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REVIEW

Ultrasound-guided core biopsy in the diagnostic work-up of tuberculous lymphadenitis in Saudi Arabia, refining the diagnostic approach. Case series and review of literature

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Summary
Objective: Tuberculous cervical lymphadenitis is the most common presentation of extrapulmonary tuberculosis (TB) in Saudi Arabia and worldwide. Obtaining a tissue biopsy for culture and histopathology is frequently needed to establish the diagnosis. The available diagnostic tools include excisional surgical biopsy, fine needle aspiration (FNA) and ultrasound-guided core lymph node biopsy. We present a single center experience of the use of ultrasound-guided core lymph node biopsy as a diagnostic tool for tuberculous lymphadenitis.

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Methods: A retrospective review of the interventional radiology database for all of the patients with cervical lymphadenopathy undergoing ultrasound-guided core biopsy at King Abdulaziz Medical City-Riyadh, Saudi Arabia from January 1 2008 to December 30 2011. The data were the patient demographics, clinical characteristics, biopsy method and pathological and clinical diagnoses.
Results: Five cases underwent ultrasound-guided cervical lymph node biopsy during the study period. A total of 55 cases underwent excisional cervical lymph node biopsy in the same period. The age of the patients who underwent the core biopsy ranged from 18 to 76 years old. All of the biopsies were performed as one-day surgery, and all of the patients were discharged on the same day with no complications. The final diagnosis was confirmed in all of the cases (100%); with tuberculosis being the diagnosis in four of the five cases (80%), and one case being diagnosed as lymphoma.
Conclusion: Ultrasound-guided core biopsy is an underutilized procedure in our hospital and could be a very valuable asset in the diagnostic algorithm of tuberculous lymphadenitis in Saudi Arabia. The widespread use of the procedure would positively affect patient care, providing earlier diagnosis and treatment.

Contents

Background

Tuberculosis is a leading cause of death globally among immunocompromised and immunocompetent patients [1]. In Saudi Arabia, tuberculosis remains a major health burden [2]. The factors aggravating the magnitude of the problem include the influx of large number of laborers and pilgrims, poor compliance with therapy and delay in diagnosis [3,4].

Globally, including in Saudi Arabia, tuberculous cervical lymphadenitis is the most common presentation of extrapulmonary tuberculosis [5—7]. Despite being a common presentation, mycobacterial cervical lymphadenitis remains a diagnostic challenge because it mimics other disease presentations including solid malignancy, lymphoma, connective tissue disease and other infections such as brucellosis. The available diagnostic tools include excisional surgical biopsy, fine needle lymph node aspiration and ultrasound-guided core lymph node biopsy [8—11]. The former is considered the gold standard diagnostic tool; however, it might not always be feasible and is increasingly being replaced by less-invasive techniques [12].

Ultrasound-guided core needle biopsy is increasingly being used as a diagnostic tool for evaluating malignant and non-malignant lymphadenopathy [13—16]. It provides a larger tissue sample that retains its architecture and permits the use of a range of histochemical and immuno-histochemical stains. The experience with this diagnostic tool in the diagnosis of tuberculous lymphadenitis in Saudi Arabia is very limited. We present our center's experience with cases of cervical lymphadenopathy that were ultimately diagnosed as tuberculous lymphadenitis using ultrasound-guided core lymph node biopsy. We propose that this approach be routinely used in the diagnosis of cervical lymphadenopathy in Saudi Arabia. The required skills could be taught to physicians in peripheral hospitals, minimizing the need for excisional biopsy and ultimately expediting the diagnosis and treatment of these patients.

Table 1 Summary of cases.

