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Approach to lymphadenopathy: how to diagnose tuberculosis lymphadenitis

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Abstract: *lymphadenopathy is considered as abnormal finding local or generalized that can be caused by neoplasm or infection, as tuberculosis lymphadenitis. Cervical localization has prevalence in the variety of disorders, can has a similar kind of clinical presentation and to differentiate them becomes extremely difficult. We provided a case report of the new onset of extrapulmonary tuberculosis lymphadenitis in 42-year-old Indian man. The patient complained of multiply enlarged painful lymph nodes on left anterior neck and was also concerned about sore throat persistent for a year. Objective examination and analysis were without evident inflammatory signs. Previous ultrasound, pulmonary and abdominal CT-scan investigations also revealed conglomerate of left mediastinal lymph nodes, moderate splenomegaly. The preliminary diagnosis of lymphoma was excluded due to confirmation of typical tuberculosis lymphadenitis with specific testing and morphological changes of the resected lymphatic node. Sputum microscopy was found to be negative, which meant that the patient was negative for social transmission of tuberculosis. Affected lymph nodes resolved completely after appropriate therapy during one-year treatment. This case report of extrapulmonary tuberculosis highlights the importance of tissue diagnosis in unclear situations. We used clinical protocol for unspecified lymph node enlargement as complete history taking and physical examination that is preliminary for diagnosis, while laboratory tests, imaging diagnostic methods and tissue samplings are gold standard evaluation for definite lymphadenopathy. Tuberculosis lymphadenitis is popularly known as collar stud abscess and is the most common benign cause of cervical lymphadenopathy in endemic areas. This observation determined the details of the immunocompromised state of the patient, conclusion was supported by the evidence of Pseudomonas putida associated pharyngitis. The main differential signs between lymphoma as immunoproliferative disorder and infectious tuberculosis lymphadenitis were provided.*

Key words: Lymphadenopathy, Tuberculosis, Lymph Node, Lymphadenitis, Lymphoma.

Introduction

It is well-known that usual local increase in cervical lymphatic nodes (LN) is a consequence of infections of the upper respiratory tract, nasopharynx, infectious mononucleosis, tuberculosis as well as also necessary to exclude both lymphoproliferative tumors (lymphomas) and metastases in the LN of tumors of different localization (head and neck, lungs, mammary and thyroid glands) (Freeman, & Matto, 2020).

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Aim

To show peculiarities of tuberculosis lymphadenitis diagnosis, to analyze the cause of misdiagnosis and to point out the details of immunocompromised state of the patient.

Case report

The 42-years old patient from India asked for general physician's appointment in private clinic in Kyiv. He complained of multiply enlarged painful LN on left anterior neck for almost two weeks and was also concerned about sore throat persistent for a year. He stopped smoking two years ago, consumes alcohol socially, his living condition and job were satisfactory. He didn't have any drug allergy, without surgeries or injuries, his family history was unremarkable. He had malaria in childhood and spine spondylosis previously which was well controlled by exercise.

After confirming lymphadenopathy (LAP) in a cervical area, we examined all the LN accessible for palpation:1) location: anterior neck LN involved in the process 2) texture and tenderness: soft painful LN, even fluctuant that suggested progressive enlargement, typical for acute inflammation 3) mobility of the LN relative to the skin and surrounding tissues: fixed LN and conglomerates of the LN are found in patients with chronic inflammation or with malignancy, that have to be determinate.

Other objective examination was without evident inflammatory signs as cough, fever, chills, night sweats, weight loss and fatigue. While reviewing the latest tests results it was excluded the preliminary diagnosis of lymphoma against TB infection, therefore the further diagnostic work up consistent of: TB cito testing, HIV elisa test, TB quantiferon test, Genetic test for TB, Gene Xpert MTB/RIF test, anterior neck LN biopsy, TB microscopy of the resected LN, culture and sensitivity of the resected LN. We provided the main objective patient's results concerning of obvious diagnosis in that case report: The new onset extrapulmonary tuberculosis of lymphatic nodes (Table 1).

