Tuberculous lymphadenopathy: An Approach To Diagnosis And Management

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Original

Tuberculous Lymphadenopathy :

An Approach To Diagnosis And Management

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الأهداف :-
تحديد تكرار حدوث السل في الغدد الليمفاوية في منطقتنا و أعراضه المرضيه وتشخيص وتقييم فاعلية العلاج الكيماوي ذو المدى القصير.

الطرق :-
دراسة مستقبلية لحالة 64 مريضاً مصابون بمرض السل في الغدد الليمفاوية

النتائج :-
تم معاينة 64 مريضا متتاليا مصاباً بالسل في الغدد الليمفاوية في هذه الدراسة المستقبلية 17 مريضاً أي 26.6% من الرجال و 47إناث أي 73.4 % تتراوح أعمارهم من 18 إلى 96 سنة بمتوسط عمري 40 سنة. بلغ عدد المرضى اللذين لديهم أعراض السل 33 أي مانسبته 51.6%. كان هنالك غالبية من النساء فبلغ نسبة النساء إلى الرجال 2.7% إلى 1% كما بينت الدراسات الأخرى. كان هنالك غدد متجمعه و أخرى ثابته عند 24 مريضاً أي مانسبته 37.5% بينما كانت الغدد متباعده عند بقية المرضى. لوحظ تشكل الخراجات والحمم الغدديه في 10.9% عند من لديهم غدد متجمعه و 7.8% ممن لديهم غدد متباعده.

الاستنتاجات :-

- يمكن زيادة محصلة أخذ عينات عن طريقة السحب بالابر بإجراء محاولتين ترسل أحداهما لفحص الأنسجة والأخرى للزراعة.
- كان لإعطاء جلسات قصيره من العلاج الكيماوي لمدة ستة أشهر أثر فعال وكان علاجاً مرضياً في حالات المرض مما دل عليه عدم حدوث انتكاسه حتى خمسة سنوات من المتابعه.

كلمات البحث: السل - الغدد الليمفاوية - العلاج الكيماوي

Abstract

Objectives

The aim of the study is to determine the incidence of peripheral tuberculeus lymphadenopathy in western region of Saudi Arabia, its clinical presentation, the diagnosis and the assessment of the value of short-term chemotherapy.

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Methods

A prospective study of 64 consecutive patients with proven tuberculous lymphadenopathy were included in this study, using FNA and / or lymph node excisional biopsy.

Results

Of the sixty-four patients included in the study, seventeen (26.6%) were males and 47 (73.4%) females. Their ages ranged from 18 to 96 years with a mean age of 40 years. The number of patients who presented with constitutional symptoms was 33(51.6%). There was a preponderance of females; the female to male ratio was 2.7:1, consistent with other studies. Matting and fixation of the nodes to the surrounding structures was present in 24(37.5%) patients, while the nodes were discrete in the rest. Among which discharging sinuses and abscesses were noted in 10.9% and 7.8% of the cases respectively.

Conclusions

The diagnostic yield of FNA can be augmented by performing two FNA attempts .One to be sent for cytopathological examination and the other for AFB smear examination and Mycobacterial culture. A short course of combined chemotherapy consisting of rifampicin (600 mg orally once daily), INH (10mg/ kg daily) and pyrazinamide (15 mg / kg) for 6 months and ethambutol (15mg / kg) for 2 months was an effective and satisfactory therapy in our patients, as proven by the lack of recurrence or relapse after 5 years of follow up.

Key words

Tuberculosis, Lymph nodes, Antimicrobial

Introduction

Tuberculosis is still causing a major health problem worldwide. Mycobacterium tuberculosis is estimated to infect 1.6 billion people worldwide, approximately one-third of the world's population.[1] The World Health Organization (WHO) had declared tuberculosis a global emergency, killing nearly 3 million people annually[2]. The annual incidence of active tuberculosis in Saudi Arabia is estimated to be 30 cases per 100,000 [3].

