International Journal of Tropical Medicine 7 (1): 53-56, 2012
ISSN: 1816-3319

Diagnosis of Tuberculous Lymphadenitis in Red Sea State, Sudan

Ali K. Ageep
Department of Pathology, Faculty of Medicine, Red Sea University, Port Sudan, Sudan

Abstract: Tuberculous lymphadenitis remains both diagnostic and therapeutic challenge because it mimics other pathologic processes. In this study, researchers tried to find the best way for diagnosis of tuberculous lymphadenitis in Red Sea State. About 222 patients suspected to have tuberculous lymphadenitis were examined in the period from March 2008 to October 2011 in a histopathology laboratory in the Red Sea Medical center, Port Sudan, Sudan. This is the only regional laboratory to which fine needle aspiration cytology and histopathological samples were sent. Slides were stained by Papanicolaou, May-Grunewald Giemsa (MGG) and Ziehl-Neelson stains. Cultures were also done from the aspirate. Serum samples were obtained for Immuno-Chromatography Test (ICT). In 57 patients biopsies were taken and stained by Haematoxylin and Eosin (H and E). Cervical lymph nodes were the common lymph node group affected by tuberculosis (94.5%). Studied females were more than males (M:F = 1:1.2). About 94.6% of the cytology show positive result for TB. The mycobacrium grow in 88% of the culture media. Acid fast bacilli were seen in 61 patients (41.6%). Serological test was positive in 68% of the patients. So in a short facility region like the study area, FNAC remain the best method for the diagnosis of tuberculous lymphadenitis. PCR and culture may be considered in few cases whenever highly needed.

Key words: Tuberculosis, lymphadenopathy, FNAC, PCR, Port Sudan

INTRODUCTION

There are nearly 9 million new cases and 2 million deaths from Tuberculosis (TB) worldwide every year (WHO, 2005). Tuberculous Lymphadenitis (TBLN) is seen in nearly 35% of extra-pulmonary TB which constituted about 15-20% of all cases of TB (Sharma and Mohan, 2004; Corbett *et al*., 2003). Infection with the Human Immunodeficiency Virus (HIV) is associated with an increased frequency of both pulmonary and extra-pulmonary tuberculosis particularly lymphadenitis (Aguado and Castrillo, 1987; Finfer *et al*., 1991). Although, cases of tuberculous lymphadenitis are common in Red Sea State, Sudan no data was reported to highlight the actual incidence and prevalence of the disease.

Medical staff will get benefits from many lessons illustrated by this research. This research confirms the presence and diagnosis of TBLN in the region since this is the first documented study in Red Sea State regarding the diagnosis of TBLN. This study will also open the light to the local staff on the importance of diagnosing atypical mycobacteria in granulomatous lymphadenitis since this has a different treatment protocol other than the conventional anti-TB therapy (Balasubramanian and Ramachandran, 2000; Castro *et al*., 1985).

The method selected in this research for first line diagnosis of TBLN could be used in other regions of the world where short heath facilities are present. The globally used protocol of the combination of history and physical examination, tuberculin test, staining for Acid-Fast Bacilli (AFB), radiologic examination and Fine-Needle Aspiration Cytology (FNAC) will help to arrive at an early diagnosis of mycobacterial lymphadenitis which will allow early institution of treatment before a final diagnosis can be made by biopsy and culture (Paredes *et al*.,1990; Ibekwe *et al*., 1997). However, this long list of investigations is impractical and could not be applied to the local short income population. So, researchers aimed at this study to find the best way for diagnosis of tuberculous lymphadenitis in Red Sea State, Sudan.

MATERIALS AND METHODS

About 222 patients suspected to have tuberculous lymphadenitis were examined in the period from March 2008 to October 2011 in a histopathology laboratory in the Red Sea Medical center, Port Sudan, Sudan. Port Sudan city is the capital of the Red Sea State and it is the major sea port of the Sudan. The total number of the whole population was (739,300) according to the national census of 2002 with adjusted growth rate. The laboratory is the only regional laboratory, to which fine needle aspiration cytology and histopathological samples were sent. The product of the aspirate was divided in to three parts for

cytology, ZN staining and culture. Cytology slides were stained by Papanicolaou and May-Grunewald Giemsa (MGG) stains. Ziehl-Neelson stain was used to detect Acid Fast Bacilli in the prepared smears. The third part of the aspirate was used to culture mycobacteria in Lowenstein Jensen (LJ) media. Serum samples from the same patients were obtained for immuno-chromatography test (Boson Biotech Co., China). Surgical biopsies were taken in 57 patients and stained by Haematoxylin and Eosin (H and E).

