

## CHAPTER 2

### LITERATURE REVIEW

Cervical tuberculous lymphadenitis (TB node) is the most common form among tuberculosis that occurs outside pulmonary system<sup>(1)</sup>. TB in total had the average reported incidence of 46.5 per 100,000 last three years<sup>(16)</sup>. Ninety percent was pulmonary TB. No national record for TB node was given. However, the record of Pulmonary and TB Clinic at King Chulalongkorn Memorial Hospital showed 2-4 new cases of lymph node tuberculosis monthly<sup>(2)</sup>. Usually patients manifest palpable nodes that persist more than two weeks. Differential diagnoses of prolonged lymphadenopathy include lymph node hyperplasia, TB node, lymphoma, metastatic carcinoma and others<sup>(2)</sup>. Biopsy is practical standard management after ENT exam having ruled out tumor in the nasopharynx, oropharynx and larynx<sup>(1)</sup>. FNA has been accepted as alternative mean for the first line approach<sup>(2,15)</sup>. It is efficacious for the diagnosis of TB node as well as the lymphadenopathy in general<sup>(17)</sup>. The benefit of this method is that it is economic, rapid and safe. Furthermore, no scar happens<sup>(4)</sup>. But it cannot reach 100% sensitivity rate. Therefore, when the test is negative for diagnosis of TB node, a significant number of patients need surgical excision. The sensitivity for the diagnosis of TB node by FNA is low (48%) in United State<sup>(18)</sup> but is modest to high in the disease prevalent regions, ranged from 71-90%<sup>(5,6)</sup>. The sensitivity of the test in Thailand is not documented but it is possible around 70%<sup>(4,19)</sup>.

The discrepancy of the sensitivity between the non-prevalent and prevalent centers is the criteria used for the diagnosis. In non-prevalent region, the identification of the causative agent is mandatory. In prevalent region, granulomatous tissue response with typical caseating necrosis is regarded as hallmark for diagnosis even though acid fast bacilli cannot be identified<sup>(20)</sup>.

The author has described cytologic features of tuberculosis of lymph node in correlation with histopathology<sup>(4)</sup>. Diagnostic features can be classified into two main categories that are principal and subordinate categories. The former correlates with histomorphology of caseating granulomatous inflammation. Depending upon the

component that is aspirated, the FNA finding belonging to this granulomatous inflammation can manifest caseous necrosis fragments or epithelioid cell aggregates or both. This feature is reported as highly suggestive of tuberculosis when acid-fast bacilli are not identified. And it is in this category that acid-fast stain is rarely positive. The subordinate category is itself not specific but will remind cytopathologist not forget to do acid-fast stain. AFB detection yield rate is high<sup>(4,21)</sup>. Only with positive AFB that allow cytopathologist to report the case as tuberculous lymphadenitis. The feature correlates with necrotizing liquefaction. Gross feature is like abscess or pus-like discharge.

To enhance the sensitivity of FNAC, tuberculin test (TT) has been suggested and it was proven that combined FNA and TT could increase the sensitivity from 77% to 90%<sup>(9)</sup>. This article is the only single article in the English written papers reviewed to date; the study was taken place in Hong Kong between July 1987 and March 1989. Firstly, tuberculin test was performed on 59 volunteer subjects who had no history of tuberculosis or cervical lymphadenopathy in order to define the value to be used as cut-off. The diameter of 24 mm was regarded as the upper limit of normal. The tuberculin reaction was graded into three categories: strong, moderate, and negative reaction. The tuberculin reaction was defined as strong when one of the following was present: (1) the size exceeded the upper limit of normal (>24 mm); and (2) association with a vesicle, local ulceration, or lymphangitis. A moderate reaction was called when it was not more than mean  $\pm$  2 SDs of the control and was not 0. The TT reaction size was measured and recorded at 72 hours after intradermal injection (Mantoux method). In the Hong Kong study, all of 74 patients with clinical diagnosis of suspected TB node received FNA, TT and subsequent surgery to the aspirated cervical lymph node. Forty-eight patients had TB node proven histologically or bacteriologically. Forty-five of the cases were due to *M tuberculosis* as proven by positive culture. Three patients were culture negative. The weakness of this study when efficiency is concerned is the inclusion of cases with positive AFB in the smears as one of the three criteria for diagnosis of TB node by combined test. The event accounted for 31% of TB node patients. The two other criteria were (1) tuberculin reaction was strong and (2) FNA cytologic findings showed granulomatous inflammation with moderate TT reaction.

Though TT is a simple technique, it is not recommended for the diagnosis of tuberculous lymphadenitis<sup>(2)</sup>. In the book<sup>(12)</sup> under patronage of the International Union Against Tuberculosis and Lung Disease (IUATLD) states clearly that the tuberculin reaction measures the degree of allergy; it does not measure immunity. Furthermore, it does not indicate the presence or extent of disease. Nevertheless, in the same book, it mentions that the larger the diameter (above 10-15 mm) the greatest the support for a diagnosis of tuberculosis. It is also written that if the test is strongly positive, this is strongly in favor of recent TB infection or clinical tuberculosis (though not conclusive proof). Therefore, it is justified to make diagnosis of clinical TB node only when the TT is unequivocally strong reaction. The moderate reaction has to be in agreement with cytologic finding, or in the other word, to diagnose TB node by cytologic finding with absence of AFB, it has to be in agreement with positive tuberculin test.

The value of TT coupled with FNAC seems rational but its practical benefit for Thai patients meets with challenge and argument from the experts. There are three points of practical benefit concern. Firstly, the test may benefit to prevent pitfalls of the cytologic findings. Secondly, the test may disclose more TB node cases that are missed by cytology. And thirdly, how can it be efficient at the Hospital setting.

The tuberculin available in Thailand is the batch RT-23 PPD, prepared by State Serum Institute of Denmark<sup>(22)</sup>. It has been estimated that the amount of the protein on this batch production of 670 g can be used for 27,000 million tests. The high prevalence of BCG vaccine has no effect for the interpretation if the cut off point is set at over 10 mm<sup>(23)</sup>.

The high prevalence of tuberculous infection among Thai patients is another debated issue for the interpretation. However, it is agreeable from the expert's point of view that the cut off of above 24 mm (used in the previous study in Hong Kong) can be regarded as recent infection. Since there is lack of available data, a prospective study is needed. Furthermore, if it is efficacious, is it also cost-effective compared with FNAC alone? The issue of efficiency is another question that has not been answerable in the literature review.

Nowadays, there are many diagnostic tests such as PCR and other molecular technique<sup>(14)</sup>, but these are all expensive. It is not economically for the service at the Hospital setting.