Lethal pulmonary thromboembolism associated with decreased thyroid hormone levels

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SUMMARY

Thyroid pathology is rarely involved in the pathogenesis of sudden death in young people. We report here the cases of two young patients with decreased levels of thyroid hormones whose death was caused by an increased thrombotic status, with venous thrombosis and pulmonary thromboembolism. In both cases the thyroid pathology was not considered as the underlying cause of death as the association between this condition and venous thrombosis is still debatable. However its presence may be considered a circumstantial factor, which could increase the severity of the disease and subsequently the lethality rate in pulmonary thromboembolism. An increased awareness for hypothyroidism or subclinical hypothyroidism in clinical practice may lead to a decrease in mortality secondary to thromboembolic disease. Also, increased awareness for thyroid pathology during forensic autopsy in sudden deaths may lead to potentially significant results, that could explain some of the sudden death with an unknown cause, and decrease the number of the so called blank autopsies. Arch Endocrinol Metab. 2015;59(4):355-8

INTRODUCTION

Thyroid pathology is rarely involved in the pathogenesis of sudden death in young people, and usually, when this is the case, is associated with acute changes of thyroid hormone blood levels. There are three main thyroid causes of sudden death that are known and used in explaining the causes of death: thyrotoxicosis, myxedematous coma (1) and, as of recently, lymphocytic thyroid infiltration (2). Coagulation disorders associated with thyroid disease are usually mild and not associated with sudden death. There are some studies showing an increased risk for unprovoked deep venous thrombosis in patients with subclinical hypothyroidism (3-5), but there is none, to our knowledge, showing a correlation between hypothyroidism, deep venous thrombosis and sudden death. Overt hypothyroidism is known to be associated with an increased risk of bleeding (6). Pulmonary thromboembolism is a relatively frequent cause of sudden death (7-10), but not always with an identifiable origin. The purpose of this article is to present two cases in which hypothyroidism was identified in patients with sudden death due to venous thrombosis complicated with pulmonary thromboembolism.

CASE PRESENTATION

Case 1

A 42-year-old female, complaining of chest pains for three weeks died suddenly at home. The family denied the presence of any other symptoms or preexistent diseases.

Autopsy findings. External examination found nothing except for a slightly increased circumference of the superior part of the right calf and bilateral 2nd degree calf varicosities. Internal examination revealed cerebral edema, a moderate degree of myocardial sclerosis, multinodular thyroid, bilateral pulmonary atelectasis, massive, bilateral pulmonary thromboembolism, hemorrhagic ovarian cysts, moderate adrenal hyperplasia, a Copper based intrauterine device (IUD), and a right saphenous thrombosis with an inflammatory reaction (Figure 1).

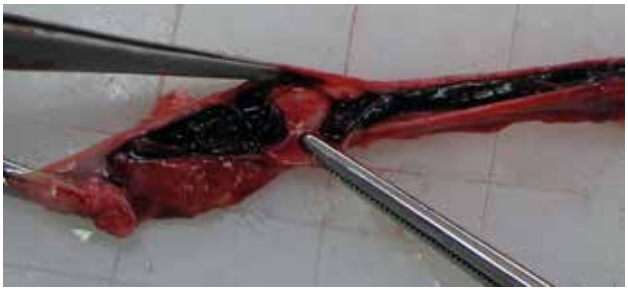

Figure 1. Saphenous vein thrombosis.

Histology findings. In both pulmonary arteries we identified thrombo-emboli with Zahn lines and hematic lysis. Right saphenous vein contained a mixed thrombus with Zahn lines and hematic lysis. The wall of the right saphenous vein contained a polymorph inflammatory reaction. Thyroid examination revealed a colloid-cystic multinodular goiter, with a rich inflammatory reaction containing mostly lymphocytes and plasma cells, with formation of germinative centers, suggestive for Hashimoto's thyroiditis. Other organs didn't have significant pathological changes. Thanatochemistry examination revealed a total T3 value of 3.15 ng/mL (normal range, n.r. 0.58-1.59), a total T4 value of 5.45 ug/dL (n.r. 4.87-11.72), a TSH value of 67.3 uUI/mL (n.r. 0.35-4.94), and a CK-MB of 244 U/L (n.r. in the pericardial fluid 105-154).

Case 2

A 15-year-old boy, basketball player, was brought by the Ambulance at the Emergency Department with cardiorespiratory arrest installed five minutes before their arrival. An ECG done at arrival showed electromechanical dissociation. The patient was successfully resuscitated but remained in a deep coma (GCS = 3). The cause of the cardiac arrest has proven to be a massive thromboembolism, for which was started emergency thrombolysis. In the first hour after thrombolysis the patient has numerous episodes of electromechanical dissociation and asystole, resuscitated each time. However, in less than 24 hours after admission the patient entered in multiple organ failure and was pronounced dead. In his personal history is to be noted a prior orthopedic intervention about a month ago for femur slipped epiphyses, followed by cast immobilization with abduction bar at the knee level.

Autopsy findings. The right pulmonary artery presented a massive, adherent thrombo-embolus. Right lung had moderate atelectasis and stasis. We also found an enlarged thyroid, hepatic and kidney stasis, slipped epiphyses of the right femur, consolidated and bilateral thrombosis in the popliteal veins. Histology findings revealed a lung with acute respiratory distress syndrome (incipient exudative phase), severe septum stasis, alveolar edema, areas of pulmonary atelectasis, and a relatively recent thromboembolism, partially occlusive in major right pulmonary branches associated with hemorrhage around the affected pulmonary vessels (Figure 2). The thyroid was normal. Popliteal veins showed thrombophlebitis with incipient organization. Thanatochemistry examination revealed a total T3 of 0.44 ng/mL, a total T4 of 2.05 ug/dL, total TSH of 11.62 uUI/mL, anti-peroxidase antibodies of 13.3 UI/mL (n.r. < 12), and CK-MB from the pericardial fluid of 14945 U/L.

