

## The Interest of Calcitonin in The Diagnosis And the Treatment of Medullary Thyroid Cancer

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**Summary:** Thyroid medullary carcinoma (MTC) is a rare cancer representing only 5 to 10% of thyroid cancers. Early and adequate surgery is capable of healing in 40% to 60% of cases. Plasma calcitonin is a sensitive and specific marker, useful for diagnosis, healing and evolution. Our work is a retrospective study of 25 patients with medullary thyroid carcinoma, followed at the endocrinology department of the CHU BEO. It was about 16 women and 09 men. The average age was 41.5 years (19 - 75 years). Nodular goitre was the main reason for consultation. Preoperative determination of calcitonin was performed in 68% of our patients. The familial form of MT C integrating into multiple familial neoplasia type 2A (MEN2A) was observed with a frequency of 52%. The follow-up of our patients was based essentially on the calcitonin dosage of base its elevation was in favor of presence of metastases. 36% of our patients are in remission, ganglion metastases observed with a frequency of 36%, and distant metastases found in 28%. The distance metastasis in our patients is dominated by pulmonary, bone metastases.

**Keywords:** MTC, TCT, surgery, MEN 2a , metastases

### I. Introduction

Medullary Thyroid Cancer (MT C) is a rare and severe cancer. It accounts for 5-10% of thyroid cancers. Its incidence in nodular pathology is around 1-2%. It occurs in 2 forms ; It can be sporadic in the majority of cases, or familial in nearly 30-35% of cases; In this case, it is transmitted in an autosomal dominant mode with variable penetrance. It is then integrated into multiple endocrine neoplasia type 2 (MEN 2a). The diagnosis of MTC is multiple: thyroid nodule, cervical adenopathy (ADP), metastasis (pulmonary, bone, and hepatic), an associated pathology (pheochromocytoma, hyperparathyroidism) or in a fortuitous discovery on a piece of thyroidectomy The calcitonin dosage is very specific; It allows for early diagnosis and especially adequate care. Treatment of MTC is primarily surgical ; Follow-up is based on the calcitonin dosage, and its elevation indicates local recurrence and or presence of metastases The aim of this study is to clarify the clinical and evolutionary profile of MTC and the value of basic calcitonin in the follow-up.

### Population, methodology

This is a retrospective study of 25 patients with medullary thyroid carcinoma hospitalized in the endocrinology department. All patients underwent complete clinical and paraclinic assessment including calcitonin, thyroid (FT4, TSH), cervical ultrasound, thoracoabdominal computed tomography and bone scintigraphy as well as a genetic study of the RET gene ; After surgery, all patients were regularly re-evaluated clinically, biologically by the determination of calcitonin and radiologically according to the biological results

### II. Results

The average age of our patients is 41.5 years with extremes of 19 and 75 years. The average age for men is 43.11 years the average age for women is 40.37 years. Women are much more affected than men: 16 for women against 09 men, with a sex ratio of 02 women for 01 men The preoperative diagnosis of CMT by calcitonin was 68% (n: 17 patients); It was performed in 50% as part of a family survey. Preoperative baseline TCT was greater than 100 ng / ml in 12 patients and less than 100 µg / ml in 5 patients. For the rest of the patients, MT C was diagnosed postoperatively;

The mode of revelation was cervical ADP associated with goitre in 4 patients (17%), and pheochromocytoma in 03 cases (17%), in patients with MEN2A. MTC was sporadic in 8 patients. The familial form integrating within asymptomatic MEN 2A, was found in 13 patients (52%) including 5 cases index. The most frequent mutation is the C634R germ mutation. The remaining 4 patients, in whom the genetic study is not available, did not allow the appearance of other endocrinopathies of MEN 2A, awaiting the results of the genetic study total thyroidectomy with lymph node dissection was performed in patients with high preoperative TCT. In the other patients (15 patients or 60%) a surgical recovery was indicated The preoperative baseline TCT was greater than 100 ng / ml in 12 patients and less than 100 pg / ml in 5 patients.

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The follow-up of the patients was regular with a calcitonin dosage of base. Immediate and postoperative TCT was normal (baseline TCT <6pg / ml and after calcium load <100pg / ml) in all patients without metastases, of which there were 9 patients. Ganglion metastases (cervical ultrasound) were frequent, found in 09 subjects (36%). These patients had either a persistence of a high level of TCT at the time of diagnosis or a reassistance of the TCT at the time of the appearance of these ADPs, with rates of TCT varying between 25 and 90 pg / ml. Distant metastases were observed in 07 patients (43%). They were pulmonary (in 5 patients) and bone (in 4 patients); One patient had hepatic metastasis.