Case	Age	Gender	Presentation	Quantiferon TB gold	Pathology	AFB stain	PCR	Culture
1	18	F	Non-painful right-sided neck swelling for 2 weeks; no fever; no night sweats	Not Done	Chronic necrotizing granuloma with caseation	Negative	Not done	Positive
2	19	M	Right-sided neck swelling for 4 weeks; low grade fever and night sweats	Negative	Lymphoma	Not done	Not done	Negative
3	26	F	Bilateral neck swelling; no fever no night sweats; no weight loss	Positive	Chronic necrotizing granulomatous inflammation with caseation	Negative	Not done	Positive
4	64	F	Three months of left neck swelling	Indeterminate	Focally necrotizing granulomatous lymphadenitis	Negative	Positive	Positive
5	76	M	Right submandibular swelling for one month; night sweats and weight loss	Positive	Necrotizing granulaoma	Positive	Positive	Positive

Materials and methods

This study is a retrospective review of the surgical, pathology and invasive radiology database for a number of cervical lymph node biopsies performed as open surgical excisional biopsy or core ultrasound-guided biopsies from January 2008 to December 2011. For the patients undergoing ultrasound-guided biopsy, we gathered information regarding the demographics, clinical characteristics at presentation and final pathological and clinical diagnoses. We collected information about the length of stay and complications post ultrasound-guided core biopsies.

Results

A total of 55 cases underwent excisional cervical lymph node biopsy between January 1 2008 and December 30 2011. Of these, only five cases underwent ultrasound-guided cervical lymph node biopsy.

For the ultrasound-guided core biopsy, a definitive diagnosis was achieved in 100% of the cases. Extrapulmonary tuberculosis was diagnosed in four cases, and one diagnosis was of lymphoma. All of these procedures were performed as one-day surgery (outpatient clinic), and all of the patients were discharged 2 h post procedure with no complications. A summary of the five cases is presented in Table 1.

Discussion

A delay in the diagnosis of tuberculosis is a major obstacle to tuberculosis control programs and might contribute to a worse outcome and increased transmission in the community in cases of pulmonary tuberculosis [17—19]. Late presentation, a low index of suspicion, the lack of appropriate diagnostic tools, and the absence or ineffectiveness of tuberculosis prevention programs are factors that might contribute to a diagnosis delay and worse outcome [18].

The mean delay duration between the onset of symptoms and the treatment of pulmonary tuberculosis ranged from 46 days in Iraq to 127 days in the Islamic Republic of Iran [18]. Although most of the data on the delay of diagnosis and treatment focus on pulmonary tuberculosis, similar findings are expected for extrapulmonary TB. A delay in the diagnosis of tuberculous cervical lymphadenitis would be expected to be less related to a patient's late presentation and more related to a lack of availability of simple and reliable diagnostic tools [18].

Historically, excisional biopsy has been the gold standard diagnostic tool in tuberculous lymphadenitis. It permits adequate histopathological examination and provides an adequate sample for culture and nucleic acid amplification tests. Excisional open lymph node biopsy is invasive and painful, and it requires hospital admission or at least one-day surgery admission, an operating room, surgeon and anesthetist, all of which might be unavailable, particularly at peripheral hospitals. All of these procedures ultimately delay diagnosis and treatment. Fine needle aspiration cytology (FNAC) has emerged as an accepted part of the investigation logarithm in the diagnosis of tuberculous lymphadenitis [8—12], and the procedure could be performed by non-physicians. Blind FNAC might result in false-negative diagnoses and could further delay the disease management. The fine biopsy procedure is not acceptable for the diagnosis of lymphoma, in which core biopsies are needed [20]. In studies involving multiple sites, AFB positivity by Ziehl-Neelsen staining or fluorochrome staining ranges from 23% to 45%, with an average of 35.5% [21]. The positive rate of mycobacterium culture from FNA material ranges from 20.8% to 83%, with an average of 57.6% [21]. The correlation between open biopsy and fine needle aspiration varies; it is generally between 78% and 97% for all lymphadenopathy cases. FNAC performed under ultrasound guidance marginally increases the diagnostic accuracy for tuberculosis; however, it will not increase the yield of lymphoma diagnosis.

