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Fine needle aspiration cytology findings in cases diagnosed as oropharyngeal tularemia lymphadenitis

Orofaringeal tularemi lenfadeniti tanısı alan olgularda ince iğne aspirasyon sitolojisi bulguları

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ABSTRACT

Francisella tularensis is a gram-negative coccobacilus that causes zoonotic disease tularemia. Histopathological examination of lymph node biopsy in tularemia reveals suppurative granulomatous inflammation potentially associated caseous necrosis. Diagnosis is mainly made on the evidence of elevated agglutinating antibodies against F. Tularensis. In this study we aimed to evaluate the cytological features of ulceroglandular tularemia cases and to demonstrate the role of fine needle aspiration cytology in the diagnosis of tularemia.

Fine needle aspiration cytology findings of six cervical lymphadenopaties that had established diagnoses of tularemia both clinically and serologically, were evaluated and the cytomorphological features were described.

All of the cases revealed suppurative inflammation and some caseous necrosis and in four cases epithelioid histiocytes and multinuclear giant cells were observed additionally.

The differential diagnosis of tularemia principally from tuberculosis and other types of bacterial lymphadenitis was made and the place of fine needle aspiration cytology among other diagnostic laboratory tests for tularemia was evaluated.

Key words: Tularemia, fine needle aspiration, cytology

ÖZET

Tularemi gram negatif kokobasil olan Francisella tularensis'in etken olduğu zoonal bir hastalıktır. Histopatolojik olarak lenf nodu biyopsisinde tulareminin yol açtığı değişiklikler genel olarak kazeifikasyon nekrozu ile birlikte seyredebilen granülomatöz pürülan lenfadenit şeklinde gözlenmektedir. Tularemi tanısı esas olarak klinik bulguları destekleyen Francisella tularensis'e karşı aglütinasyon gösteren antikorların yüksek seviyelerinin gösterilmesi ile konmaktadır. Bu çalışmada ise serolojik olarak orofaringeal tularemi tanısı alan olguların ince iğne aspirasyon sitolojisi materyallerindeki sitolojik özellikler gözden geçirilerek tularemi tanısında iğne aspirasyonunun değerinin ortaya konulması amaçlandı.

Klinik ve serolojik olarak tularemi tanısı alan altı hastanın servikal lenf nodu ince iğne aspirasyon sitolojisi sonuçları değerlendirilmiş ve sitomorfolojik özellikleri tanımlanmıştır.

Altı olgunun tamamında süpüratif inflamasyon bulguları yanı sıra kazeifikasyon nekrozu gözlenirken, ayrıca dördünde epiteloid histiyositler ve multinükleer dev hücreler izlendi.

Bu bulgular ile klinik ve histopatolojik olarak başta tüberküloz olmak üzere granülomatöz hastalıklar ve diğer bakteriyel lenfadenitler ile ayırıcı tanı yapılmış, ince iğne aspirasyon sitolojisinin tularemi tanısındaki laboratuvar tanı yöntemleri arasındaki yeri değerlendirilmiştir.

Anahtar sözcükler: Tularemi, ince iğne aspirasyonu, sitoloji

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INTRODUCTION

Francisella tularensis is a gram-negative coccobacillus that causes zoonotic disease, tularemia and it was first demonstrated as a plaque-like disease of rodents in Tulare County, California, by McCoy (1-3). This zoonotic bacterium is carried both with arthropod vectors, and wild and domestic animals (particularly with cats that have eaten infected rodents or rabbits). Transmission through water contaminated by infected rodents has also occurred (1,4).

Clinical features of the disease depend on the source of inoculation. Six clinical forms have been recognized: ulceroglandular, oculoglandular, lymphadenoid, typhoidal, oropharygeal and pulmonic (3).

Clinical diagnosis of tularemia is difficult to make, as symptoms are nonspecific and often initially resemble influenza or other respiratory tract infections. Laboratory diagnosis is also problematic. Serologic studies (including ELISA and agglutination assays) are the most commonly employed diagnostic methods. Immunohistochemical studies, fluorescent antigen testing and immunoelectron microscopic examination have also been used to detect *Francisella tularensis* (1,4,5).