Discussion

TB is one of the most widespread systemic bacterial infectious diseases worldwide. The frequency of TB in underdeveloped nations is believed to coexist with poor hygiene environment. TB chiefly affects the pulmonary system besides involving extrapulmonary locations comprising head and neck region, occurring in 0.05-5% of the patients with acquired immunodeficiency syndrome (Brown, & Skarin, 2004). The disease can begin acutely, with fever and severe intoxication, and the inflammatory process can spread from the LN to the subcutaneous tissue and skin. Chronic TB of the external LN is manifested by soft dense nodules, sometimes a chain of small nodules. One group of LN is affected more often: the cervical and submandibular LN diagnosed in children and adolescents, less often - in adults and the elderly, the axillary ones extremely rare as well as other localization. Tuberculous lymphadenitis is popularly known as collar stud abscess due to its proximity to the collar bone and its superficial resemblance to a collar stud, although this is just one of the five stages (Weinstock et al. 2018). The diagnosis consists of anamnesis (contact with patients with TB, pulmonary involvement and other organs, scars on the neck, eye diseases), objective data, tuberculin testing (sharply positive), detection of Mycobacterium tuberculosis in pus, punctate, cytological examination of punctures and histological analysis a biopsy for the diagnosis confirmation. The outcome of the disease depends on the timeliness of diagnosis, the form of LAP and the effectiveness of treatment. At a favorable course there are reduction and consolidation of the LN (sometimes with the subsequent petrification's formation in them), fistulas are closed. Drainage do not provide according to the effect from anti-tuberculosis medications: isoniazid, rifampicin, pyrazinamide, ethambutol. In our case due to appropriate treatment for almost 12 months the patient completely recovered, at regular follow-up visit one year later LN were not detected.

It is known, that seventy-five percent of all LAPs are localized, with more than 50% being seen in the head and neck area (Brown, & Skarin, 2004). Cervical LN are involved more often than the other lymphatic regions. Based on different geographical areas, the etiology is various, and TB is the main benign cause of LAP in adults and children in tropical areas. For the adequate diagnosis, the affected enlarged LN ≥1 cm in adults should be examined completely. Previous ultrasound, pulmonary & abdominal CT-scan

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Table 1. Objective patient's results and their assessment

Objective	Data	Results assessment
Vital Signs Unremarkable	BP: 107/64 mm Hg PR= 70 RR=17 per/min SPO2=96%, T – 36,9°C, BMI = 19 kg/m^2	Appears healthy and responds appropriately throughout the exam. Lungs were clear for auscultation and percussion. Cardiac regular rhythm, S1 and S2, no murmur. Abdomen soft, non-tender in palpation. Negative Pasternatsky sign. No neurological deficit
CBC+ESR, Creatinine, BUN	Within normal range	Lymphoma? is doubtful
CRP	Elevated	Sign of inflammation
Pulmonary CT	Proliferative conglomerate of the left mediastinal lymph nodes	Sign of lymphadenopathy
Abdominal CT	Moderate splenomegaly	Malaria in childhood
HIV Elisa Test	Negative	Absence of HIV
TB Cito test	Indeterminate, more positive than negative	Suspicious
TB Quantiferon test	Positive	NIL (the control test) =0.12 IU/ml Referent range <8.0 TB1-antigen (CD4+) =0.68*IU/Ml Ref.range <0.35 TB2-antigen (CD8+) =0.56*IU/ml Ref.range <0.35 Mitogen=5.03*IU/ml Ref.range <0.5
Anterior neck lymph biopsy	Pus, excised specimens: LN with thickened capsule, infiltrated by coalescent epithelioid histiocytic granuloma with areas of central caseous necrosis – "cottage cheese" consistency.	Morphological pattern responds to chronic necrotizing granulomatous lymphadenitis of TB etiology Positive (+++)
Resistance to Rifampicin	Negative	Sensitivity to treatment
Gene Xpert MTB/ RIF test	G+/R-	Gene for MBT was positive Resistant to Rifampicin – neg
2 TB Sputum microscopies	Negative	Negative for social transmission of TB
Treatment prescribed	Rifampicin 600mg Ethambutol – 1200 mg Isoniazid – 300 mg Pyrazinamide – 1500 mg	Follow-up visit after one-year treatment reveals an inactive extrapulmonary TB of lymph nodes, LN were not detected

investigations in our case revealed the proliferative conglomerate of left mediastinal LN, visceral and retro-visceral LAP and moderate splenomegaly that were very suspicious for general pathological involvement (Freeman, & Matto, 2020). Patient was also concerned about his sore throat persistent for a year. The throat was erythematous, without exudates, oral mucosa was dry. There was revealed of Pseudomonas putida associated chronic pharyngitis in patient's case without definite complaints: is an uncommon cause of skin and soft tissue infections that is often associated with trauma or immunocompromised state. LN that are inaccessible to physical examination (mediastinal and retroperitoneal) can be assessed using imaging studies (radiography, ultrasonography, CT, PET-CT, MRI, scintigraphy). In equivocal cases histologic examination of the LN is necessary and

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achieved through biopsy or excisional removal. Tissue diagnosis by fine needle aspiration biopsy or excisional biopsy is the gold standard evaluation (Brown, & Skarin, 2004; Freeman, & Matto, 2020).

