

Surgical Lymph Node Biopsy in the Diagnosis of Tuberculous Lymphadenopathy

الخرز الجراحية للعقد اللمفاوية في تشخيص تضخم العقد اللمفاوية التدرني

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Abstract:

Background: Lymphadenopathy is a common problem in medical practice. Tuberculous lymphadenitis is among the commonest causes of lymphadenopathy in the developing world.

Objectives: To describe the clinical presentations and the investigations for the diagnosis of lymphadenopathy. To study cases of tuberculous lymphadenitis with a view to determining the value of clinical and investigative diagnostic indices.

Materials & Methods: A prospective observational study was conducted to describe the clinical presentations and the pathological diagnoses resulting from (76) surgical lymph node biopsies in patients (44 male, 32 female) with enlarged lymph nodes admitted to Al-Yarmouk Teaching Hospital in Baghdad (during the period from 1st Jan. 2001 to 31st Dec. 2002).

Results: 30 patients out of 76 (39.4%) had Tuberculous Lymphadenitis, while 20 patients (26.3%) had Non-specific lymphadenitis, 12 patients (15.8%) had Lymphoma, 10 patients (13.1%) had Neoplastic metastases, and the rest 4 (5.4%) had other diagnoses like brucellosis & toxoplasmosis.

The epidemiological, clinical, and investigative results of 30 patients with tuberculous lymphadenopathy were analyzed. While cervical lymphadenopathy predominated (60%), the classical clinical features of tuberculous infection both local and general were frequently absent. Almost only third of the cases (33.33%) had a normal ESR (< 20mm/hr) and only (30%) had lymphocytosis. A clinical diagnosis of tuberculous lymphadenopathy was accordingly made in only (18) patients (60%).

Conclusion: This study emphasizes the need of a high index of diagnostic suspicion of tuberculosis when confronted with peripheral lymphadenopathy in developing countries, and the need of surgical LN biopsy in confirming the diagnosis.

الخلاصة :

خلفية البحث: تضخم العقد اللمفاوية المحيطية هو مشكلة شائعة في العمل الطبي، يعتبر تدرن العقد اللمفاوية من اهم الاسباب له في العالم النامي.

الاهداف: دراسة الصفات السريرية والفحوصات المجرأة لتشخيص مرضى تضخم العقد اللمفاوية.

طريقة البحث: تم دراسة الصفات السريرية والتشخيص النسيجي للعقد اللمفاوية لـ (76) مريضاً مصاب بتضخم العقد اللمفاوية في مستشفى اليرموك التعليمي في بغداد للفترة من 2001/1/1 لغاية 2002/12/31

النتائج: تبين أن (39.4%) منهم كانوا يعانون من تدرن العقد اللمفاوية بينما شكل التهاب العقد اللمفاوية غير المحدد (26.3%) اما ورم العقد اللمفاوية الابتدائي (اللمفوما) فكان (15.8%) والأورام الثانوية المنتشرة إلى العقد اللمفاوية (13.1%).

تبين أن معظم العقد اللمفاوية المصابة بالتدرن هي العقد الرقبية . كما لوحظ غياب الميزات السريرية التقليدية للتدرن في معظم المرضى سواء الموضعية أو الجهازية . تم ملاحظة أن معدل ترسيب كريات الدم الحمر E.S.R لم يرتفع في (33.33%) من المرضى المصابين بالتدرن كما أن (30%) من المرضى فقط لديهم زيادة في عدد كريات الدم البيض اللمفاوية (اللمفوسايت) . لذلك كان التشخيص السريري لتدرن العقد اللمفاوية مطابق مع الفحص النسيجي في (53,3%) فقط من المرضى المصابين.

الاستنتاجات: سلطت هذه الدراسة الضوء على الحاجة إلى توقع الأطباء للتدرن بشكل كبير لدى المرضى المصابين بتضخم العقد اللمفاوية كون التدرن من الأمراض المنتشرة في الدول النامية ومنها قطرنا العزيز . كذلك الحاجة الى الخرز الجراحية للعقد اللمفاوية لتثبيت التشخيص .

