

## Thyroid tuberculosis

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**Key words:** thyroid, tuberculosis, infection, thyroiditis, aspiration.

**Summary.** The aim of this article is to collect and to review reference data about thyroid tuberculosis from all-over the world and to analyze urgency and changeability of this problem since 19<sup>th</sup> century until now. Data show that there are cases of thyroid tuberculosis still occurring in many countries of the world, including highly developed countries. It turned out that the disease can manifest in various ways and that it does not have specific symptoms characteristic only to thyroid tuberculosis. The main method for establishing diagnosis is fine-needle aspiration with subsequent bacterioscopic, bacteriological or biological investigation. Still, for verification of diagnosis, ultrasonography, even computerized tomography and the newest serological diagnostic methods of tuberculosis may be necessary. In conclusion, thyroid tuberculosis should be differentiated from other diseases of thyroid: various types of thyroiditis, Graves disease and nodular goiter. It is particularly vital to distinguish thyroid tuberculosis from thyroid cancer; in attempt to avoid unnecessary thyroid surgery. While treating thyroid tuberculosis, there is a choice of thyroid surgery, antituberculous drugs and repeated puncture drainage procedures. Sometimes these methods can be combined.

### Introduction and historical data

Combination of thyroid disorders and tuberculosis has been known for a long time. In 1862 Lebert reported the first case of tuberculous thyroid involvement in a patient with disseminated tuberculosis (1). In 1878 Chiari described 7 cases of microscopic involvement of thyroid in patients who died from disseminated tuberculosis (1). Bruns in 1893 described the first case of tuberculous thyroiditis diagnosed in a middle aged woman with a rapidly enlarging goiter, who had cervical lymphadenopathy but no evidence of pulmonary tuberculosis (1). The first report of successful drainage of tuberculous thyroid abscess was by Schwartz in 1894 (1). Five cases of thyroid tuberculosis were described in 1926 by Coller and Huggins in a series of thyroid-operated patients (1). A historical border should be outlined between thyroid tuberculosis before the discovery of anti-tuberculous drugs in 1944 and after it: upon administration of these drugs, epidemiology, symptomatology and methods of treatment of thyroid tuberculosis changed considerably.

Tuberculosis and thyrotoxicosis have many common symptoms. Therefore sometimes it is difficult to find out which disease has come first, which of them is dominating and which one is to be treated first. Thus the term of "thyroid tuberculosis" has been formulated (2). One should make difference between tuberculosis in general which can affect thyroid gland and hinder its function due to intoxication, and tuberculosis of the thyroid gland

when the tuberculous agent is located in the gland and it directly damages thyroid tissue and alters its function.

Dr. A. Aleknavičius was the first to describe thyroid tuberculosis in Lithuania in 1935 (3).

### Epidemiology

Most authors mention thyroid tuberculosis 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 according to its symptoms and by insufficient knowledge of physicians on the subject of differential diagnostics of thyroid tuberculosis (4). The true incidence of the tuberculous thyroiditis is difficult to determine, as there are considerable differences in the criteria used to establish the diagnosis in these cases (5).

### Pathogenesis

Tuberculosis may involve thyroid gland in two main forms. One of them is miliary spread to thyroid gland as a part of generalized dissemination, but this form has never been shown to give rise to clinical thyroid disease. Alternatively, focal caseous tuberculosis of thyroid may occur, presenting as localized swelling mimicking carcinoma, as cold abscess appearing superficially or very rarely – as an acute abscess (1, 6–8). Thyroid tuberculosis can also manifest itself as a common thyroid nodule or lump (1, 9) or as a nodule with a cystic component (10). Therefore

there are referrals in modern scientific literature stressing that tuberculosis of the thyroid gland should be included in the differential diagnosis of thyroid masses (11–13), not excluding children (10). Chronic fibrosis of thyroid has been described in association with tuberculosis particularly by European authors (1).

Spread of the disease to the thyroid occurs by hematogenous or lymphogenous route or directly from larynx or tubercular cervical lymphadenitis (1).