Ethical clearance of this study was approved from the regional Ethical Review Committee (ERC), Ministry of Health, Red Sea State Government. Data regarding the age, sex and the site of the involved lymph nodes was recorded in predesigned forms. The diagnosis of tuberculosis was considered as positive when either of the following criteria was met:

- Presence of epithelioid cell granulomas with or without multinucleate giant cells and caseation necrosis on H and E staining
- Demonstration of acid fast bacilli on Z N staining
- Isolation of mycobacteria on culture (Nataraj *et al*., 2002)

Leukemic patients are referred to the hematology department of the laboratory for bone marrow aspiration or biopsy, so they were excluded from this research.

Statistical analysis: Data were analyzed by using a computer Statistical Package for Social Sciences (SPSS) program Version 16 and results are presented as frequency and percentage.

RESULTS AND DISCUSSION

A total of 222 patients were enrolled in to this study. 40 patients were clearly diagnosed as having non TBLN lesions (like metastatic carcinomas or reactive changes) on FNAC. These 40 patients were excluded from the research. In 150 patients (1st group) from the remaining 182 cases, aspiration of the lymph nodes was done. In this group, 17 patients underwent surgical biopsy because the treating doctors were not convinced with FNAC result. Surgical biopsies were also taken from the 8 patients who have negative FNAC result for TBLN. In a second group, 32 patients underwent surgical biopsy of the lymph nodes.

Cervical lymph nodes were the commonest superficial lymph nodes group affected by tuberculosis (94.5%) (Table 1). This followed by the axillary group (3.8%) and the inguinal group (1.7%), respectively. Studied females were more than males (M:F = 1:1.2). The incidence of the disease increases in the age of twenties and peaks in the third decade of life and declines after that.

Table 2 shows the results of the different diagnostic techniques used in this study. Of the 150 cases of the FNA, 94.6% of patients show positive result for TB in the cytology smears. These patients received anti-tuberculous therapy and they were improved after 2 weeks follow up. So, the specifity of FNAC method for detection of TB was 100% in this study. The mycobacrium TB grow in 88% of the culture media. Acid fast bacilli were seen in 61 patients (41.6%). Serological test was positive in 68% of the patients. Histopathology of the 57 lymph nodes shows caseous granuloma in 98.2% of the sections. Of these 57 patients, 17 were already examined by FNAC method and they were all positive for TB. Although, this number of patients is small but it also supported the finding that FNAC is 100% specific for diagnosis of TB lymphadenitis. The 8 negative cases for TB by FNAC were proved to be positive cases by histopathology. So in this research the false negative cases for FNAC were 0.05% and no false positive cases.

Lymphadenitis is the most common clinical presentation of extrapulmonary tuberculosis (Brizi *et al*., 1998). In this study, tuberculous lymphadenitis most frequently involves the cervical lymph nodes. This is highly consistent with Khirey study in the center of Sudan (Kheiry and Ahmed, 1992) and reports from other different countries (Thompson *et al*., 1992). TBLN most frequently affects patients in their second and third decades but may afflict patients of any age. There is slight female predominance (approximately 1.2:1). This is also consistent with most of other studies (Enarson *et al*., 1980).

The diagnosis of TBLN in this region faces many obstacles. The first is ignorance and the less awareness of the rural population about the importance of early diagnosis and treatment of their illness. Secondly, the poverty of this population limits them from seeking medical advice and care. The third reason is the short medical facilities with few equipped laboratories that could make the diagnosis possible for all people in the

Table 1: Illustrates the sex and age (per years) presentations of tuberculosis in superficial lymph nodes in Red Sea State, Suda

Site affected	M	F	<10	11-20	21-30	31-40	41-50	51-60	>60	Total
Cervical	80.0	91.0	3.0	11.0	47.0	61.0	23.0	18.0	9.0	172
Axillary	2.0	5.0	0.0	0.0	2.0	3.0	1.0	1.0	0.0	7
Inguinal	1.0	2.0	0.0	0.0	0.0	0.0	1.0	1.0	1.0	3
Total (%)	84 (46.2)	98 (53.8)	3 (1.7)	11 (6.0)	49 (26.9)	64 (35.2)	25 (13.7)	20 (11.0)	10 (5.5)	182 (100)

M = Males, F = Males

Table 2: Shows results of positive cases by different types of investigations

Type of investigation	Positive cases	Frequency (%)
Cytology	142	94.6
Ziehl-Neelson stain	61	41.6
Culture	92	61.3
Immuno-chromatography	102	68.0
Histopathology	56	98.2

studied area. Empirical use of anti-tuberculous drugs by some junior doctors (who work in rural hospitals) which will lead to delay in diagnosis and treatment of some other serious illnesses like metastatic cancers and incorrect management of some cases of atypical mycobacteria is also added to the list of the problems in this region.