The preliminary diagnosis of lymphoma in our case was excluded due to the confirmation of typical TB LAP with specific testing and morphological changes of the resected LN. Since lymphoma is cell-mediated immunodeficiency, it may result in infections with several pathogens, such as Mycobacterium species and the presence of these pathogens can precede lymphoma or even can contribute to its development (Centkowski et al. 2005). In lymphoma affected LN have a dense-elastic consistency, not fused with the skin, painless: supraclavicular and mediastinal LN are the most often affected. Thus, the main differences between suspicious LAP are (Table 2):

Table 2. Differential diagnosis between lymphoma and lymphadenitis

Lymphadenitis	Lymphoma
Surrounding inflammation	Sharply delineated
Heterogeneous structure of LN	Homogeneous disruption of LN
Central Liquefaction	Hypoechogenic on Ultrasound
Unilateral, often one level only	Several levels involvement
Tender/mobile LN	Non-tender/ non-mobile LN
Young age, adolescent	Adults, elderly persons
Favorable prognosis	Less favorable prognosis

Conclusion

Tuberculosis is still wide-spread in endemic areas, undeveloped countries, its extrapulmonary occurrence is often missed. Misdiagnosis or delay in diagnosis of TB and immunodeficiency patterns may occur because of similar signs and symptoms, such as fever, cough, loss of appetite, loss of weight, night sweats, hepatosplenomegaly and mediastinal lymphadenopathy. History of prior TB infection, residence in a country where TB is endemic, close contact with a TB patient, or positive tuberculin skin test should raise suspicion of extrapulmonary TB. Fine needle aspiration with polymerase chain reaction or culture may accurately identify cervical TB lymphadenitis as well as excisional biopsy. This case report highlights the risk of misdiagnosis of generalized lymphadenopathy and determinate the details of immunocompromised state of predisposed patient from endemic area.

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Conflict of interest

There is no potential conflict of interests.

Consent to publication

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Підхід до лімфаденопатії: як діагностувати туберкульозний лімфаденіт

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Анотація: *лімфаденопатія розглядається як патологія місцевого або генералізованого характеру, що може бути спричинена новоутворенням або інфекцією, як туберкульозний лімфаденіт. Шийна локалізація переважає при різноманітних захворюваннях, може мати схожу клінічну картину і диференціювати їх стає вкрай важко. Ми представляємо випадок позалегеневого туберкульозного лімфаденіту у 42-річного індійця. Хворий скаржився на багаторазово збільшені болючі лімфовузли на шиї зліва, а також турбував біль у горлі, що не зникав протягом року. При об'єктивному огляді та загальних аналізах виражених ознак запального процесу не виявлено. При попередньому УЗД, комп'ютерній томографії легенів та черевної порожнини виявлено проліферативний конгломерат лімфатичних вузлів середостіння зліва, помірну спленомегалію. Попередній діагноз лімфоми виключено у зв'язку з підтвердженням типового туберкульозного лімфаденіту специфічним дослідженням та морфологічними змінами видаленого лімфатичного вузла. Мікроскопія харкотиння виявилася негативною, що означало, що хворий не був схильним до соціального поширення туберкульозу. Уражені лімфатичні вузли повністю розсмоктались після відповідної терапії протягом року лікування. Цей випадок позалегеневого туберкульозу підкреслює важливість діагностики тканин у незрозумілих ситуаціях. Ми застосували клінічний протокол при неуточненому збільшенні лімфатичних вузлів, оскільки повний збір анамнезу та фізикальне обстеження є попередніми для діагностики, тоді як лабораторні тести, візуалізаційні діагностичні методи та зразки тканин є золотим стандартом оцінки для точної лімфаденопатії. Туберкульозний лімфаденіт у народі відомий як абсцес шиї високого комірця і є найпоширенішою доброякісною причиною шийної лімфаденопатії в ендемічних регіонах. Подальше спостереження визначило деталі імунодефіцитного стану пацієнта, висновок підтверджено фарингітом, асоційованого з Pseudomonas putida. Наведено основні диференційні ознаки між лімфомою як імунопроліферативним захворюванням та інфекційним туберкульозним лімфаденітом.*

Ключові слова: лімфатичні вузли, лімфаденопатія, лімфаденіт, лімфома, туберкульоз.