic method provided that conducted by experienced histopathologists and some authors recommend repeating the procedure in cases of uncertain or non-diagnosis histology [20]. Surgical biopsy in such cases is controversial, due to the reported adverse effects on neck disease control and high incidence of local recurrence yet some studies found no such effects provided that the biopsy was followed by definitive treatment [21].

The incidence of lymphoma in this study is lower than that reported in other studies [7, 12, 15] yet higher than that reported elsewhere [5]. Abdulnabi [12] found a higher incidence of lymphoma after surgical biopsy of cervical lymph nodes in comparison to FNAC which may highlight the superiority of surgical biopsy in establishing an accurate diagnosis. Matsumoto et al. suggested predictive criteria to perform surgical biopsy when definitive diagnosis of lymphoma cannot be made by FNAC, these criteria are advanced age, large lymph node size and high level of soluble interlukine-2 receptor (sIL-2r) [2]. On the other hand Tsuji et al. [7] suggested that US and CT scan evaluation and high level of thymidine kinase might be useful in

determining the need for surgical biopsy in cases of lymphoma.

Non-specific inflammatory reaction is the third cause of cervical LAP (25%), this is in contrast to other Iraqi studies [12, 15] and reports from Asian and African countries that found that this cause was the most common diagnosis in LAP [8, 22, 23]. Mohan et al. in 2007 [8] found that in 3% of patients a second pathology could be identified within 6 months of the initial biopsy and they maintain that this group of patients may require further investigations and should be followed up to detect whether they develop additional conditions.

FNAC is reported as an efficient diagnostic tool with high accuracy rate in cervical LAP [2, 12], but in this study about 45% of the cases (5 of 11 patients) that underwent FNAC before surgical biopsy had inconclusive or non-diagnosis results. In the institutions where this study was conducted surgical biopsy is preferred as a more accurate diagnostic tool than FNAC especially when serious diseases are suspected since their treatment may be associated with high morbidity or even mortality, thus minimizing the risk of misdiagnosis and subsequent over-treatment.

This study is limited in its small number of patients and its retrospective methodology, but, nevertheless, it emphasizes the importance of surgical lymph node biopsy in establishing a definitive diagnosis in patients presenting with cervical LAP. The results show that cervical LAP is caused by benign diseases more than malignant diseases; they also reveal the high incidence of TB lymphadenitis and malignant diseases in Iraq.

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