Tularemia is an emerging disease in Turkey with the outbreaks during last years (6-7). Endemic and sporadic tularemia cases were seen predominantly in Marmara and Western Black Sea region and also in Zonguldak province in 2004 and 2005 (8-11).

In this study we aimed to detect the cytological features of ulceroglandular tularemia cases diagnosed by serological methods and to demonstrate the role of fine needle aspiration cytology in the diagnosis of tularemia.

MATERIALS and METHODS

We reviewed cytologic, histologic and clinical features of six cases with a serologically established diagnosis of tularemia. In each case fine needle aspiration cytology was performed using 23-25 Gauge needles. Also in two cases the palpable lymph nodes were surgically excised. A portion of the smears were air-dried and stained with Giemsa, while the remaining smears were wet-fixed with alcohol and subsequently stained by hematoxylin-eosin. In two cases histochemical Ziehl-Neelsen staining for acid fast bacilli was also performed.

RESULTS

The age of our 4 female and 2 male patients ranged from 16 to 64 years. All of the patients presented with a soft to firm cervical masses varied between 4 to 10 cm in diameter and they were associated with fever (38-40°C), generalized body aches, often prominent in the lower back and sore throat. Three patients had a history of close relation with rodents. Serologically their serum agglutinating antibodies against *F. tularensis* were diagnostic for tularemia and their titers ranged between 1:320 and 1:2560.

Grossly all aspirated materials were purulent. All smears showed an abscess-like image with multiple neutrophils, macrophages, necrotic materials and also amorphous basophilic material consisted of caseification necrosis (Figure

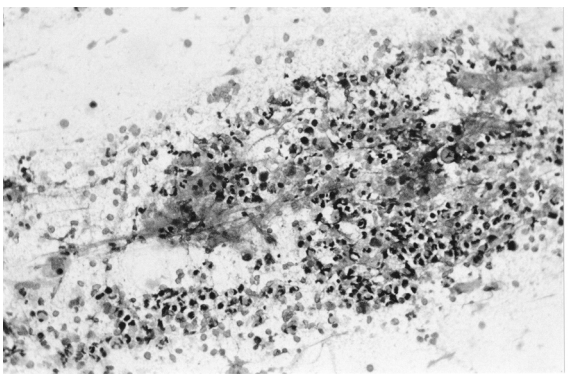

Figure 1. Suppurative inflammation and abcess formation (HE x40).

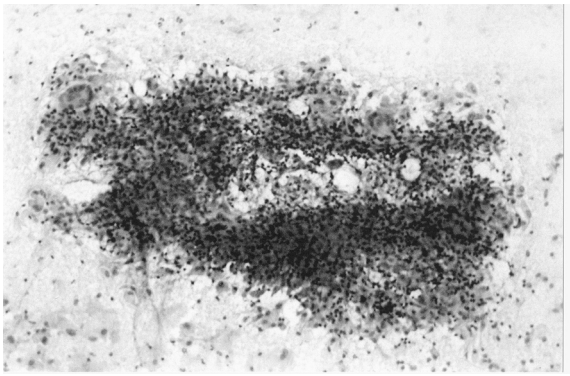

Figure 2. Granulomatous inflammation in the cytological material (Giemsa's stain x10).

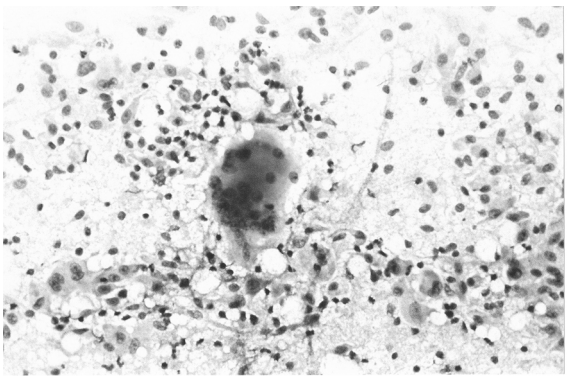

Figure 3. A multinuclear giant cell with an amphophilic cytoplasm (HE x100).