### Pathohistological findings

Four morphological variations of thyroid tuberculosis are distinguished: 1) multiple tubercles in case of miliary tuberculosis, 2) solitary and sometimes merging tubercles, 3) foci of caseation necrosis (4) or cold abscesses (13), and 4) cicatrized tubercular foci (4). Cases of thyroid amyloidosis occurring during the course of long-lasting cavernous pulmonary tuberculosis are described (14). Most authors indicate predominance of productive thyroid tuberculosis (4). Histological demonstration of epithelial cell granulomas with peripheral lymphocytic cuffing, Langhans giant cells and central caseation necrosis prove the diagnosis of thyroid tuberculosis (1).

### Course of the disease

Two variations of course of thyroid tuberculosis are known. The first one resembles toxic goiter or acute thyroiditis (4). This is not surprising as the role of tuberculosis is well known for many years in etiology (14) and pathogenesis of thyrotoxicosis, particularly in young patients (15). On the other hand, it is admitted that tuberculous infection is one of the agents causing acute thyroiditis (14). The second variation has chronic or subacute course when the disease develops gradually, after penetration of infection into pre-existing diffuse or nodular goiter. In this case new symptoms of the disease occur or previous symptoms are exacerbated (4). According to Werner's classification, this is chronic nonsuppurative thyroiditis, encompassing infectious and infiltrative processes, tuberculosis among them (16, 17). Rare presentation of thyroid tuberculosis is pyrexia of unknown origin (18).

### Diagnosis

Fine needle aspiration or aspiration needle biopsy is performed in order to detect tuberculosis of the thyroid gland (11, 12, 19, 20). This is an effective method to confirm the diagnosis (13). Diagnosis is made with acid-fast bacilli staining and culture from fine needle aspiration material (11). 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 (21). Another case of thyroid tuberculosis showed multifocal, heterogeneous, hypoechoic lesions with ill-defined margins in both lobes of the thyroid and several small, oval lymph nodes in the left lower internal jugular chain (22). But pre-operatively and even during surgery correct diagnosis is established rarely, and thyroid tuberculosis is diagnosed basically by histological findings during examination of surgically removed thyroid material (1, 8, 23, 24).

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) (25) to the most modern rapid tests – serological assays, when antibodies to *Mycobacterium tuberculosis* are detected in human serum or plasma (26, 27). It is important to know that in order to identify tuberculosis infection, it should be found in sufficient concentration in the examined material, and this concentration is different for each diagnostic method. Cytological investigation allows to detect *Mycobacterium tuberculosis* provided there are not less than 10000 microorganisms in each ml of the examined material; culture from the investigated material is effective when there are not less than 50 tuberculous bacilli in each ml; biological test (infecting susceptible animals with tuberculosis) is informative in case when there are 1–5 such bacilli in each ml; polymerase chain reaction gives a positive result when each ml of the tested material contains solitary bodies of microorganisms (25).

The following prerequisite conditions present for diagnosis of thyroid tuberculosis were described in early 1939: 1) demonstration of acid fast bacilli within thyroid, 2) a necrotic or abscessed gland, 3) demonstration of tuberculous focus outside. Histological and bacteriological confirmation is adequate and fulfillment of third criterion is not essential (1). Nowadays it is stated that acid-fast bacilli are not always found, therefore multiple coalesced and caseated epithelioid cell granulomas along with giant cells are considered to be diagnostic of tuberculous affection of the gland (28). However, it is obligatory to stress that this is the specific reply of human organism to the tuberculous agent. Massive use of antibacterial drugs has caused alteration of the course of tuberculosis and adjustment of mycobacteria to antituberculous drugs; therefore the immune response of human organism to this agent may be paraspecific or even non-specific. In the latter case only common features characteristic to inflammation can be found in any organ, including the thyroid gland: these are macrophages, lymphocytic infiltrations, etc. (29). Within tubercle (tuberculous granuloma), beside characteristic epithelioid and giant cells, one

can find macrophages, lymphocytes, plasmocytes, monocytes and fibroblasts (cells producing connective tissue) (29), and in the case of autoimmune thyroiditis, beside characteristic Hurthle cells, one can also find the same infiltration of thyroid with lymphocytes, plasmocytes and increased development of connective tissue (30).

These data prompt to reconsider whether thyroid tuberculosis is as rare as it is claimed (1, 19, 28, 31, 32). An essential question occurs – is it rare disease or rarely diagnosed (33)?

