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Screening in Medullary Thyroid Carcinoma

C. Calmettes*

The four-year experience of the French collaborative study on medullary thyroid carcinoma (MTC) has permitted improvement in family screening by a common discussion of data and a network of coordinators throughout France involved in the detection of new cases. Investigations have been directed at improving the discrimination between sporadic and hereditary forms of MTC and between individuals who have or have not inherited the disease within families. (Henry Ford Hosp Med J 1987;35:99-100)

Most clinicians lack experience in handling cases of medullary thyroid carcinoma (MTC); these tumors are not only rare but also difficult to manage. The French medullary thyroid study group was created in 1982 to collaboratively support research on the disease and to help physicians caring for patients with MTC. A common protocol was established for patient management and for screening within families. Specialized study groups, a central registry of cases, and a network of regional coordinators were created to collect and analyze data.

Tools for Screening

The first objective of the group was to test the various tools for MTC screening. Since the diagnosis depends on calcitonin (CT) assay (1) and/or pathological examination, the efficacy of these techniques was analyzed and the network of coordinators was organized to study family members throughout France.

CT assay

A comparison of the different assay methods used in France confirmed and provided several conclusions:

1. Artifacts can be excluded by means of serial dilutions of the plasma and the use of pentagastrin-stimulated CT test, which also allows discrimination between elevations of CT of thyroid or of ectopic origin (2).

2. Any technique provides good results when the basal CT level is high, but variations in normal values obtained by different assays must be appreciated (3), and at times it is useful to have duplicate aliquots assayed in different immunoassay systems.

3. The pentagastrin-stimulated CT test is efficient in early detection of MTC, but the upper limits of normal must be known for the particular assay used. This provocative test must be performed in all cases of family screening, though an upper age limit needs to be determined [MTC can be still very small even after age 60 (4), as also observed in cases of our group]. This procedure also eliminates artifacts found in using basal CT levels only (5).

Pathology

Realizing the benefits of CT and thyroglobulin (Tg) immunopathological studies in the diagnosis of the type of thyroid cancer (6), these studies were performed in specialized laboratories. The use of these techniques allowed confirmation of the diagnosis of MTC and an estimation of C-cell hyperplasia. Interestingly, this allowed recognition of atypical MTC, especially those with a trabecular, follicular (7), or papillary pattern, or Tg-secreting carcinoma with amyloidosis mimicking MTC.

Research on Criteria for Diagnosing Hereditary Forms of MTC

Efforts of the group have been directed toward determining the criteria by which the hereditary form of MTC can be differentiated from the sporadic form. If screening efforts can be concentrated to the families of those with the hereditary disease, much effort of screening can be saved and the costs decreased.

Family screening

Clinical screening may not always discriminate between the hereditary and sporadic forms of MTC because of unknown parentage, a limited number of available relatives, lack of family cooperation, and lack of knowledge of the type of cancer or thyroid disease in family members.

Utilizing CT assay within families has limitations since it is not always possible to test enough family members to establish whether or not the disease is hereditary or sporadic.

Pathology

In our collaborative study, over 190 MTC cases have been collected, with most cases reviewed by ten histopathologists

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(8). Cancers and/or C-cell hyperplasia are bilateral in hereditary MTC but also may occur, in our experience, in the sporadic form. Preliminary results suggest that a cancer limited to only one lobe of the thyroid gland without evident C-cell hyperplasia is a feature of the sporadic form only if adequate sections of the thyroid are available for study.

Endocrinology

Studies have been carried out for ACTH, β -lipotropin, endorphin, somatostatin (9-11), and CT-gene-related-peptide in plasma and in tumors. The increase in plasma of β -lipotropin seems to be more frequent in the hereditary form and of somatostatin in the sporadic form.

HLA determination

No linkage was observed between MTC and HLA type in several families as presented in Cambridge by Guillausseau et al (12) and as reported by Simpson and Falk (13).

Meta-iodo-benzylguanidine (MIBG) scintigraphy

The results of the study of more than 50 cases have led Baulieu et al (14) to conclude that MIBG uptake in MTC is usually a feature of hereditary MTC.

In summary, no technique has yet been able to discriminate between the hereditary and the sporadic form of MTC in all cases. Unfortunately, repetitive screening of family members remains necessary despite its difficulties.