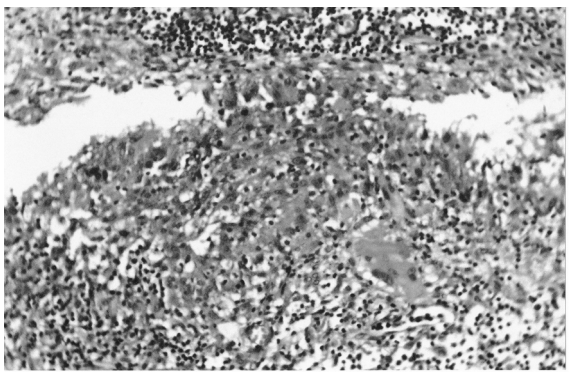

Figure 4. Epitheliod histiocytes with multinuclear giant cell and a suppurative inflammation at the center (HE x100).

1). In three cases epithelioid histiocytes with multinuclear giant cells were demonstrated (Figure 2-3).

Paraffin sections of two cases revealed suppurative granuloma formation with abscess-like material in the center and epithelioid cells and some multinuclear giant cells in the periphery (Figure 4). These sections were stained histochemically, but no microorganism was detected.

DISCUSSION

Fine needle aspiration cytology is the first method to be performed on the superficially enlarged lymph nodes. With this technique, reactive, inflammatory and neoplastic conditions of lymph nodes are correctly diagnosed in nearly every case. So using this cytological method, the number of the surgical excisions will be decreased (12-13).

In tularemia lymphadenopaty, the histopathological features vary with the stage of the disease. In the very early stage, there are only reactive changes without necrosis. Abscess formation with or without epithelioid cell reactions is observed during the second and caseous necrosis during the fourth week (3,5,14). Stellate necrosis may also be seen (15).

When caseous materials with epithelioid cells are present in the fine needle aspiration materials, firstly tuberculosis should be considered in the differential diagnosis. In tuberculosis lymphadenitis, when lymph nodes are secondarily infected, abscess formation which is almost similar to tularemia abscesses may appear (16-17). Also in a large number of tuberculosis cases showing suppurative inflammation, acid fast bacilli were masked with excessive purulent exudate (16). However tularemia cases reveal more dense inflammation which extends beyond capsule (18). In these instances the serological and clinical features will aid in establishing the correct diagnosis (3,15,18).

Cat-scratch disease and lymphagranuloma venerum demonstrate focal areas of necrosis with accumulation of polimorphous nuclear leu-

kocytes with granulomatous organization. In tularemia cases with stellate necrosis, the differential diagnosis from cat-scratch lymphadentis will be difficult. The identification of microorganism is necessary for the diagnosis. Although lenfogranuloma venerum has a similiar histopathological appearance, clinical features, predilection for male gender, localization of the lesion and laboratory findings will lead to diagnosis (3,15).

Other bacterial infections such as yersiniosis, typhoid fever, melioidosis and listeriosis can cause suppurative infections in the lymph nodes. Gram's stain is useful in identifying the presence and type of the bacteria. Bacteriologic study of smears and cultures may be indispensable for specific etiologic identification (15).

One of the major difficulties with interpretation of cytologic findings of lymph nodes is that some suppurative lymphadenopaties may mask malignant disease. Necrosis and massive neutrophilic infiltrate can occur spontaneously and be prominent findings in smears obtained from patients with Hodgkin's disease (19).

In conclusion, necrosis and massive neutrophilic infiltrate with epithelioid histiocytes and multinuclear giant cells is a prominent finding in smears obtained from patients with tularemia. However other bacterial and fungal infections with granulomatous and suppurative lesions may reveal similiar features. Therefore fine needle aspiration cytology for the diagnosis of tularemia is not a useful method per se. However this technique is a safe procedure which does not require hospitalisation. It is also more cost effective and less time consuming than a surgical excision.

Moreover fine needle aspiration will provide rapid diagnosis for the clinically suspect cases of tularemia and the cytological evaluation of the aspirate will play an important role in the identification of other pathological entities responsible for lymphadenopathy. Furthermore the aspirate can be cultured or used for the more complex investigations if required.

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