CALCITONIN SCREENING FOR MEDULLARY THYROID CARCINOMA

Chambon G, Alovisetti C, Idoux-Louche C, Reynaud C, Rodier M, Guedj A-M, Chapuis H, Lallemant JG, Lallemant B. The use of preoperative routine measurement of basal serum thyrocalcitonin in candidates for thyroidectomy due to nodular thyroid disorders: results from 2733 consecutive patients. J Clin Endocrinol Metab. September 29, 2010. doi:10.1210/jc.2010-0162.

SUMMARY

BACKGROUND AND METHODS

The utility of routinely measuring basal calcitonin (CT) levels "under appropriate conditions" was assessed on 2733 consecutive patients from southern France who had nodular thyroid disorders and who were already scheduled to undergo thyroid surgery. Thyroid and cervical ultrasonography was performed, but fine-needle aspiration (FNA) biopsies were not performed on lesions <10 mm. A total of 43 patients had a basal CT level >10 pg/ml, which triggered additional preoperative, intraoperative or postoperative procedures or tests, and all these patients underwent at least a total thyroidectomy.

RESULTS

Of the 43 with high CT levels, 12 were found to have some form of medullary thyroid cancer (MCT): 7 were larger tumors (mean diameter, 2.5 cm), while 5 were called "micro-MCT" or "subclinical latent MCT" (mean diameter, 4.4 mm). All of the remaining 31 patients with high CT levels had benign C-cell hyperplasia when detailed immunohistochemical examination of the entire gland was performed. These 31 patients had no cervical lymph nodes on preoperative ultrasound, and their serum CT levels had normalized when assayed at least 6 weeks postoperatively. None of the patients with an elevated basal CT level turned out to have *ret* proto-oncogene mutations, and pentagastrin stimulation testing did not provide any additional diagnostic information. Two of the 2690 patients with normal basal CT levels had a focus of micro-MCT on detailed immunohistochemistry. In conclusion, all the macro-MTCs could have been detected by ultrasonography, FNA, and/or histopathology at surgery, but basal CT screening did pick up five (of seven) patients with micro/subclinical latent MTC, one of whom had clinically unappreciated central compartment nodes.

COMMENTARY

Similar to a number of previous studies that have used basal CT determination to screen all patients with nodules, MCT was found in ~0.5% of cases. The positive predictive value of the CT screening was only about 25%. The ATA has not taken a position for or against routine screening (1), based on the total associated costs and in view of the large fraction of false positive tests, which do have associated risk (note that approximately three fourths of the patients with elevated CT levels in this study underwent total thyroidectomy for an apparently benign disease). Still, the central compartment nodes of one patient with subclinical latent micro-MCT probably would have been missed if the screening CT had not been performed. In another three cases, the nodule was not on the side where the MCT was found, so the simple lobectomy that probably would have been performed would have missed the MCT, if the high CT level had not been recognized preoperatively. However, data are lacking to support the idea that C-cell hyperplasia without germline mutation or subclinical latent MCT develop with time into macro-MTC, so it isn't clear whether those latter three cases would ever have developed clinical symptoms.

— Stephen W. Spaulding , MD

What fraction of patients with micro-MCT detected by intensive immunohistochemistry actually benefit from aggressive surgery? The following paper addresses another side of this risk/benefit problem. —JMH, MD

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Valle LA, Kloos RT. The prevalence of occult medullary thyroid carcinoma at autopsy. J Clin Endocrinol Metab. October 13, 2010. doi:10.1210/jc.2010-0959.

SUMMARY

BACKGROUND AND METHODS

A total of 24 autopsy reports containing detailed thyroid histology on approximately 7900 individuals with no clinical evidence of thyroid disease were reviewed for cases of occult MCT.

RESULTS

The weighted mean prevalence of occult medullary and papillary carcinomas of the thyroid (defined as ≤1 cm) was 0.14% for MCT and 7.6% for papillary thyroid cancer (PCT). Excluding reports that used only thick tissue sections (>3 mm), the mean prevalence of occult MTC was 0.18% and of occult PTC was 8.4%. Focusing on the studies that performed calcitonin immunohistochemistry, the MCT incidence was 0.33%. In the only two studies that assessed calcitonin immunoreactivity on thin sections through the entire thyroid, occult MCT was detected in 0.42%.

COMMENTARY

The autopsy series that were combined for this paper spanned 35 years and came from many nations with different prevalences of nodular thyroid diseases. Diet and other environmental factors have changed—as have the ways that minor thyroid nodules are detected and assessed—from 1971 when thyroid ultrasonography was in its infancy until 2006 when "thyroid incidentalomas" had burgeoned following the widespread use of MR, PET and CT scans. It is important to note that in these studies three-quarters of the patients autopsied were older than 60, which may bias the data toward benign disease, since sporadic MCT commonly presents in patients in their 40s and 50s, familial MCT tends to present even earlier, while benign thyroid nodularity increases progressively with age.

Clearly, occult subcentimeter MCTs are not always benign, even though the ones detected in these autopsies were asymptomatic up to the time of death. Even so-called benign C-cell hyperplasia (>50 C-cells per 3 low-power fields) is considered to be carcinoma in situ for patients with familial MCT or MEN2, especially those with certain *ret* mutations (1). There is a clear need for up-to-date information on the behavior of occult MCT in order to conduct meaningful risk/benefit and cost/benefit analyses. Unless country- and age-specific data on the incidence and behavior of occult MCT miraculously do become available, it seems that amalgamated temporal and global data will have to do, despite questions about its applicability, particularly to younger patients.

— Stephen W. Spaulding, MD

Reference

1. Kloos RT, Eng C, Evans DB, et al. Medullary thyroid cancer: management guidelines of the American Thyroid Association. Thyroid 2009;19:565-612.