

<p align="center">Medullary Thyroid Carcinoma, Misdiagnosed as Subacute Thyroiditis and Role of Calcitonin Measurement</p>		<p align="center">Healthcare</p> <p>Keywords: Medullary thyroid carcinoma, calcitonin, fine needle aspiration biopsy.</p>
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<p>Abstract</p> <p>The thyroid nodules are found often in the clinical practice in adults. The clinical importance of thyroid nodules is to exclude thyroid cancer, which occurs in 7-15 % of cases with thyroid nodules depending on age, sex, radiation exposure history, family history and other factors. We present a clinical case, misdiagnosed as a subacute thyroiditis, in which the lack of clinical doubt for suspecting the thyroid cancer, despite the negative result of fine needle aspiration biopsy of thyroid nodule and not measuring the calcitonin level, did not allow the diagnosis of medullary thyroid carcinoma (MTC). Based on this clinical case and also the review of literature, we recommend the routine measurement of calcitonin in screening the thyroid nodules, for the early diagnosis of the medullary thyroid carcinoma. Despite the negative result for malignancy of fine needle aspiration biopsy (FNA) of nodule, if the nodule has some echographic signs, characteristic of malignancy, the thyroid surgery must be recommended.</p>
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Introduction

The thyroid nodules are often found in the adult population. About 4-7% of the adults have thyroid nodules in palpation and this percentage is higher in the echographic examination, because of its high sensitivity. The clinical importance of thyroid nodules is to exclude thyroid cancer, which occurs in 7-15% of cases with thyroid nodules, depending on age, sex, radiation exposure history, family history and other factors (1,6). Differentiated thyroid cancer (papillary and follicular cancer) comprises the vast majority, more than 90% of all thyroid cancer (7). Medullary thyroid carcinoma accounts for 5-8% of all thyroid cancer (8). MTC occurred either sporadically or in a hereditary form such as multiple endocrine neoplasia type 2A and 2B, and the related syndrome familiar medullary thyroid carcinoma. Sporadic MTC occurs between the fourth and sixth decades of life (9).

The Case: A woman, 62 years old, presented one year ago to the endocrinologist, with pain in the anterolateral region when she palpated the neck, or pressed it on the left side. She referred a 6 points pain (for pain assessment scales from 0 to 10), neither fever, nor weight changes. The blood pressure and heart rate were normal. A thyroid ultrasound was performed and showed a heterogenic structure in both lobes and a solid hypoechoic nodule with dimensions 1.4 x 1.21 cm, with microcalcifications, irregular borders and marked intranodular blood flow, and also a heterogenic formation near the jugular vein, its dimensions 2.16 x 1.34 cm. The analysis of TSH, anti-TPO antibodies, anti-thyroglobuline antibodies and the ultrasound-guided FNA-biopsy of the nodules were performed. Calcitonin wasn't checked. Biochemical analyses, including whole blood count, were in the normal range. The erythrocyte sedimentation rate (ESR) was 25 mm/h (normal range <15).

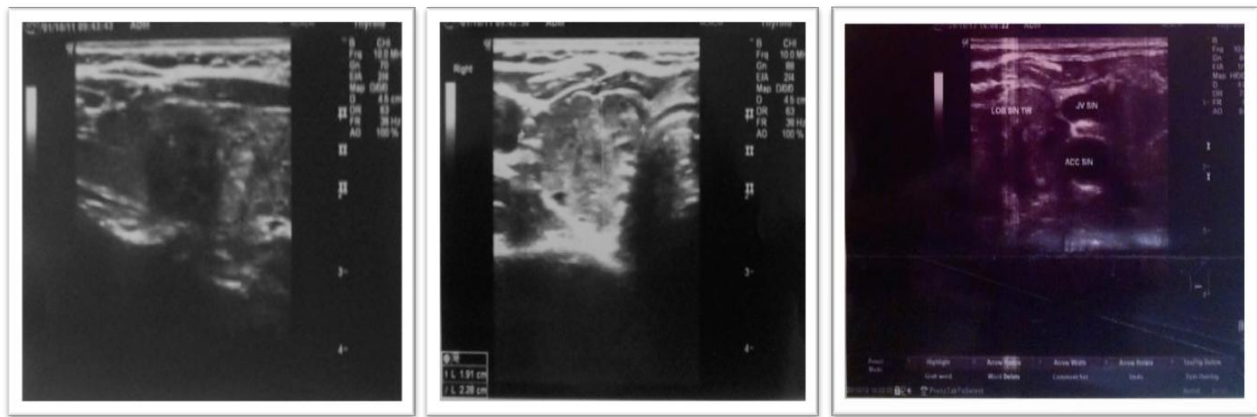
Table no 1: Laboratory data

Analysis	Values	Normal Range
TSH	1.19 mIU/ml	3.5-4.2
Ab anti TPO	12.26 UI	< 70
Ab anti Thyroglobulin	669.7 UI	< 70
FNAB of thyroid nodule	Negative for malignancy disease.	
The FNA – Biopsy of the lymph node near jugular vein	Wasn't performed.	

