

Cervical lymph node biopsy: Clinical and histological significance

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Chronic cervical lymphadenopathy (enlarged lymph node for more than 3 weeks) may result from a variety of different underlying diseases. Metastatic carcinoma from the head and neck is the most important of these and must be borne in mind of the clinician before embarking on an open lymph node biopsy. Open cervical lymph node biopsy is a common procedure in surgical practice. Traditionally, it plays an important role in the diagnosis as well as in the treatment of cervical tuberculous lymphadenopathy, especially the atypical *Mycobacterium tuberculosis* (*M.tuberculosis*). Over the last 10 years, fine needle aspiration biopsy (FNAB) has played an important role in the diagnosis of cervical lymphadenopathy with high sensitivity and specificity for malignancy, especially squamous cell carcinoma, and for tuberculosis.^{1,2}

The aim of the present study was to find out the most common cause of cervical lymphadenopathy at King Abdul-Aziz University Hospital (KAUH), Jeddah, Kingdom of Saudi Arabia and to know how many patients who had open biopsy underwent fine needle aspiration cytology (FNAC) prior to open biopsy. A total of 419 patients were studied retrospectively and who underwent an open cervical lymph node biopsy in KAUH over a 10 year period (1989-1998). There were 290 (69.2%) non-Saudi and 129 (30.7%) Saudi patients. Two hundred and seventy-nine patients (66.6%) were female and 140 patients (33.4%) were male. Most of these patients came from low socio-economic classes. There was no previous personal history of tuberculosis (TB). Three hundred and seventy-eight (90.2%) patients were adults with an average age of 40.5 years and 41 (9.8%) were considered children between 4 months and 14 years with an average age of 9.5 years. Deep cervical lymph nodes were affected in 316 (75.4%) patients and other cervical lymph nodes were less affected. Most of the patients (77%) had a multiple and bilateral lymph nodes enlargements. The size of the enlarged lymph nodes were ≤ 3 cm in 314 (75%) patients, and the rest were > 3 cm. The consistency of the enlarged lymph nodes varied; it was solid in 325 (79.6%) patients and cystic with sinus formation in 94 (22.4%) patients. *Mycobacterium tuberculosis* was present in 207 (49.5%) patients as it was

suggested histologically by the presence of tuberculous granuloma, characterized by the presence caseating necrosis, epitheloid cells, and Langhans multinucleated giant cells. Acid-fast bacilli were seen by Ziehl-Neelsen (ZN) stain on 3 patients only. Tuberculosis cultures were not followed in this study. Of those 207 patients positive for TB, there were 68 (32.9%) Saudi patients and 139 (67.1%) non-Saudi patients from different nationalities. One hundred and thirty-five (65.2%) patients were female and 72 (34.8%) were male. The majority of these patients were young adults since there were only 5 (3.4%) children. Malignancy was diagnosed in 130 (31%) patients. Hodgkin's lymphoma was the most common class of malignancy in 50 (11.2%) patients and immunohistochemically, 48 of them were B cell type and 2 were T cell type. This lesions was also classified in 4 histologic sub-types of the Rye classification system, which has been used almost exclusively in North America since its proposal in 1966, including nodular sclerosis Hodgkin's disease (NSHD), lymphocyte predominant Hodgkin's disease (LPHD), mixed cellularity Hodgkin's disease (MCHD), and lymphocyte depleted Hodgkin's disease (LDHD), these are based entirely on descriptions of the non-malignant background of the involved node rather than on the characteristics of the malignant cells themselves.¹ Nodular sclerosing Hodgkin's disease was the most common sub-type reported in 23 cases, MCHD was the 2nd most common histologic type with 8 cases. The histological type was not reported in the rest of the cases. Other major class of malignant lesions was metastatic carcinomas to cervical lymph nodes and this included squamous cell carcinoma from the head and neck, papillary thyroid carcinoma, metastatic breast carcinoma, malignant melanoma and metastasis from unknown primary site. Reactive lymphoid hyperplasia was found in 72 (17.2%) patients; 2 of them had human immunodeficiency virus (HIV) positive serology and 4 had toxoplasmosis positive serology. Surprisingly, FNAC was performed in 23 (5.4%) patients only. Thirteen of them were found to have inflammatory changes with caseation and epitheloid cells, 5 patients had malignancy, and the results of the 5 patients were not conclusive. All patients who had FNAC cytology, later had an open cervical lymph node biopsy where the FNAC findings were confirmed histologically. The significance of human *M.tuberculosis* infections has been recognized since the beginning of recorded history. Tuberculosis was the common cause of illness and death prior to the industrial revolution. Improved general public health and hygiene, as well as the introduction of anti-tuberculous treatment, had a dramatic effect on the reduction of TB in different