Fine needle aspiration cytology is a sensitive, specific and cost-effective way to diagnose mycobacterial cervical lymphadenitis (Ellison *et al*., 1999). This technique alone detects 94.6% of the cases in this research. This finding is highly comparable to the global estimation of the sensitivity and specifity of FNAC which were found to be 88 and 96%, respectively (Ellison *et al*., 1999). Adding to these findings, the other advantages of FNAC like the fewer invasions, the low cost and the short time to obtain the result make us recommend this method to be the first line technique in the diagnosis of TBLN in studied area.

Products from the FNAs tend to contain very small number of mycobacteria to be picked up by ZN smear alone. The low positive cases here may be also related to the empirical use of broad spectrum antibiotics or anti-tuberculous therapy before performing the test. Chance of finding AFB is higher in patients with cold abscess (Albright and Pransky, 2003).

The study finding of 61.3% of positive culture growth of mycobacteria is consistent with other reports where their cultures were positive in 10-69% of the cases (Kanlikama *et al*., 1993; Lau *et al*., 1990). Culture of mycobacterium is diagnostic for mycobacterial cervical lymphadenitis. However, several weeks are needed to obtain the culture result which may prolong the initiation of treatment (Lau *et al*., 1990). Broad spectrum antibiotics such as amoxicillin-clavulanic acid and fluoroquinolones have been reported to be inhibitory to *M. tuberculosis* that might lead to negative initial sputum smears and cultures (Sterling, 2004). However, there is a paucity of literature on such findings in TBLN. Researchers speculate that the cytology positive and culture negative results in this study could be due to the inhibitory effect of prior broad spectrum antibiotic or anti-TB treatment. There can also be a possibility for the presence of non viable or very few organisms that were missed by culture (Verenkar *et al*.,1996; Gupta *et al*., 1993). Never the less, the high number of negative cultures (38.9%) and absence of the culture media itself in the studied area reserve this technique to be used for limited number of patients.

The test of blood samples by the immuno-chromatography detects 68% positive cases of the studied population. The solid phase of the kits contains antigens of *Mycobacterium tuberculosis* (huminis), *Mycobacterium bovis* and *Mycobacterium africanum*. The negative serology results with a positive cytology smears make us suggest other different strains of mycobacteria to be the cause of the TBLN in the patients with the negative serology results. Further researches are needed to evaluate this method in the diagnosis of TBLN in the region.

Histopathological examination gives high index value (98.2%) in the diagnosis of mycobacterial cervical lymphadenitis in studied patients. This is consistent with reports from different authors in other different countries (Flint *et al*., 2000; Kwon *et al*., 2000). Disadvantages of this procedure are the high cost, the need of surgery to obtain the sample and the more time (than the cytology) to have the result (Kwon *et al*., 2000).

Molecular tests like the Polymerase Chain Reaction (PCR) are very sensitive (43-84%) and specific (75 and 100%) (Schuit and Powell, 1978; Manitchotpisit *et al*., 1999) but they are not included in this research because they are not available in the studied region. In this study we have not considered the HIV status of the patients. However, Sudan has not got a high HIV prevalence as compared to other African countries (El-Sony *et al*., 2002; Hashim *et al*., 1997).

CONCLUSION

Cervical group of lymph nodes are the most affected nodes by tuberculosis. Cytological smears from FNA are sensitive, rapid, cost effective and easy method for the diagnosis of tuberculous lymphadenitis. So, this technique is recommended to be the first line investigation in the diagnosis of TBLN. PCR and culture may be considered in few cases whenever highly needed. The circulating different strains of mycobacteria should be studied in the future. Researches regarding HIV cases related to TB are also recommended in this region.

REFERENCES

Aguado, J.M. and J.M. Castrillo, 1987. Lymphadenitis as a characteristic manifestation of disseminated tuberculosis in intravenous drug abusers infected with human immunodeficiency virus. J. Infect., 14: 191-193.

Albright, J.T. and S.M. Pransky, 2003. Nontuberculous mycobacterial infections of the head and neck. Pediatr. Clin. North Am., 50: 503-514.

Balasubramanian, R. and R. Ramachandran, 2000. Management of non-pulmonary forms of tuberculosis: Review of TRC studies over two decades. Indian J. Pediatr., 67: 34-40.

Brizi, M.G., G. Celi, A.V. Scaldazza and B. Barbaro, 1998. Diagnostic imaging of abdominal tuberculosis: Gastrointestinal tract, peritoneum, lymph nodes. Rays, 23: 115-125.

Castro, D.J., L. Hoover, D.J. Castro and L. Zuckerbraun, 1985. Cervical mycobacterial lymphadenitis medical vs surgical management. Arch. Otolaryngol., 111: 816-819.

Corbett, E.L., C.J. Watt, N. Walker, D. Maher, B.G. Williams, M.C. Raviglione and C. Dye, 2003. The growing burden of tuberculosis: Global trends and interactions with the HIV epidemic. Arch. Intern. Med., 163: 1009-1021.