The physician concluded the diagnosis of subacute thyroiditis in a patient with previously lymphocytic thyroiditis and recommended treatment with naproxen for two weeks and follow-up after six months. The patient didn't return to the doctor and lost the follow-up.

Figure no1: Thyroid ultrasound image (heterogenic structure in both lobes and a solid hypoechoic nodule with dimensions 1.4 x 1.21 cm, with microcalcifications, irregular borders and marked intranodular blood flow. In the right image of lymph node with characteristics of metastatic lymph node).

Figure nr.1: Thyroid ultrasound image



One year later, the patient was admitted to our hospital with pain in the neck, which became stronger even at very soft touch. The thyroid was hard, with one painful lymph node near the jugular vein. During the palpation of the lymph node, she referred an 8 point pain (from 0-10 points). The patient didn't refer flushing or diarrhea. The hormonal thyroid function, calcitonin, CEA, thyroid ultrasound, ultrasound-guided FNA-biopsy of the nodule and lymph node, and contrast enhanced magnetic resonance imaging of the neck were performed.

Table no 2: Laboratory data (after one year)

Analysis	Values	Normal Range
TSH	2.0 mIU/ml	3.5-4.2
FT4	1.4 ng/dl	0.89-1.76
CEA	36 ng/ml	<5.0
Calcitonin	2604,0 pg/ml	< 5
FNA-B of thyroid nodule and the FNA-B of the lymph node near jugular vein	FNAB of thyroid nodule, malignant disease. The result of FNAB of the lymph node: metastatic cancer, probably thyroid carcinoma (Type??)	

Based on clinical and laboratory data, the diagnosis of thyroid cancer was suspected. After the results of calcitonin and FNA-biopsy, the patient underwent surgery. The total thyroidectomy with lymph node dissections, also with removal of two parathyroid glands, which were infiltrated by cancer, was performed. The histological examination showed at least two neoplastic nodules, their size 1cm and 2.2cm, the latter showed marked extrathyroidal extension into the adipose tissue with lymphovascular and perineural invasion. The remainder of the lobes showed lymphocytic thyroiditis. Two of the four lymph nodes were metastasis of the thyroid cancer. The immunocytochemical staining was positive for CK8, mCEA and calcitonin and absence of thyroglobuline expression.

Histological diagnosis: Medullar carcinoma of thyroid PT4N1Mx. To exclude the MEN (multiple endocrine neoplasia), the analysis of DNA of RET proto-oncogen was performed. The results were without mutation of exone 8,9,10,11,13,14,15 and 16.

Figure No 2: On the left lymph node FNA-Cytology and on the right histological examination of MTC

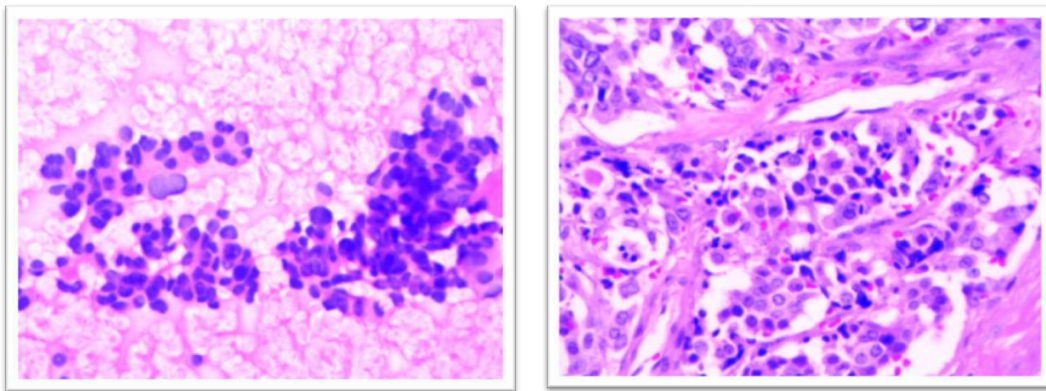
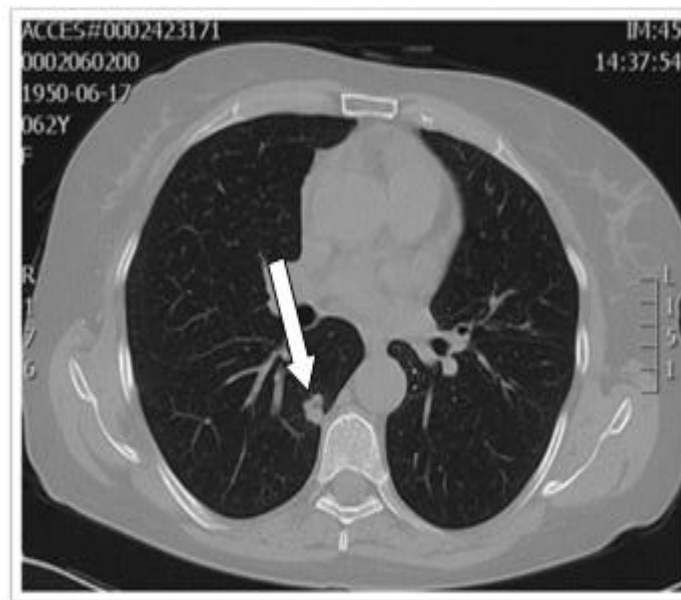


