



CHAPTER 1

BACKGROUND AND RATIONALE

Tuberculous lymphadenitis is the most common form of extra-pulmonary tuberculosis⁽¹⁾. It is prevalent in young adults. Most patients manifest palpable neck masses that challenge the clinicians to distinguish it from the other diseases in differential diagnosis. The latter vary from reactive node to malignancy⁽²⁾.

There are recently approximately 40-50 newly diagnosed cases of tuberculous lymphadenitis at King Chulalongkorn Memorial Hospital each year⁽²⁾. To diagnose the case, it is basically a tissue diagnosis based. Incisional biopsy is not recommended since it may produce scrofuloderma⁽¹⁾.

Fine needle aspiration (FNA) can replace the excisional or incisional biopsy and it has been accepted as the first line approach in the management scheme (Fig.1)⁽²⁾.

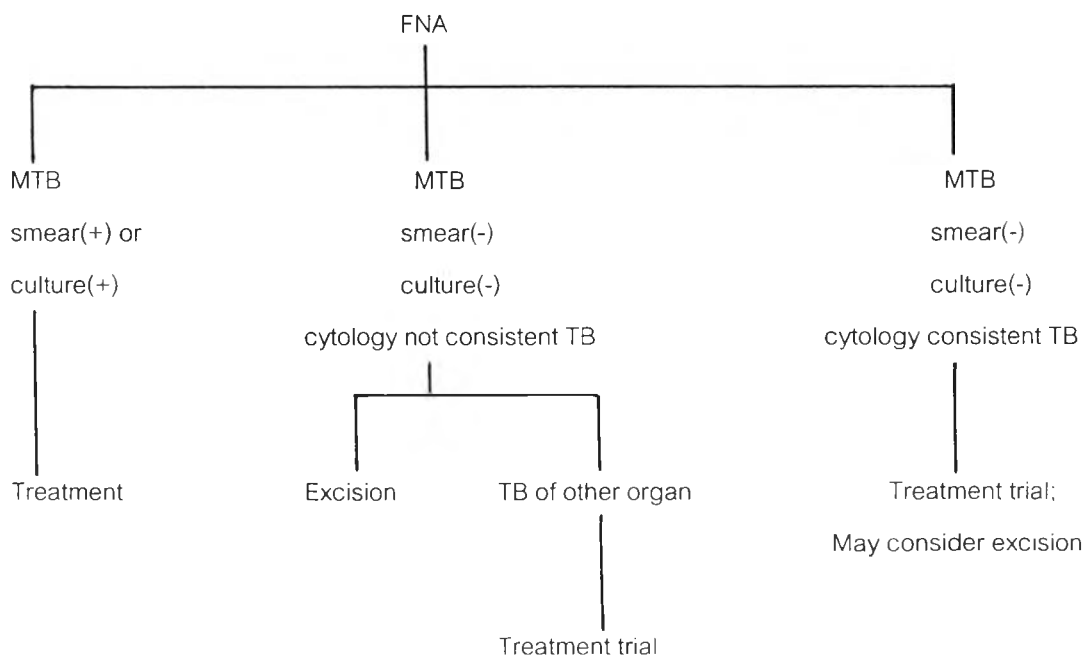


Figure 1: Diagnostic scheme for TB lymphadenopathy (MTB = *Mycobacterium tuberculosis*)

FNA procedure is simple, safe and not costly. This diagnosis-based clinic – named FNA clinic has set-up and has been running since B.E. 2532 at King Chulalongkorn Memorial Hospital⁽³⁾. Lymph node is one of the three common organs to be investigated at the clinic. TB lymphadenitis is one of the diseases that have benefit to perform FNA test. The merit of FNA in the diagnosis is that it leaves no scar⁽⁴⁾. However, the limitation is that the needle takes a rather small sampling area, thus occasionally not get the whole diagnostic histopathologic features. The sensitivity of the test to diagnose tuberculous (granulomatous) lymphadenitis in the prevalent areas varies from 71%⁽⁵⁾ to 90%⁽⁶⁾. Usually, the diagnosis is straightforward if acid-fast bacilli can be identified or the culture proves. This happens in 17%⁽⁷⁾ to 50%⁽⁸⁾ of the cases depending on how prevalence of tuberculous abscess in the series. Most of the cases are diagnosed cytologically granulomatous lymphadenitis. The latter is not conclusive but very suggestive for tuberculosis in this part of the world where tuberculosis is prevalent⁽⁹⁾.

