

CLINICAL AND PARACLINICAL ASPECTS OF THYROID TUBERCULOSIS

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Abstract- The common midline neck masses include thyroglossal duct cyst, lipomas, thyroid tumor or cyst and rarely a midline lymph node, particularly the node just above the thyroid isthmus. Thyroid tuberculosis (TTB) is a rare cause of thyroid disease and therefore only occasionally included in the differential diagnosis. In this study we tried to explain the clinical and paraclinical manifestations of TTB with a case series of 26 patients with definite or suspicious diagnosis of TTB. There were 7 cases with definite tuberculosis involvement of thyroid and 19 cases which were suspicious to have TTB. In fine needle aspiration cytology (FNAC) of 4 definite patients, acid fast bacillus was seen (57.1%). PPD skin test was positive only in 3 patients with definite TTB (42.9%). Microscopically, epithelioid granuloma, Langerhans giant cell and evidences of carcinoma, each was shown in one separate case. It is therefore important to note that tuberculosis should be considered in the differential diagnosis of anterior cervical swellings. FNAC can help in confirming the diagnosis but final confirmation is made by histopathological and biochemical examination; and patients respond well to surgery with antituberculous drugs.

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INTRODUCTION

Tuberculosis of the thyroid gland is very rarely diagnosed and extremely uncommon in recent years (1-3). It was first reported in 1862 by Lebert in a patient with disseminated mycobacterial infection (3-4). In 1878, Chiari described 7 cases of microscopic involvement of thyroid in patients who died from disseminated tuberculosis (4). The first case of primary thyroid infection, presenting as a rapidly enlarging goiter with cervical lymphadenopathy but no evidence of pulmonary tuberculosis, was reported

in 1893 by Bruns (5). In 1926, five cases of thyroid tuberculosis (TTB) were recognized by Collier and Huggins among 1200 thyroidectomies (6). In 1932, Rankin and Graham reported 21 cases out of 20,758 partial thyroidectomy specimens from the Mayo Clinic covering the period from 1920 to 1931 (7), while in 1952 only two cases were identified by Levitt among 2114 consecutive thyroid specimens.

Since then two studies using fine needle aspiration cytology (FNAC) were conducted and lesions compatible with TTB were found in 8 out of 1283 and in 18 out of 1565 cases, respectively (1, 6). The exact number of cases reported is difficult to determine, but to our knowledge at least 186 cases (not including our cases) can be found cumulatively in the English language literature, four of which were children (8, 9, 10-12). Similarly, the true incidence of TTB is difficult to estimate possibly

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due to escape of the etiologic diagnosis (13). Most authors mention TTB being diagnosed by physicians rarely, in 0.1–1% of cases. But during autopsy this disease is found much more often (2–7% of cases). This is explained by difficulties of diagnosing the disease, since the lesion can often be mistaken for carcinoma, suppurative abscess or hemorrhage into a thyroid cyst (14, 15, 16-19); and by insufficient knowledge of physicians on the subject of differential diagnostics of TTB (20).

The clinical presentation is variable and usually consists of local symptoms related to enlargement of the gland, while thyroid function is rarely affected (21, 22). Before the application of FNAC as a method of investigating thyroid nodules, all the patients underwent surgical removal of the thyroid lesion (suspected of representing a tumor) and diagnosis was established by demonstration of tubercle bacilli in the biopsy specimens (23-28). Thus when attempting to prove or deny presence of tuberculosis infection in the thyroid, it may be necessary to apply all or most of methods used to diagnose tuberculosis: from the most simple (such as chest X-ray and PPD test) (26) to the most modern rapid tests-serological assays, when antibodies to *Mycobacterium tuberculosis* are detected in human serum or plasma (29-32). Ultrasonographic and computed tomography (CT) findings can help in this matter as well; heterogeneous hypoechoic mass is seen on ultrasonogram and peripheral-enhancing low-density abscess with regional lymphadenopathy is demonstrated on CT scan (33).

In this study we tried to explain the clinical and paraclinical characteristics of TTB with a case series of 26 patients with definite or suspicious diagnosis of TTB.

MATERIALS AND METHODS

We conducted a 20-year retrospective study of all cases of TTB occurring in three academic hospitals of Tehran University of Medical Sciences including Imam Khomeini, Dr. Shari'ati and Amir A'alam between 1984 and 2003.

We prepared a case series of 26 patients with definite or suspicious diagnosis of TTB. Anatomopathological results of the removed thyroid,

when available, were gold standard for diagnosis of TTB. Diagnosis of suspicious TTB was based on presence of a history of close contact to a patient with definite tuberculosis, or tuberculosis in other organs, *etc.* Patients' demographic data, different signs and symptoms, and also paraclinical test results extracted from medical files.