Introduction:

Tuberculosis is one of the most important infectious diseases in Iraq [1]. Several reports have alluded to the significance of tuberculosis in the developing world [2,3]. The early involvement of lymphatic system in the pathogenesis of tuberculosis is universally known [4]. Clinical

lymphadenopathy is accordingly a frequent feature of tuberculosis and publications from both western hemisphere [5, 6] and Iraq [7] rate as the commonest non-respiratory form of the disease. Surgical lymph node biopsy thus plays an important role in the diagnosis of tuberculosis. The importance of lymph node biopsy in the investigation of clinical lymphadenopathy in Iraq is high because of the prevalence of lymphoma and Tuberculosis in Iraq. The studies from western hemisphere proved that malignancies were the leading cause of lymphadenopathy [8], while in developing countries tuberculosis proved to be commonest cause of lymphadenopathy. This study reviews 76 cases subjected to surgical lymph node biopsy and further analysis of 30 patients in whom the histological findings were those of tuberculous lymphadenitis with a view to determining the value of clinical and investigative diagnostic indices.

Materials & Methods:

Seventy six cases had undergone excisional lymph node biopsy at Al-Yarmouk Teaching Hospital in Baghdad from 1st January, 2001 to 31st December 2002. The biopsy procedure involved the removal of one or more entire lymph nodes by surgical operation under general anesthesia. The histological findings in each case were analyzed. Thirty cases in which pathological diagnosis was tuberculosis were studied further. The age and sex distribution were determined. The clinical features and investigations results were reviewed with particular reference to the manifestations and diagnosis of tuberculosis.

Results:

There were 20 males and 10 females among the 30 patients with tuberculous lymphadenitis. The male: female ratio being 2:1, while in non- TB patients the ratio was nearly equal. The patients' ages ranged from 2 years to 51 years (The mean age being 29 years).

The age and sex distribution of the patients is depicted in Table 1.

Table 1:

A: Age and sex distribution of Tuberculous patients

Age	Males	Females	Total	%
2-20	2	2	4	13.3
21-40	14	6	20	66.7
41-60	4	2	6	20.0
Total	20	10	30	100

B: Age and sex distribution of Non-Tuberculous patients

Age	Males	Females	Total	%
2-20	4	8	12	26.08
21-40	10	6	16	34.78
41-60	10	8	18	39.14
Total	24	22	46	100

Thirty patients (39.4%) had tuberculous lymphadenitis, 12 patients (15.8%) had lymphoma, and 10 patients (13.1%) had metastatic tumour in lymph node. There were two cases of each toxoplasmosis and brucellosis. On 20 occasions (26.3%) the lymph node biopsy was helpful in that it excluded specific diseases and the histological features were Reactive Hyperplasia.

The histological diagnoses of 76 cases subjected to lymph node biopsy are recorded in Table 2.

Table 2: Histological diagnosis of lymph node biopsy

Histological diagnosis	No. of cases	Percentage
Tuberculosis	30	39.4 %
Non specific lymphadenitis	20	26.3 %
Lymphoma	12	15.8 %
Metastasis	10	13.1 %
Brucellosis	2	2.7 %
Toxoplasmosis	2	2.7 %
Total	76	100 %

The anatomical sites of the lymphadenopathy are catalogued in Table 3.

Cervical lymphadenopathy was predominant in tuberculous cases, being seen in 18 patients (60%). Most of them had unilateral disease, bilateral lymphadenopathy being seen in only five cases. In addition to cervical lymphadenopathy, the axillary nodes were enlarged in 4 patients and inguinal nodes in 2. All three regions (cervical, axillary, and inguinal) were involved in 3 cases. A Single case had only inguinal, and 2 had only axillary lymphadenopathy.

Table 3 : Anatomical sites of Tuberculous Lymphadenopathy

Sites of LN	No. of cases	Percentage
Cervical	18	60 %
Cervical and axillary	4	30 %
Cervical and inguinal	2	
Cervical, axillary and inguinal	3	
Axillary	2	10 %
Inguinal	1	
Total	30	100 %

Most of patients had more than one palpable enlarged lymph node at the site involved. The multiple nodes were however described as being matted on 15 occasions (50%). In 8 patients the enlarged nodes were specifically notes to be rubbery in consistency (26.6%). A clinical diagnosis of cold abscess was made in 5 cases. The scars of healed sinuses or ulcers were observed in two patients. The Characters of Lymph nodes in TB Cases are shown in Table 4

Table 4: The Characters of Lymph Nodes in TB Cases

	TB LAP	Percentage
Matted	15	50%
Rubbery	8	26.66%
Cold abscess	5	16.66%
Sinus or ulcers	2	6.66%
Total	30	100%

Table 5 shows the prevalence of general symptoms suggestive of tuberculosis such as weight loss, pyrexia, night sweats and cough in all TB & non-TB cases.