countries. Cervical tuberculous lymphadenopathy has become a rare disease, even in the Western countries. In the last decade, the incidence of TB has been rising in the United States of America (USA) and other Western countries, reflecting the increase risk of the infection in acquired immunodeficiency syndrome (AIDS) patients. In India and other developing countries, the reported incidence of TB cervical lymphadenopathy was 75%.^{1,3} In the present study, tuberculous lymphadenopathy continues to be a major health problem since it represents 49.5% of cervical lymphadenopathy in this report. Most of the cases of tuberculous lymphadenitis occur in young females since it was diagnosed in 135 (65.21%) female patients and this is consistent with what has been reported by others.^{4,5} Histologically sometimes it is confusing to differentiate and recognize the caseating granulomatous reaction of TB from other necrotizing granulomatous lymphadenitis. The differential diagnosis that should be kept in mind while dealing with such cases are as follows.⁵ (i) Necrotizing lymphadenitis of Kikuchi Fujimoto is characterized by patchy necrosis, partially preserved architecture and absence of granulocytes. It is more common in Asians and young women. (ii) Necrotizing granulomatous lesions of TB, leprosy, lymphogranuloma venereum and catscratch disease can be distinguished by the presence of epithelioid cells surrounding the foci of necrosis and the identification of specific micro-organisms by special stainings. Necrotic areas of syphilis are accompanied by proliferation of epithelioid cells and by lesions of vasculitis with perivascular cuffs of plasma cells. (iii) Necrotic foci in hypersensitivity reactions are surrounded by cellular infiltrates that include eosinophils and plasma cells. Malignant lymphomas of Hodgkin and non-Hodgkin types may be diagnosed in infarction-free areas. When the tumor necrosis is extensive and complete, the diagnosis is difficult, and relies on the size and deposition of the residual ghostlike cells. Additionally sections and levels, as well as reticulin staining may be helpful in such cases. Fine needle aspiration cytologies plays a very important role in the diagnosis of cervical lymphadenopathy due to malignant conditions with a high specificity and sensitivity as well as for TB.^{1,5} In a study from India, FNAB was carried out in 180 cases of cervical lymphadenopathy followed by open biopsy. The diagnostic accuracy was 84.4% for tuberculous lymphadenitis, caseous necrosis was found in 84.2% and epithelioid cells in 73.6%. These 2 cytological findings were the most characteristic diagnostic features in the aspirated smears. Acid-fast bacilli were observed in 45.6% of the cases. In the USA where the prevalence of tuberculous lymphadenitis is relatively low, a definitive diagnosis requires microbiological confirmation.³ In HIV infected individuals, FANC was reported to be effective. Fine needle aspiration cytology specimens

from HIV seropositive individuals, unlike those from HIV seronegative individuals, usually demonstrate the presence of abundant *Mycobacterium*, most commonly, *Mycobacterium avium* intracellular. *Mycobacterial* burden correlates directly with the level of immune dysfunction. In addition, individuals with advanced immunodeficiency are less likely than their uninfected counterparts to form granulomata. Fine needle aspiration cytology was performed in 5.4% of the patients in the present study. It showed a 78% positive correlation consistent with an open biopsy and non-conclusive results in 22%. Fine needle aspiration cytology was underused in the diagnosis of cervical lymphadenopathy in this series, especially with the finding of high prevalence of tuberculous lymphadenitis in the local population. Fine needle aspiration cytology should be performed first (before open biopsy) in all cases of cervical lymphadenopathy since it is simple, non-invasive, and it requires no hospital admission. The presence of caseous necrosis and epithelioid cell granulomata on the cytology of the aspirate should be an indication for the start of anti-tuberculous therapy and open cervical lymph node biopsy should be reserved for non-conclusive FNAC results or other special situations as in the case of lymphoma.

In conclusion, tuberculous lymphadenopathy continues to be a major health problem in the local population since it represents the most common cause of isolated cervical lymphadenopathy. Fine needle aspiration cytology is a very simple, cost-effective procedure with high sensitivity and specificity in both benign and malignant conditions. It must be performed first in all cervical lymphadenopathy cases. Open cervical lymph node biopsy should not be the first diagnostic tool in this country.

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