Results of Screening for MTC in France

Although the registry was established in 1970, the common protocol was established only four years ago. The registry includes nearly 1,000 cases, with a high likelihood that 175 cases are sporadic cases (based on extensive family screening and pathological criteria) and with 206 cases hereditary in 59 families. In the past two years, one-half of the new cases have been hereditary.

The hereditary cases appear to be isolated MTC in 29 families without other components of MEN-2 syndromes, MEN-2A in 26 families and a few cases of the MEN-2B phenotype. The gene has a variable expression in MEN-2 even within the same family, with pheochromocytomas in 40% to 45% and parathyroid tumors in 16% to 18% of cases at the time of screening. The origin from the west of France (16 families) or Mediterranean area (13 families, eight of which are foreign) should make interesting genealogic studies. The registry has permitted cases to be linked from different family branches.

The evolution of MTC is quite variable in both the sporadic and hereditary form. Even though the prognosis generally appears better in the hereditary form, the tumors are very aggressive in some of these cases.

References

1. Calmettes C. Usage de la thyrocalcitonine pour la detection des cancers medullaires familiaux chez l'enfant. *Ann Med Interne (Paris)* 1984;135:335-7.
2. Calmettes C. Dosage de la calcitonine circulante pour la detection du cancer medullaire familial et sporadique. *Biomed Pharmacother* 1984;38:266-8.
3. Argemi B, Calmettes C, Deltour G, Guilloteau D. Etude multicentrique du dosage de la calcitonine plasmatique au cours des cancers medullaires thyroidiens (abstract 21). Premier symposium europeen sur les cancers thyroidiens. Montpellier, June 6-7, 1985.
4. Ponder BAJ. Medullary thyroid carcinoma: Screening the family of the apparently sporadic case. In: Muller H, Weber W, eds. *Familial Cancer*. Basel: Karger, 1985:112-4.
5. Calmettes C, Moukhtar MS. Immunoassay of human calcitonin in health and disease. In: Parsons JA, ed. *Endocrinology of calcium metabolism*. New York: Raven Press, 1982:211-33.
6. Caillou B, Calmettes C, Rougier P, Schlumberger M, Talbot M, Bellet D. Le cancer medullaire de la thyroide: modele de tumeur monoclonale heterogene? In: Lemerle J, ed. *Institut Gustave-Roussy—Actualites Carcinologiques*. Paris: Masson, 1984:271-83.
7. Calmettes C, Caillou B, Moukhtar MS, Milhaud G, Gerard-Marchant R. Calcitonin and carcinoembryonic antigen in poorly differentiated follicular carcinoma. *Cancer* 1982;49:2342-8.
8. Franc B, Caillou B, Carrier AM, et al. Immunohistochemistry in medullary thyroid carcinoma: Prognosis and distinction between hereditary and sporadic tumors. *Henry Ford Hosp Med J* 1987;35:00-00.
9. Caron J, Calmettes C, Deltour G, et al (travail du groupe d'etude des tumeurs a calcitonine [GETC]). Influence de la dexamethasone (DXM) sur l'hypercalcitoninemie dans les cancers medullaires de la thyroide (CMT) (abstract 22). Premier symposium europeen sur les cancers thyroidiens. Montpellier, June 6-7, 1985.
10. Modigliani E, Calmettes C, Girard F, et al (travail du groupe d'etude des tumeurs a calcitonine [GETC]). Taux plasmatique de la somatostatine, ACTH, beta-lipotropine et beta-endorphine dans les cancers medullaires du corps thyroide (abstract 26). Premier symposium europeen sur les cancers thyroidiens. Montpellier, June 6-7, 1985.
11. Modigliani E, Chayvialle JA, Calmettes C, et al. Reponse de la somatostatine a la pentagastrine dans le cancer medullaire du corps thyroide. *Ann Endocrinol (Paris)* 1986;47:309.
12. Guillausseau PJ, Guillausseau C, Gony J, et al. Polyadenomatose endocrinienne de type 2a (MEN 2a): Enquete familiale et etude genetique. *Ann Endocrinol (Paris)* 1986;47:323.
13. Simpson NE, Falk J. Exclusion of linkage between the loci for multiple endocrine neoplasia type-2 and HLA. *Hum Genet* 1982;60:157.
14. Baulieu JL, Guilloteau D, Delisle MJ, et al. Fixation de la meta-iodo-benzylguanidine par les carcinomes medullaires de la thyroide—etude multicentrique. *J Biophys Biom* 1986;10(suppl 2):42-4.