SPSS 11.0 was applied for descriptive analysis.

RESULTS

There were 7 cases with definite tuberculosis involvement of thyroid and 19 cases with suspicious diagnosis of TTB. Patients' demographic data and various clinical and paraclinical presentations have been abstracted in table 1.

Among patients with definite TTB, there were 3 males and 4 females (42.9% vs. 57.1%); while suspicious patients constituted of 11 males (57.9%) and 8 females (42.1%).

Table 1. Clinical and paraclinical presentations*

Data/Manifestations	Definite (n = 7)	Suspicious (n = 19)
Demographic Data		
Gender		
Male	3 (42.9)	11 (57.9)
Female	4 (57.1)	8 (42.1)
Age Range(yr.)	42-55	39-53
Mean	50.1	49.4
Clinical Presentations		
Dyspnea	4 (57.1)	9 (47.4)
Dysphagia	2 (28.6)	3 (15.8)
Neck Mass	3 (42.8)	7 (36.8)
Fever	1 (14.3)	2 (10.5)
Paraclinical Presentations		
Euthyroidism	5 (71.4)	12 (63.2)
Hypothyroidism	2 (38.6)	3 (15.7)
Thyrotoxicosis	-	3 (15.7)
Acute Thyroiditis	-	1 (5.2)
Extra-TTB	2 (28.6)	3 (15.7)
Cervical TB	1	-
Pulmonary TB	1	3
Cold nodule in thyroid scan	6 (85.7)	15 (78.9)
Acid Fast Bacillus in FNAC	4 (57.1)	-
Positive PPD skin test	3 (42.9)	-
Epithelioid granuloma	1 (14.3)	-
Langerhans Giant Cell	1 (14.3)	-
Evidences of carcinoma	1 (14.3)	-

Abbreviations: n, number; Pts, Patients; yr, year.

*Data are given as number (percent).

The mean age of definite and suspicious ones was 50.1 and 49.4 years, respectively. In suspicious cases, thyrotoxicosis, hypothyroidism and acute thyroiditis were observed in 7 cases (3, 3 and 1 cases, respectively). The remaining 12 cases (63.2%) were euthyroid. In definite cases of TTB, there were only 2 cases with hypothyroidism and the remaining 5 patients (71.4%) were euthyroid.

Extra-thyroid TB was reported in 2 definite and 3 suspicious patients including 1 cervical and 4 pulmonary tuberculosis. Thyroid scan demonstrated cold thyroid nodule in 6 definite (85.7%) and 15 suspicious (78.9%) patients. In FNAC of 4 definite patients, acid fast bacillus was seen (57.1%). PPD skin test was positive only in 3 patients with definite TTB (42.9%). Microscopically, epithelioid granuloma, Langerhans giant cell and evidences of carcinoma, each was shown in one separate case.

As an example, a thyroid ultrasonography and a chest X-ray of a typical case with definite diagnosis of thyroid tuberculosis in a 48-year old male patient have herein been presented. These are possibly denoting reactivation of a latent pulmonary mycobacterial infection. The thyroid ultrasonography (Figure 1) shows heterogeneity and the presence of a hypoechogenic nodule on the lower part of the right lobe, with a diameter of 55 mm. The nodule is heterogeneous and has cystic degeneration. The chest X-ray (Figure 2) and a computed tomography (CT) of the chest of the patient show a lesion with distinct calcification in the basal region of the right lobe. No other focal lesion is observed in the remaining pulmonary parenchyma. A heterogeneous nodule of the right thyroid lobe with irregular margins is again visualized in the CT, causing mild displacement of the trachea without infiltration. No lymph node enlargement is present.

DISCUSSION

TTB has been recognized since 19th century but since it does not have any consistent symptoms and symptoms of the disease may vary, establishing correct diagnosis may be difficult (33-36). While TTB is a rare condition, it is also one that frequently may go un- or misdiagnosed.