Lymphadenitis is the most common form of extra pulmonary tuberculosis and is among the most common causes of peripheral lymphadepathy in the developing world [4,5,6]. Tuberculous lymphadenitis typically presents as a painless and firm enlargement of the lymph node. The usual diagnostic tests are fine-needle aspiration (FNA) and/or excisional biopsy of a lymph node[7,8,9].

This prospective study was carried out to determine the incidence of peripheral lymph node tuberculosis in our area, its clinical presentation, diagnosis and to assess the value of short-term chemotherapy.

Materials And Methods

All the patients who attended the Surgical and other Outpatient Clinics of King Khalid National Guard Hospital as well as inpatients with peripheral lymphadenopathy over a 2-year period were enrolled in the study. Our hospital is a 400 bed tertiary care Medical Institution of the National Guard Health Affairs, serving the National Guardsmen and their dependants in the Western Region of the Kingdom of Saudi Arabia. The referral area of the hospital covers the western region of Saudi Arabia. All the patients included in this study had given full history and underwent a thorough physical examination, with particular attention given to peripheral lymph nodes examination. The group understudy underwent diagnostic workup, which included complete blood count, liver and renal function tests, ESR, Mantoux Test, chest radiograph, FNA and/ or lymph node excisional biopsy. Two attempts of fine needle aspiration (FNA) were carried out for every patient. The first one was to obtain 6 smears; 4 fixed in alcohol and 2 air dried. Two of the wet fixed slides were stained by H&E and the other two slides by PAP stain. One air-dried slide was stained by Giemsa. All were screened by a Cytotechnologist and reported by cytopathologist. The remaining one air-dried slide was sent to Microbiology Department for Ziehl-Neelsen staining. The second FNA attempt was performed to obtain material for microbiological investigations. The

Table- 1: Site of involved lymph node groups

Location	Frequency	Percent
Cervical	42	65.6
Axillary	5	7.8
Inguinal	3	4.7
Multiple sites	14	21.9
TOTAL	**64**	**100.0**

aspirate was injected into a liquid media (MB Bact Alert bottles) with an addition of antibiotic (prepared on request for the number of cases required) for culture and the residual material left in the needle was rinsed out with 100 ul of saline and sent in a sterile container to the Microbiology laboratory for a routine bacteriological culture.

In the Microbiology Department, the material from the lymph node was ground and subjected to microbiological and mycobacterial examination after suitable digestion and decontamination. The sediments were inoculated into Lowenstein-Jensen medium and BacT/Alert TB medium for the isolation and identification of Mycobacteria using a standard technique. In addition, routine culture was performed for pyogenic bacteria. Smears were made from the sediment, and stained with Ziehl-Neelsen (ZN) for AFB and Gram's stain for other bacteria. Mycobacterial isolates were confirmed as M. tuberculosis if positive by Ligase Chain Reaction (LCR). Isolates negative by LCR were regarded as Non-tuberculous Mycobacteria. Only the patients proven micro-biologically or cytopathologically as tuberculous lymphadenopathy were included in the study. Drug sensitivity tests were performed on culture-positive specimens, using the BacT/Alert liquid method.

Three early morning sputa were collected from each patient and submitted for ZN and Grams staining. The sputa were cultured on routine media for pyogenic bacteria as well as in a separate LJ media and BacT/Alert media for Mycobacteria. Standard Microbiological techniques were used for the identification of the isolates.

After confirmation of the diagnosis, all patients were given short-term chemotherapy consisting of rifampicin (600 mg orally once daily), INH (10mg/kg daily) and pyrazinamide (15 mg / kg) for 6 months and ethambutol (15mg / kg) for 2 months. All the drugs were taken as a single dose orally, preferably on an empty stomach, on an outpatient basis. Treatment was continued until the results of mycobacterial cultures were available.