El-Sony, A. I., A.H. Khamis, D.A. Enarson, O. Baraka, S.A. Mustafa and G. Bjune, 2002. Treatment results of DOTS in 1797 Sudanese tuberculosis patients with or without HIV co-infection. Int. J. Tuberc. Lung Dis., 6: 1058-1066.

Ellison, E., P. Lapuerta and S.E. Martin, 1999. Fine needle aspiration diagnosis of mycobacterial lymphadenitis. Sensitivity and predictive value in the United States. Acta Cytol., 43: 153-157.

Enarson, D.A., M.J. Ashley, S. Grzybowski, E. Ostapkowicz and E. Dorken, 1980. Non-respiratory tuberculosis in Canada epidemiologic and bacteriologic features. Am. J. Epidemiol., 112: 341-351.

Finfer, M., A. Perchick and D.E. Burstein, 1991. Fine needle aspiration biopsy diagnosis of tuberculous lymphadenitis in patients with and without the acquired immune deficiency syndrome. Acta Cytol., 35: 325-332.

Flint, D., M. Mahadevan, C. Barber, D. Grayson and R. Small, 2000. Cervical lymphadenitis due to non-tuberculous mycobacteria: Surgical treatment and review. Int. J. Pediatr. Otorhinolaryngol., 53: 187-194.

Gupta, S.K., T.D. Chugh, Z.A. Sheikh and N.A. Al-Rubah, 1993. Cytodiagnosis of tuberculous lymphadenitis: A correlative study with microbiologic examination. Acta Cytol., 37: 329-332.

Hashim, M.S., M.A. Salih, A.A. El Hag, Z.A. Karrar and E.M. Osman *et al*., 1997. AIDS and HIV infection in Sudanese children: A clinical and epidemiological study. AIDS Patient Care STDS, 11: 331-337.

Ibekwe, A.O., Z. Al Shareef and S. Al Kindy, 1997. Diagnostic problems of tuberculous cervical adenitis (Scrofula). Am. J. Otolaryngol.-Head Neck Med. Surg., 18: 202-205.

Kanlikama, M., C. Ozsahinoglu, E. Akan and K. Ozcan, 1993. Mycobacterial species causing cervicofacial infection in Turkey. Eur. Arch. Otorhinolaryngol., 250: 237-239.

Kheiry, J. and M.E. Ahmed, 1992. Cervical lymphadenopathy in Khartoum. J. Trop. Med. Hyg., 95: 416-419.

Kwon, K.S., C.K. Oh, H.S. Jang, C.W. Lee and E.S. Jun, 2000. Detection of mycobacterial DNA in cervical granulomatous lymphadenopathy from formalin-fixed, paraffin-embedded tissue by PCR. The J. Dermatol., 27: 355-360.

Lau, S.K., W.I. Wei, C. Hsu and U.C. Engzell, 1990. Efficacy of fine needle aspiration cytology in diagnosis of tuberculous cervical lymphadenopathy. J. Laryngol. Octol., 104: 24-27.

Manitchotpisit, B., S. Kunachak, B. Kulapraditharom and T. Sura, 1999. Combined use of fine needle aspiration cytology and polymerase chain reaction in the diagnosis of cervical tuberculous lymphadenitis. J. Med. Assoc. Thai, 82: 363-368.

Nataraj, G., S. Kurup, A. Pandit and P. Mehta, 2002. Correlation of fine needle aspiration cytology, smear and culture in tuberculous lymphadenitis: A prospective study. J. Postgrad Med., 48: 113-116.

Paredes, C., F. Del Campo and C. Zamarron, 1990. Cardiac tamponade due to tuberculous mediastinal lymphadenitis. Tubercle, 71: 219-220.

Schuit, K.E. and D.A. Powell, 1978. Mycobacterial lymphadenitis in childhood. Am. J. Dis. Child, 132: 675-677.

Sharma, S.K. and A. Mohan, 2004. Extrapulmonary tuberculosis. Indian J. Med. Res., 120: 316-353.

Sterling, T.R., 2004. The WHO/IUATLD diagnostic algorithm for tuberculosis and empiric fluoroquinolone use: Potential pitfalls. Int. J. Tuberc. Lung Dis., 8: 1396-1340.

Thompson, M.M., M.J. Underwood, R.D. Sayers, K.A. Dookeran and P.R.F. Bell, 1992. Peripheral tuberculous lymphadenopathy: A review of 67 cases. Br. J. Surg., 79: 763-764.

Verenkar, M.P., K. Kamath, W.M.J. Pinto, S. Rodrigues and R.G. Wiseman Pinto, 1996. Mycobacteriological study of fine needle aspi-rates in cervical lymphadenitis. Indian J. Tuberc., 43: 187-189.

WHO, 2005. World Health Organization Global Tuberculosis Control Surveillance, Planning and Financing. WHO, Geneva.