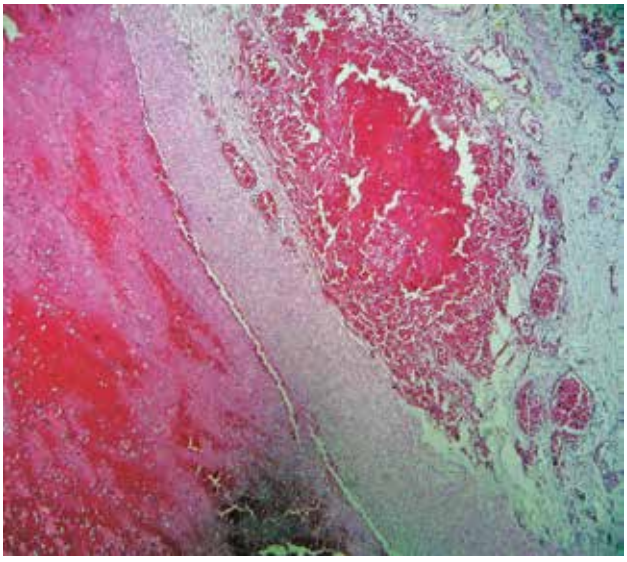

Figure 2. Pulmonary thromboembolism, with partial lysis and hemorrhage around the vessel.

DISCUSSION

Subclinical hypothyroidism is defined by increased TSH levels associated with normal free T3 and T4 levels, and the absence of clinical symptoms. Clinical diagnosis of subclinical hypothyroidism is suggested by a slight increase in the TSH levels (usually up to 10-20 uUI/mL), associated with a stable thyroid function for weeks or more, a normal hypothalamic-pituitary-thyroid axis, and in the absence of recent or ongoing severe illness (11-13). It affects between 1 and 15% of the general population, is more frequent in women, elderly and persons with a positive family history for thyroid disease (14). Thyroid hormones can be used with caution for the diagnosis of either hypo or hyperthyroidism after death. T4 levels tend to decrease starting with 2.75 hours af-

ter death (15,16) except for cases with prolonged agony (when thyroxin levels may start decreasing before death) (17). Therefore high postmortem T4 levels can be used to diagnose hyperthyroidism. T3 levels tend to have a variable course after death (16) (values either higher than before death, mainly caused by T4->T3 conversion or lower, mainly due to bacterial degradation) and therefore they cannot be used in postmortem diagnosis of thyroid dysfunction. TSH levels however are known to be stable in serum at least 24 hours after death and are positively correlated with the values before death (15), being useful for the diagnosis of either hypothyroidism or hyperthyroidism. In our cases, the first patient had a TSH value of 67.3 uUI/ml with an elevated T3 value and a normal T4 and the second one had a slightly high TSH value with decreased values of T3 and T4. In both cases, even if we identified increased values of TSH, we could not specifically state that the patients had hypothyroidism or subclinical hypothyroidism.

After death the vascular department of the body suffers profound changes, making the analysis of clotting disorders extremely difficult. Immediately after the cessation of the blood flow blood cells tend to settle under the action of gravity; this, together with increased fluid losses to the perivascular tissues significantly increases the hematocrit (often reaching values of 80% or more) (18). Platelets and serum proteins retain their normal function a few hours after blood cessation; afterwards stasis, hypoxia, decreased pH, and endothelial alterations lead to the formation of postmortem blood cloths concomitant with fibrinolysis processes (19,20). In deaths in which increased levels of catecholamine or plasminogen activator are released in the agonal period (as is the case with most sudden deaths) the thrombolytic events are increased and the cadaveric blood is liquid; if the agonal period is prolonged thrombotic events are dominant, leading to an increased density of postmortem clots (21-23). For this reason we could not perform coagulation tests, that might have revealed the presence of additional risk factors for thromboembolism. The first case did not have any significant risk factors for thromboembolic disease (except for obesity); therefore the presence of a hypothyroidism/subclinical hypothyroidism may be considered a circumstantial factor, explaining the unfavorable prognosis. In the second case, the patient had a significant risk factor for the development of thrombo-embolic disease (orthopedic surgery followed by cast immobilization with bed-rest), able to explain by itself the unfavorable course. However the presence of an altered thyroid status may have increased the severity of the disease.

CONCLUSIONS

In both cases hypothyroidism/subclinical hypothyroidism was not considered as the underlying cause of death as the association between these diseases and venous thrombosis is still debatable [see for details a discussion by Hostiuc and cols. (14)], and overt hypothyroidism is known to be associated with an increased risk of bleeding. However the presence of an altered thyroid status may be considered a circumstantial factor, which can increase the severity of the disease and subsequently the lethality rate in pulmonary thromboembolism. Prospective studies with a larger number of patients should be conducted in order to identify more precisely the risk of deep venous thrombosis and pulmonary thromboembolism in patients with an altered thyroid status.

An increased awareness for subclinical hypothyroidism in clinical practice may lead to a decrease in mortality secondary to thromboembolic disease. Also, increased awareness for thyroid pathology during forensic autopsy in sudden deaths may lead to potentially significant results, able to explain some of the sudden death with an unknown cause (and reduce the number of the so called blank autopsies).

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