Patients were assessed every month for the first 3 months and every third month thereafter, including a local and general examination ,determination of the ESR and haemoglobin concentration. The total follow up period was 5 years in order to detect any recurrence or drug toxicity.

Statistical analyses were performed using the SPSS 10 (Statistical Package for Social Sciences). Mean -+SD was determined for quantitative data, and frequency was determined for categorical variables. A logistic regression model using maximum likelihood estimates was used for multivariate analysis of clinical improvement predictors; the odds ratio and the Confidence Interval were also calculated. A P-value of <0.05 was considered significant.

Results

Of the sixty four patients included in the study, 17 (26.6%) were males and 47 (73.4%) females. Their ages ranged from 18 to 96 years with a mean of 40 years. The number of patients who presented with constitutional symptoms was 33(51.6%). All patients were of Saudi nationality. The distribution pattern the lymph node locations are shown in Table1. The cervical region was the most affected site 42 (65.6%). There was history of previous tuberculosis in 13 patients and 27 patients were of low socio-economic status while 37 were of middle socio-economic status.

The method of diagnosis in the 64 cases of tuberculous lymphadenitis was a positive FNA alone in 40 patients (62.5%), a positive excisional lymph node biopsy alone in 24 (37.5%). All sputum specimens were negative for AFB smears and/or culture for M. tuberculosis. The independent contribution of age and socioeconomic class on the clinical improvement of tuberculous lymphadenitis were analyzed as shown in (Table- 2) Firstly, a better prognosis was found among patients of younger age group. Those who were less than 40 years had a better prognosis by 4.43 folds compared to those who are older than 40 years, which could be as low as 1.313 or as high as 14.94 (95% CI), p=0.016. Secondly, a better prognosis was found to exist among the low socioeconomic class, who had a better prognosis by 3.708 times when compared to middle social class, which could be as low as

Table -2 :Factors affecting prognosis

Factor	P-value	odds ratio	Confidence Interval	
			Lower	Upper
Age	.016	4.430	1.313	14.943
Socioeconomic status	.034	3.708	1.104	12.462
Gender	.659	1.330	.375	4.710
History of tuberculosis	.269	2.248	.534	9.461
Constitutional symptoms	.199	2.116	.674	6.648
Multiple sites	.706	.768	.195	3.028
Complications	.866	1.105	.346	3.528
Constant	.070	.006		

1.104 or as high as 12.462 (95% CI), p=0.034.

The chemotherapy schedule used in our study included Isoniazed, Rifampicin for 6 months and Pyrazinamide, Ethambutol for 2 months. After six months of treatment, all the constitutional symptoms disappeared in all patients. The lymph nodes were either no longer palpable or reduced significantly in size as shown in (Table- 3).

Twelve patients had persistent lymph nodes, which were reduced in size of which six patients had persistent nodes at 1 year and 2 patients only presented to have palpable lymph nodes by the end of the second year.

Discussion

Tuberculous Lymphadenitis is the commonest form of extra pulmonary tuberculosis. It is among the commonest causes of peripheral lymphadenopathy in the developing world.[4,5,6] There was a preponderance of females (female/ male ratio of 2.7:1) as noted by other studies.[9,10] The most common site is the neck [7,8,9]. The most common location is along the upper border of the sterno-cleidomastoid muscle where it presents as a painless and firm mass growing over several months. Matting and fixation of the nodes to the surrounding structures was present in 24(37.5%) patients; while the nodes were discrete in the rest.[6,9] Discharging sinuses and abscess formations were noticed in 10.9 and 7.8 percent of all cases respectively.

Unlike what is described classically, constitutional symptoms like fever, weight loss, fatigue and malaise were present in only 33 (51.6%) patients while the others were asymptomatic, which has also been described by other authors.[6,11].