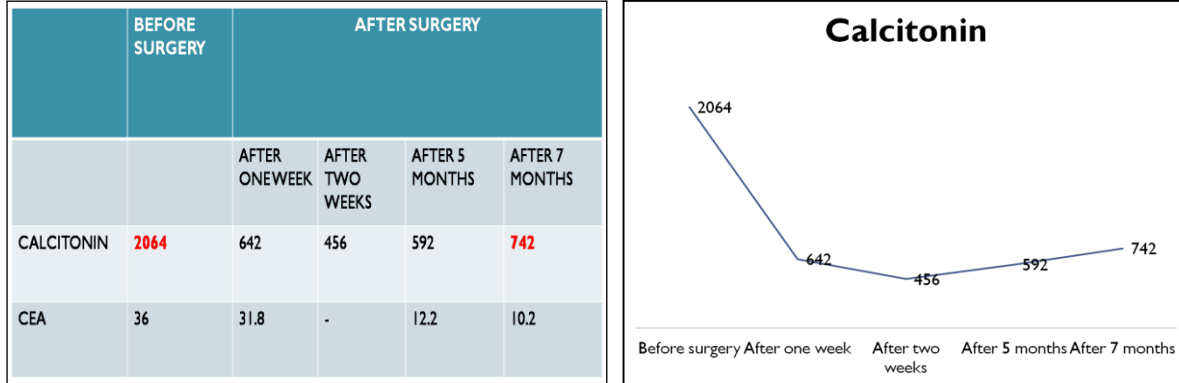
Figure no.3: CT Scanned thorax (lung metastasis from thyroid cancer)



The values of calcitonin and CEA decreased after surgery and stayed constant during follow-up. Seven months after the surgery the patient continued the treatment with Levothyroxine, calcium, cholecalciferol. Even the imaging data from neck ultrasound, chest computed tomography scan, liver magnetic resonance imaging and

bone scan were without evidence of new metastasis and the lung metastasis which was present even before surgery was without changes of dimensions. We continued the follow-up of the patient and evaluated even the calcitonin double time.

Figure no.4: Calcitonin and CEA values during follow up



Discussions

We presented a clinical case with MTC carcinoma, misdiagnosed as subacute thyroiditis. An elevated level of serum calcitonin is a highly sensitive marker for MTC, but is not especially specific (10,11). The routine measurement of calcitonin to screen for MTC is still controversial, but in our case the lack of measurement of calciton and CEA and not taking the decision of thyroidectomy, despite the negative results of FNA-biopsy in the first clinical examination, delayed the exact diagnosis. In the Essig GF study in 2013, among multiple international centers, the diagnostic accuracy of fine-needle aspiration biopsy (FNAB) to preoperatively diagnose MTC had low sensitivity of cytological evaluation alone in sporadic medullary thyroid cancer, limits its ability to command an optimal preoperative evaluation and initial surgery in over half of affected patients (12).

Conclusions

Based on the report of this clinical case and the calcitonin sensitivity in MTC, we recommend a routine measurement of calcitonin level, alongside with the use of the fine needle aspiration biopsy of the thyroid nodules, despite the low percentage of MTC among thyroid carcinomas, with the aim of increasing the accuracy of diagnosis and the therapeutically decision in the thyroid nodules.

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