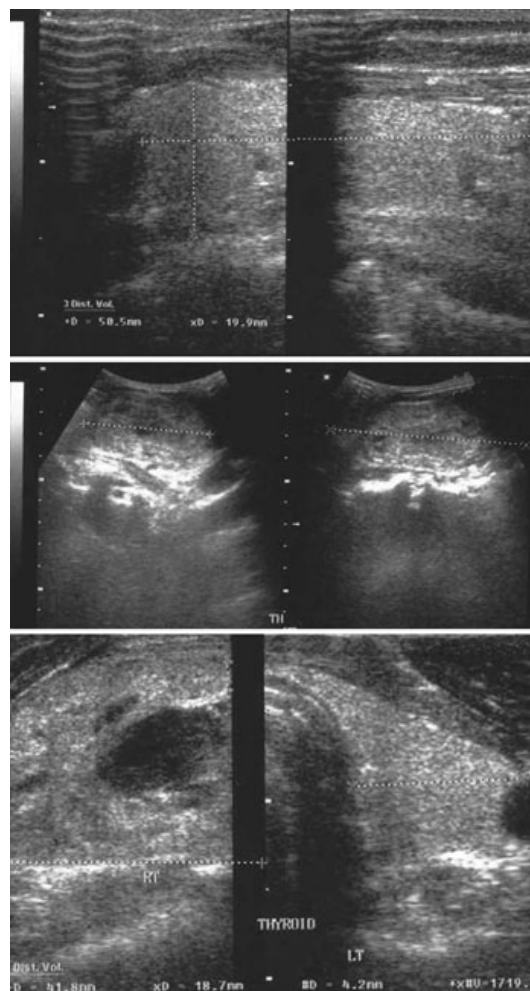


Fig. 1. Thyroid ultrasound showing heterogeneity and the presence of a nodule on the lower right lobe, measuring 55mm. The nodule is heterogeneous and hypoechogenic and has cystic degeneration.



Fig. 2. Patient's chest X-ray showing a lesion with distinct calcification in the lower lobe of the right lung. No other focal lesion is observed in the remaining pulmonary parenchyma.

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A chest X-ray and a tuberculin skin test (PPD) should be performed if mycobacterial infection is suspected. Our results, in agreement with El Malki *et al.* and Terzidis *et al.* (9, 37), showed that FNA of the thyroid gland is a helpful method for confirming the diagnosis and can result in the avoidance of surgery. Definite diagnosis is established by characteristic histological findings such as epithelial cell granulomas with central caseous necrosis, peripheral lymphocytic infiltration and Langhans giant cells. In fact, caseous necrosis is a cytologic finding specific to tuberculosis. The simultaneous demonstration of acid fast bacilli (AFB) makes diagnosis almost certain. On the other hand, the smear may not reveal AFB positive staining, but this fact does not preclude the diagnosis if the histological features and the clinical presentation are compatible (38).

TTB should be differentiated from all the main diseases of the thyroid such as various types of thyroiditis, Graves disease and nodular goiter. It is particularly important to distinguish it from thyroid cancer in order to avoid unnecessary thyroid surgery. The imaging techniques are not very helpful in establishing the diagnosis. Ultrasonography usually reveals a heterogeneous, hypoechoic mass similar to a neoplastic lesion. Contrast-enhanced CT may help localize the caseous necrotic lesion. This finding consists of a necrotic center with a peripheral rim enhancement due to acute inflammation causing thickening of adjacent tissues (“dermal sign”) (39).

The differential diagnosis of tuberculous thyroiditis depends on the presence or absence of local pain. If pain is the predominant clinical finding, the differential diagnosis lies between an infectious form of thyroiditis (bacterial, fungal, *etc*) and subacute granulomatous thyroiditis (De Quervain’s, thyroid sarcoidosis, *etc*). The culture of aspiration material and the distinct histological findings confirm the diagnosis of tuberculous thyroiditis. De Quervain’s thyroiditis may have similar histopathological features with thyroid sarcoidosis and thyroid tuberculosis but caseous necrosis is absent. In the event that pain is absent, thyroid tuberculosis might be falsely diagnosed as thyroid malignancy; these conditions may even coexist (40). Rarely a tuberculous abscess of the supra-sternal

notch region may cause dysphagia and mimic an anterior neck mass or thyroid tumor.

Treatment of thyroid tuberculosis consists of antituberculous drugs combined with surgical removal of the affected parts of the thyroid gland (4) or surgical drainage (7). Lately it has been recognized that antituberculous drugs alone could be efficacious (14, 41). A combination drug therapy consisting of isoniazid, rifampicin and vitamin B6 with or without the addition of ethambutol or a fluoroquinolone seems to be effective. This can lead to significant clinical improvement and avoidance of surgery in the event that preoperative diagnosis is established (13). Finally, if a thyroid tuberculous abscess is present, drainage combined with antituberculous drug therapy is considered as sufficient and further surgery is rarely required (42).

According to similar studies such as Simkus (36), the consequences strongly suggest that tuberculosis should be considered in the differential diagnosis of anterior cervical swellings. FNAC can help in confirming the diagnosis but final confirmation is made by histopathological and biochemical examinations. Patients respond well to surgery with antituberculous drugs (43, 44). However, more investigation is warranted to better understand the definition, diagnosis and treatment of TTB among thyroid problems.

Conflict of interests

The authors declare that they have no competing interests.

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