### Differential diagnosis

The first thyroid tuberculosis course variation should be distinguished from toxic goiter (thyrotoxicosis) and acute thyroiditis, the second – from thyroid cancer, Riedel thyroiditis (4) and thyroid nodules (1, 11–13). Lymphocytic infiltration and presence of granulomas may also be seen in sarcoidosis, subacute thyroiditis and goitrous autoimmune thyroiditis (5). There is a description of cases of isolated tuberculosis found in surgically removed goiter without any signs of tuberculosis in other organs before surgery and after it. In fact it was de Quervain thyroiditis (34). The most distinct feature of subacute thyroiditis is the granuloma, consisting of giant cells clustered about foci of degenerating thyroid follicles; due to resemblance with granulomatous tissue reaction in thyroid tuberculosis, the term of pseudotuberculous thyroiditis arose (35). Sometimes thyroid tuberculosis is mistakenly thought to be carcinoma (36, 37), however there are reports of tuberculous thyroiditis coexisting with thyroid carcinoma in the same patient (38, 39). A differentiation from thyroid cancer is essential to avoid unnecessary thyroid surgery (5).

### Treatment

Treatment of thyroid tuberculosis is complex: administration of antituberculous drugs is combined with surgical removal of the affected parts of thyroid gland (1, 4) or surgical drainage (5). Repeated puncture drainage and antituberculous drugs are the least invasive mode of treatment (40). Lately treatment with antituberculous drugs has been recognized as the preferred method (13). In case of tuberculous abscess in the thyroid, drainage is sufficient; surgery is required rarely (13).

### Conclusions

Thyroid tuberculosis has been an important problem since 19th century. Tuberculous infection spreads to the thyroid by lymphogenous, hematogenous route or directly from adjacent organs. Thyroid tuberculosis does not have any specific symptoms. Symptoms of the disease may vary, thus causing difficulties in establishing correct diagnosis. Fine needle aspiration is the main diagnostic method to verify thyroid tuberculosis. Acid-fast bacilli staining and culture from aspirated thyroid material sometimes are insufficient to detect tuberculosis mycobacteria, therefore the newest and the most modern tests may be necessary to identify them. The disease can cause only non-specific alterations in the thyroid. Thyroid tuberculosis should be differentiated from all the main diseases of the thyroid. It is particularly important to distinguish it from thyroid cancer in order to avoid unnecessary thyroid surgery. Antituberculous therapy and surgical removal of affected parts of the thyroid gland are the most common methods of treatment of thyroid tuberculosis. Repeated puncture drainage in combination with antituberculous drugs is applied nowadays as well.

## Skydliaukės tuberkuliozė

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**Raktažodžiai:** skydliaukė, tuberkuliozė, infekcija, tiroiditas, punkcija.

**Santrauka.** Darbo tikslas. Apžvelgti pasaulinės mokslinės literatūros duomenis apie skydliaukės tuberkuliozę, išnagrinėti šios problemos aktualumą bei kintamumą nuo XIX amžiaus iki šių dienų. Į apžvalgą įtrauktos citatos iš mokslo žurnalų straipsnių bei monografijų. Paaiškėjo, kad šios ligos klinika labai įvairi, ji neturi tik jai vienai būdingų simptomų. Pagrindinis tyrimo metodas – skydliaukės punkcija plona adata ir gautos medžiagos bakterioskopinis, bakteriologinis arba biologinis ištyrimas. Bet diagnozei patikslinti gali prireikti echoskopijos arba net kompiuterinės tomografijos bei naujausių serologinių imunofermentinių tuberkuliozės diagnostikos būdų. Skydliaukės tuberkuliozę reikia skirti nuo kitų skydliaukės ligų: tiroiditų, toksinio ir mazginio gūžio. Ypač svarbu skirti nuo skydliaukės vėžio siekiant išvengti nereikalingos skydliaukės operacijos. Gydant skydliaukės tuberkuliozę, tenka rinktis operaciją, prieštuberkuliozinius vaistus arba gydymą pakartotinėmis skydliaukės punkcijomis. Kai kada šiuos gydymo būdus reikia derinti.

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