In the published data from Saudi Arabia, the utilization and yield of FNAC in the diagnosis of tuberculous lymphadenitis varies between centers; the average ranges of utilization are 8—70%, and the yield for specific diagnosis is 46—97% [22—24]. The factors that might be associated with lower yield were not mentioned in these studies, however, they might include paucibacillary disease, adequacy of the sample provided and the experience of the pathologist.

Ultrasound-guided core biopsy is an alternative diagnostic tool that is increasingly being used in medical practice to diagnose cervical masses. It offers logistic advantages over other procedures because it is performed under local anesthesia in outpatient clinics and results in fewer complications and increased patient satisfaction. It has a high diagnostic accuracy, and it technically provides a larger tissue sample that retains its architecture and permits the use of a range of histochemical and immunohistochemical stains. Compared

with FNA in the diagnostic work-up of malignancies, it has a lower rate of false-positive and false-negative results in biopsy-proven specimens; inadequate sampling is more often encountered with FNAC, particularly when the submitted specimens are sampled by physicians lacking experience with the FNAC procedure [25]. FNAC requires the presence of experienced cytologists and the immediate assessment of the adequacy of the material at the bedside to determine whether additional aspirations are needed, which is frequently not logistically possible.

Kim et al. retrospectively evaluated the efficacy of ultrasound-guided core needle biopsy for the diagnosis of cervical lymphadenopathy in patients without a known malignancy [26]. In their series of 155 patients, of whom 37 had tuberculous lymphadenitis, the sensitivity, specificity and accuracy of ultrasound-guided core biopsy were 97%, 99% and 97.9%, respectively. The procedure had equal accuracy and safety in other diagnostic challenges such as lymphoma [27]. McAllister et al. recently compared FNA, core biopsy and excisional biopsy in the diagnosis of neck tuberculosis. He found that FNA had a significantly lower sensitivity compared to core and excisional biopsies. There was no statistically significant difference between the sensitivities of core biopsy and excisional biopsy [28].

Ultrasonography is inexpensive and requires almost no investment in the infrastructure. It requires relatively inexpensive equipment, and its use is easily understandable; the development of small, multifunctional portable US systems has helped ensure that the method has increased interdisciplinary utilizations. A better understanding of the specific clinical context of a patient might better qualify other clinical specialists in the performance and understanding of ultrasound studies compared to radiologists. More than 50% of ultrasound examinations worldwide are performed by clinical specialists rather than by radiologists or radiographers [29]. Percutaneous biopsies performed by non-radiologists at many anatomical sites constituted approximately 45% of all of the procedures, with general surgeons and pulmonologists leading the non-radiology clinical subspecialties.

Ultrasound-guided biopsy has not been well documented for use in Saudi hospitals as a diagnostic tool for extrapulmonary tuberculosis. This study clearly demonstrated the under-utilization of this procedure in our hospital because only five of 55 9% patients underwent ultrasound-guided core biopsy. The underutilization of this convenient and simple-to-operate tool is not justified because of the demonstrated efficacy of these procedures. Ultrasonography is inexpensive, and almost no investment in the infrastructure is needed. It requires little training, and the procedures are easy to perform and delay in the diagnosis of the patient is avoided with the procedure.

We recommend a change in our practice regarding the diagnostic approach of cervical lymphadenopathy and suggest that we should use it as a first step to obtain a definitive tissue biopsy and avoid using more invasive and costlier procedures such excisional biopsy. Ultrasound-guided core biopsy is safe and is more likely to aid in the establishment of a diagnosis.

We hypothesize that ultrasound-guided core biopsy could be a markedly valuable asset in the diagnostic algorithm of tuberculous lymphadenitis in Saudi Arabia and that the widespread use of the procedure will positively affect patient care, providing earlier diagnosis and treatment. Structural efforts to train physicians managing patients with cervical lymphadenitis, including surgeons, internists and family physicians, would significantly reduce the need for more invasive surgical procedures.

Conflicts of interest

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