Immediate postoperative TCT was normal in 3 patients with a rate less than 10 pg / ml, but a marked increase in the rate was observed at the time of distant metastasis with rates > 250 pg / ml. The rate remained high in the postoperative period between 60 and 1100 pg / ml in the 4 patients who metastasized at the time of diagnosis of MTC.

### **III. Discussion**

Thyroid medullary carcinoma (MTC) is a rare tumor that accounts for 5 to 10% of thyroid cancers. MTC is developed at the expense of C, or parafollicular thyroid cells responsible for calcitonin secretion (TCT). The C-cells have a neuro-ectodermic origin and are derived from the formation of the bronchial arches. They come by migration to occupy the part. Upper or middle thyroid lobes. The C cells represent between 1 and 2% of the thyroid cell population, (98 to 99% of follicular cells). In most cases, CMT is sporadic, it is hereditary in 25% of cases and is integrated into multiple neoplasia 2 (NEM2). It is characterized by an autosomal dominant mutation of the RET proto oncogene (1). In our study, the finding of a higher frequency of hereditary form (52%) is due to the inclusion of NEM2A-screened cases. It is a disease that affects the young adult between 40 and 50 years (1). The average age of our patients was 41.5 years. The diagnosis of CMT can be revealed by a thyroid nodule usually of small size of variable age and in euthyroidism. Several elements of the nodule can orient towards the CMT: its sensitivity to palpation, its location at the middle and upper third union of the thyroid, and it is associated in half of the cases with large lymph nodes. (2) Calcitonin is a specific marker of CMT, a high rate of TCT before a thyroid pathology is in favor of a CMT. However, its dosage is not recommended systematically for thyroid nodule exploration, some scholarly societies such as the French Society of Endocrinology (SFE) (2), indicates the dosage of calcitonin at least in one. In case of suspicion of a malignant thyroid nodule (clinical, ultrasound or cytological), and before any surgical intervention for thyroid nodule, when there are symptoms (vasomotor flush, motor diarrhea). In our study the calcitonin dosage was performed in 17 patients (68%), but almost 50% was performed as part of a family survey.

A calcitonin level of > 100pg / ml is very suggestive of CMT (3), this is the case of 70% of our patients, but 23% had a rate between 20pg / ml and 100pg / ml. Our results are similar to those of Scheuba et al. (4), only one patient had a normal baseline TST rate but a positive calcium charge rate (RET mutation).

Several studies have demonstrated a positive correlation between the baseline TCT rate and the largest tumor diameter (TCT sup 1000pg / ml if the tumor exceeds 2.5cm) (5). Our results agree with those of the literature: 8 cases out of 10 with a rate of TCT > 1000pg / ml have a tumoral size greater than 2cm. The TCT rate allows not only to make the diagnosis of CMT and already gives an idea on the evolutionary stage of the disease before the surgery. In the study of Giraudet et al (4), for a median calcitonin at 196 pg / mL, no secondary lesion was associated, but in the ganglion metastases the median calcitonin was higher (565 pg / ml). In our small series, 2 patients among 8 patients with ganglion metastases had TCT rates <100pg / ml, while 6 had a TCT > 500pg / ml.

Giraudet also demonstrated that when there was a visceral metastasis the median calcitonin was at 1510 pg / mL, when there were two to four visceral metastases the median calcitonin was higher at 18450 pg / mL. In our study the preoperative rate did not predict the presence of metastases even with rates > 1500pg / ml.

Postoperative calcitonin predicts the persistence or remission of the disease. An undetectable calcitonin was in favor of complete remission with a 10-year survival in 97.7% (7). In our patients, normalization of TCT was obtained in 17 patients, 68% of whom were in remission for the 8 others: 05 developed ganglion metastases and 03 metastasis at a distance. Calcitonin less than 150 pg / mL is in favor of cervical residual disease because rarely associated with distant metastasis [6,7]. In our patients a rate > 250pg / ml was in favor of the presence of metastasis at a distance. The calcium charge test is indicated primarily for early diagnosis of C-cell hyperplasia, or CMT microplasia in patients with RET mutation, or in the post-operative assessment of a CMT-1 patient (1). In our series this test is not carried out in a systematic way. It allowed us to diagnose a CMT in a patient with a RET mutation with a normal baseline TST.

The treatment of a CMT is primarily surgical. It is essential to approach a trained team. It is necessary to first eliminate an associated pheochromocytoma before thyroidectomy, even in apparently sporadic forms. The surgical procedure advocated consensually is the total thyroidectomy associated with lymph node dissection.

#### **IV. Conclusion**

Medullary thyroid carcinoma (CMT) is a rare but serious disease. Only early diagnosis at a sub-clinical stage and complete surgical excision of the tumor can provide hope for a cure.

Calcitonin is a sensitive and specific marker. It makes it possible to make an early diagnosis, to appreciate the pre and post-operative prognosis and to follow the patient in the long term

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