It is known that some malignancy can give the feature of associated granuloma or mimicking appearance and is the important source of falsely interpreted cases^(10,11). In 1991, Lau SK et.al. has proposed tuberculin skin test (TT) as a complementary test to FNA cytology in order to enhance the sensitivity as well as support the diagnosis. The rationale was that TT and FNA were inexpensive tools, each had its own limitation. The combined test proved to have higher sensitivity in diagnosis of tuberculous lymphadenitis than cytology alone⁽⁹⁾. The finding interested the author. However, there are some concerns on implementation. This is the single paper in the literature review to date. Most clinicians still doubt if it works and about its efficiency in our situation, although Thailand is prevalent for TB like Hong Kong where the mentioned study was taken place. The combined protocol may have to adjust. Therefore, this study is conducted, aimed at cost-effectiveness evaluation of the combined test if it will launch in the diagnosis scheme at King Chulalongkorn Memorial Hospital.

There are reasons for the need of TT as a complementary test, as following.

1. FNA cytology cannot achieve 100% sensitivity. The probable sensitivity is 70%. That means there are a substantial number of TB patients that have to undergo excisional

biopsy of lymph node after the test. If TT can enhance the sensitivity, it can save more cases not need surgery and leaves no scar.

2. AFB positive rate is low^(7,8). It is more likely detectable in a tuberculous abscess lymph node than a solid tuberculous node. Most cases will show cytologic feature of granulomatous inflammation without detectable organism. TT is usually positive in person who has at some time been infected with TB⁽¹²⁾. Therefore, the test is speculated to verify cytologic finding with negative acid-fast stain.

3. Culture which is the definitive diagnosis tool can be made from FNA material⁽¹³⁾ but again, the rate of success is low for the solid node. Moreover, it is time-consuming, not suitable to use in every case in practice. On contrary, TT is feasible and can be read the result within 48-72 hours.

4. TT is cheap, well-known and feasible comparing with ancillary tests like PCR and molecular methods⁽¹⁴⁾. Although it is not reliable diagnostic tool, it can be used for complementary test. If the test is strongly positive, this is strongly in favor of recent TB infection or clinical tuberculosis (though not conclusive proof)⁽¹²⁾.

On the other hand, there are some concerns that the combined test needs to be proved before launching.

1. In countries with high prevalence of disease and BCG immunization, more than half of the population are TT reactors. It is the cut-off value that makes significance. How to define the suitable value to classify the reaction as strongly positive. In Hong Kong, the upper limit of normal value in controls was used, the value was set at above 24 mm⁽⁹⁾. The value will be used in this study.
2. The National guideline for interpretation of positive tuberculin test for general person has set the value at above 14 mm⁽¹⁵⁾. The value will be used in this study as confirmatory test for granulomatous lymphadenitis by cytology.
3. HIV patients may react tuberculin in different way⁽¹²⁾. It's prevalence may effect in economic analysis. Since TB infection is common in HIV patients as well as in other underlying diseases, it is not rational to separate in this study.
4. TT is not specific for *Mycobacterium tuberculosis* complex, non-tuberculous mycobacterium can give the reaction too, however, the latter usually gives small induration size and its incidence is very low comparing with tuberculosis⁽¹²⁾. Therefore, the identification of species is not much needed in this study.

Expected benefit of the study

If the combined test can be proved to be efficient, it will implement for routine investigation. For the patients who are suspected for tuberculosis but FNAC cannot give conclusive diagnosis, these patients will forward to have tuberculin test. More TB node cases will have the benefit of avoiding unpleasant surgical scars. On the other hand, with complementary test of TT, the patients will have the benefit of correct diagnosis for tuberculous lymphadenitis. The small risk of false positive from FNAC diagnosis alone can be prevented.