Table 5: General symptoms in cases of TB and non-TB lymphadenopathy

Symptoms	TB cases		Non-TB cases		All cases	
	No.	%	No.	%	No.	%
Fever	8	26.66	7	15.21	15	19.73
Weight loss	6	20.0	4	8.69	10	13.15
Night sweats	4	13.33	4	8.69	8	10.52
Cough	5	16.66	3	6.52	8	10.52
Total symptomatic	20	66.66	21	45.65	41	53.92
Total asymptomatic	10	33.33	25	54.35	35	46.08
Total	30	100	46	100	76	100

The known duration of lymphadenopathy was not more than 2 year in the majority of cases 80% , the shortest being a fortnight and in this group the mean duration was 5.5 months.

Only Two patients gave a family history of tuberculosis. No other patient admitted a contact history of the disease.

The results of some Laboratory Investigations done for TB and non-TB cases is shown in Table 6

Table 6: Laboratory Investigations of TB and non-TB cases

Table 6-A: Total White Blood Cells (WBC)

WBC	TB cases		Non-TB cases	
	No.	%	No.	%
Normal ($4-11 \times 10^3$)	12	40%	8	17.4%
$>11 \times 10^3$	14	46.66%	24	52.2%
$< 4 \times 10^3$	4	13.33%	14	30.4%
Total	30	100%	46	100%

Table 6-B: Erythrocyte sedimentation rate (ESR)

ESR	TB cases		Non-TB cases	
	No.	%	No.	%
$\leq 20\text{mm/hr}$	10	33.33	16	34.78%
21-40mm/hr	12	40%	11	23.91%
41-60mm/hr	6	20%	13	28.26%
$> 60\text{mm/hr}$	2	6.6%	6	13.04%
Total	30	100%	46	100%

The total white cell count of 30 patients ranged from $3.1-15 \times 10^3$ with a mean value of 6.17×10^3 . The differential count revealed a lymphocyte percentage greater than (35%) in 9 patients (30.0%). The range of lymphocyte percentage was (13-63%) and the mean was (34%). Four patients (5.2%) had a polymorphonuclear leukocytes percentage over (70%), the range for 30 patients being (24-78%) and the mean was (56%).The erythrocyte sedimentation rate (E.S.R.) in one hour was below 10mm in 8 out of 30 patients (20.66%) and above 60mm in 2 patients (6.6%), the highest rate being 80mm. The mean E.S.R. for tuberculous lymphadenopathy patients in this series was 25.5mm.Chest X-ray (CXR) was done for all patients; only 4 out of 30 patients (13.33) had evidence of pulmonary TB in their CXR.

Discussion:

Tuberculosis is still a major health problem in Iraq [9]. Lymphatic spread from the primary complex is an integral component of the pathogenesis of tuberculosis. Lymphadenopathy is consequently a characteristic feature of the disease and frequently comprises the only clinical manifestation of tuberculous infection[10].The total number of tuberculous lymphadenopathy recorded in Iraq was (632) cases in 2002 which represent (5.3%) of all recorded cases of tuberculosis. Chest and Respiratory Diseases Institute in Baghdad reported that peripheral lymphadenopathy accounted for (18.3%) of cases of extrapulmonary tuberculosis [11].This study has shown that tuberculous lymphadenopathy was the histological report on as much as (39.4%) of surgical lymph node biopsy. Lymphoma and metastatic malignancy were the pathological finding in (15.5%) and (13.8%) respectively. The study thus illustrated that while reticuloendothelial neoplasia and disseminated carcinoma compete with tuberculosis for the diagnostic decision in cases where lymphadenopathy dominates the clinical picture in Baghdad, tuberculosis maintains the foremost position whatever the age of the patient.This conclusion contrast with clinical experience in developed countries of the western hemisphere where as a rule: "any lymph node enlargement in an adult of more than 2 cm diameter is likely to be due to secondary spread from a malignant growth" [12], While in India 75% of lymphadenopathy was tuberculous [13,14]. In this study, Cervical TB Lymphadenopathy was predominant (60%) compared with other study in Saudi Arabia which revealed that Cervical TB Lymphadenopathy constituting (80%) of the involved sites[15].A high index of diagnostic suspicion with reference to tuberculosis must therefore be kept by the clinician in Iraq when dealt with cases of established lymphadenopathy. While this suspicion may be enhanced by other allegedly characteristic clinical features of tuberculosis and by the commonly expected results of investigative procedures relevant to the disease, the diagnostic decision must not be determined by their absence, as what is found in a study done in USA that constitutional symptoms were rare [16]. In this study as much as (46.08%) of patients had none of general symptoms supportive of a diagnosis of tuberculosis like : weight loss, low-grade fever, night sweats and chronic cough.Clinical teaching frequently emphasize, that tuberculous lymph nodes are typically: "matted" while "rubbery" consistency is described of lymphomatous lymphadenopathy, while in this study: matted node 50%, rubbery node 26.6%, cold abscess and sinus 23.4%.Almost a third of the cases had a normal ESR and in those in whom the rate was elevated the rise was usually moderate the mean value for the series being 25.5 mm/hr. The classically expected lymphocytosis in tuberculosis was seen in only (34%).Radiological evidence of pulmonary tuberculosis were present in only (13.3%) of Chest X-Ray of patients, as compared to (27%) of patients in Saudi Arabia [15].Tuberculine test and TB culture were not included in our study because of unavailability at the time of study, while Fine Needle Aspiration Cytology (FNAC) was not done because of its lower diagnostic yield as was seen in a study in Saudi Arabia which gave only (46%) positivity of FNAC [15].Although the prevalence of tuberculosis in developing countries is well known, a clinical diagnosis of tuberculosis was made in only (60% = 18 patients) of the patients in this study who were subsequently proven to have tuberculous lymphadenopathy by surgical biopsy.

Recommendations:

This study emphasizes the need for an increased awareness of the probability of tuberculous lymphadenopathy as a likely diagnosis in cases of chronic lymph nodes enlargement, despite the absence of general features of the disease and the lack of the expected results of standard investigative procedures.A high index of diagnostic suspicion and its prompt confirmation by lymph node biopsy would lead to early effective therapy and the reduction of the incidence of this debilitating disease thereby enhancing the development of those parts of the world where it is still prevalent.

References:

1. I.U.A.T. "International Union Against Tuberculosis". *Conference in Baghdad, 1979*.
2. Raviglione MC, Kochi A. "Global epidemiology of tuberculosis" *JAMA* 1995 ; 273 :220-226.
3. W.H.O. / *T.B.* / 1991 "First Program Report 1988-1991 and Future plan 1991-1995". 159: 2.
4. Seal ME : "The pathology of tuberculosis". *Br. J. Hosp. Med.* 1971: 783-792.
5. Enderson DA, Dorken E. "Non-respiratory tuberculosis in Canada" . *Am. J. Epidemiol* 1980 , 112 : 341-351.
6. Monie RD, Hunter A.M, Kilpatrick GS : "Management of extra-pulmonary tuberculosis in South and Wales". *Br. Med. J.* 1982, 285: 415-418.
7. Chest and respiratory Diseases Institute. "Tuberculosis Annual Report In Iraq, 2002".
8. Martin DA, James OA. "Clinical oncology". 2nd ed. London (UK): *Chruchill Livingstone Inc.*, 2000 , P. 2620-2629.
9. Al-Khamese A.S. "T.B. in children", *Iraq Med.* 1982 ; 30 : 9.
10. Innes JA: "Non respiratory tuberculosis". *Medicine International* 1984, 2: 209- 213.
11. Ibrahim M: "*Cervical lymph node biopsy*", *Saudi Med. Journal.* 2002, 23:1291-1292.
12. Cady B: "*Evaluation of neck mass*". *North Am.* 1970 ; 50 : 559-566.
13. Bowling MC. "Lymph node specimens": *Achieving technical excellence laboratory Med* 1979; 10 : 457-476.
14. Kissane M. Gephardt GN. "Lymphadenopathy in childhood" *Hum. Pathol.* 1974; 5:431-439 .
15. Memish ZA et al "Clinico-diagnostic experience with tuberculous lymphadenitis in Saudi Arabia": *Clin Microbiol Infect.* 2000 Mar;6(3):137-41.
16. Artenstein AW et al "Isolated peripheral tuberculous lymphadenitis in adults: current clinical and diagnostic issues": *Clin Infect Dis.* 1995 Apr;20(4):876-82.