The majority of the cases (78 percent) presented within 3 months from the onset of illness. The ESR was raised in all but 4 cases and was a useful index during follow-up. The Mantoux test was positive in 51.6 percent of cases. Instead of excision of lymph nodes for histological and microbiological examination to confirm the diagnosis of mycobacterial lymphadenitis, fine needle aspiration cytology (FNA) has become an alternative easy procedure for collection of material for histological diagnosis and microbiological examination.[6,7].

We avoided the low yield FNA as in other studies,[9-12] by standardization of the procedure, performing 2 FNA attempts and also performing both AFB smear examination and culture on each FNA sample, resulting in a positive diagnosis in 40 (62.5%) without any complications.

The diagnosis of Mycobacterial lymphadenopathy by the pathologist depends on the histological assessment of granulomatous lesions and/or the detection of acid-fast bacilli (AFB). In most cases, the disease is suspected clinically and confirmed histologically. However, in some cases, histological changes may be equivocal or a search for AFB by Ziehl-Neelsen or fluorescent staining may be unfruitful, since its sensitivity depends on the number of organisms present.[13]

Culture remains the gold standard for the diagnosis of Mycobacterial infection as it allows for not only identification of the species of infecting Mycobacteria but also the determination of its drug susceptibility

Table- 3: Lymph Node Follow-Up

Status	Number	%
Disappear	46	81.2
↓ in size	12	18.8
Total	64	100

pattern.[6] . This is very crucial in view of the increasing number of multi-drug resistant M. tuberculosis strains are being reported worldwide. Biopsy of the largest node gave histopathological confirmation in all FNA negative cases 24(37.5%). Culture in Lowenstein-Jensen medium showed that 42(65.6%) were positive for Mycobacterium tuberculosis of human type.

Although culture of the gland in Lowenstein-Jensen medium confirmed the diagnosis in 65 percent cases in this study, a negative culture did not exclude the diagnosis, as all enlarged lymph nodes do not necessarily contain live bacilli [6,9] .

The factors predicting prognosis were age less than 40 years and low socio-economic class were found to carry a favorable prognostic outcomes, while on the other hand, other factors such as sex, history of tuberculosis, constitutional symptoms, multiple sites and presence of abscess or sinuses were not found to be of any prognostic value.

The main goal in the treatment of tuberculosis is to adopt the shortest effective course with minimum drug toxicity. Unlike pulmonary tuberculosis, the progress in chemotherapy seems to be slow in extra pulmonary tuberculosis, because of the difficulties in the diagnosis or in the assessment of response to the therapy. There are studies which showed that 9 months treatment was adequate for tuberculous lymphadenitis[9,11,14], but many other studies showed that 6 months with combination of antibiotics were enough [15-19]. After six months treatment all constitutional symptoms disappeared and the lymph nodes were no longer palpable or had decreased considerably in size (<5mm) as shown in (Table- 3). During follow up of the 12 patients in whom the lymph nodes did not disappear but decreased in size, only 6 persisted after 1 year and 2 of which remain after 2 year which is similar to the findings by Campbell [14] who found that after 5 years of follow-up, only 4% of patients had palpable residual nodes. Surgery, apart from an excisional biopsy, in any form was not used in the present series even in the presence of discharging sinuses or cold abscesses, where aspiration only was performed and most of these disappeared within 6 months of follow-up. No Toxic effects were seen in relation to any of the drugs used and to date we have not encountered any form of recurrence after 5 years of follow up, but 2 patients had persistent palpable lymph nodes, as has been encountered in similar studies.

In conclusions, the diagnostic yield of FNA can be augmented by performing 2 FNA attempts .One to be sent for cytopathological examination and the other for AFB smear examination and Mycobacterial culture. A short course of combined chemotherapy consisting of rifampicin (600 mg orally once daily), INH (10mg/kg daily) and pyrazinamide (15 mg / kg) for 6 months and ethambutol (15mg / kg) for 2 months was an effective and satisfactory therapy in our patients, as proven by the lack of recurrence or relapse after 5 years of follow up.

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