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Results of a prospective thyroid ultrasound screening program in adenomatous polyposis patients

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Abstract

BACKGROUND: Patients with adenomatous polyposis may be at increased risk for developing thyroid cancer (TC). However, screening guidelines for TC in these patients are not well established.

METHODS: Patients with a diagnosis of familial adenomatous polyposis, attenuated familial adenomatous polyposis, and gene mutation-negative adenomatous polyposis enrolled in our Hereditary Colorectal Cancer Family Registry were eligible for a screening thyroid ultrasound (US). Findings were reviewed by the study endocrinologist and intervention and/or follow-up determined.

RESULTS: Fifty patients underwent screening thyroid US. Thirty-four (68%) patients had abnormal findings on US, including 27 (79%) with thyroid nodules. In 7 patients, US-detected thyroid nodules met established criteria for fine-needle aspiration. Of the 6 patients who underwent fine-needle aspiration, 2 (4%) were diagnosed with papillary TC. Both of these patients were female.

CONCLUSIONS: A large proportion of adenomatous polyposis patients will have abnormal results on thyroid US, including suspicious-appearing thyroid nodules that when biopsied are malignant. Female patients have an apparently greater risk of developing TC. Polyposis patients, especially women, should be offered participation in a thyroid US screening program.

Familial adenomatous polyposis (FAP) is a rare, autosomal-dominant condition that is characterized by numerous colorectal adenomatous polyps and is associated with an increased risk of colorectal and extracolonic cancers. Because nearly all individuals with FAP will develop colorectal cancer (CRC) if their colons are left in situ, prophylactic colectomy has become the standard of care to reduce the risk of CRC-related morbidity and mortality. As the rate of mortality from CRC continues to decrease, there is increasing concern about extracolonic malignancies associated with FAP.[1–3]

The association between thyroid cancer (TC) and FAP was first suggested by Crail et al[4] in 1949. The prevalence

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of TC in the FAP population is thought to be .4% to 12%.[5–12] Prospective registry screening programs for TC in FAP patients have reported incidences of 2.6% to 7%,[12,13] compared with .01% to .2% in the general population.[9,14] As a result of these findings and a retrospective review of our registry data, which demonstrated a prevalence rate of 6.1% for TC,[15] we began offering screening thyroid ultrasound (US) to our patients affected by adenomatous polyposis syndromes. We now report on our findings to enrich the cohort of patients with these rare syndromes.

Methods

All gastrointestinal polyposis patients were prospectively enrolled in the institutional review board-approved Hereditary Colorectal Cancer Family Registry at Memorial Sloan-Kettering Cancer Center. The registry requested source documentation for all prior cancer diagnoses and treatments, related screening tests, and other relevant diagnoses and treatments. All patients were referred for clinical genetics consultation at the time of polyposis diagnosis. All data were prospectively maintained. Patients aged 16 years and older with an adenomatous polyposis syndrome were offered a screening thyroid US during clinic visits from November 2010 to August 2012.

Patients with either a clinical or molecular diagnosis of FAP or attenuated FAP were eligible for inclusion. Patients with *MYH*-associated adenomatous polyposis or Lynch syndrome were excluded. Five patients with a previous history of TC were also excluded.

Abnormal thyroid US scans were reviewed by institutional radiologists as well as the study endocrinologist, and all patients were referred for appropriate follow-up and/or treatment. Recommendations for fine-needle aspiration (FNA) of suspicious-appearing thyroid nodules were based on the American Thyroid Association Guidelines, as interpreted by the study endocrinologist.[16] Patients with normal US were recommended to repeat US every 2 years, and patients with abnormal US were recommended to repeat US annually.

Results

Fifty-three of the 90 (59%) adenomatous polyposis patients enrolled in our registry were seen in clinic during the study period and were referred for screening thyroid US. Fifty of the 53 (94%) referred patients from 43 kindreds underwent screening thyroid US as part of our program and constitute our study population. Nineteen (38%) were female. Thirty-one (62%) patients had a documented *APC* mutation, 8 (16%) had undergone testing and no detectable mutation was found, and 11 (22%) have not been tested.

The median age at the time of US was 34 years (range 19 to 70). The median age at the time of diagnosis of adenomatous polyposis was 26 years (range 10 to 56). Five of the 50 patients had undergone thyroid US before commencement of our screening program. Two patients had normal US and 3 had benign findings, which included multinodular thyroid gland, goiter, and a cyst without evidence of TC. However, one patient was found to have evidence of papillary thyroid carcinoma (PTC) in a subsequent US approximately 7 months later as part of our screening program.

Thyroid US findings detected during our screening program are summarized in Fig. 1 and Table 1. A total of 34 (68%) patients had abnormal findings, including 12 (35%) women and 22 (65%) men. The abnormal findings included 7 (21%) patients with heterogenous thyroids and 27 (79%) with thyroid nodules. Of the 52 nodules found, 12 (19%) nodules were at least 10 mm (range 2 to 35). Fourteen patients had sonographically suspicious-appearing thyroid gland findings, including increased vascularity, hypoechoicity, microcalcifications, or irregular margins. Three patients were diagnosed with benign thyroid disease (ie, hyperthyroidism or thyroiditis) based on workup for abnormal US findings. These patients were referred to the study endocrinologist for further evaluation.

Seven (14%) patients with thyroid nodules were recommended to undergo FNA based on the American Thyroid Association Guidelines. Four of these patients were female. Six patients—3 women and 3 men—underwent FNA. Three patients had benign histology. The results of the FNA are discussed below.

One 21-year-old female had PTC. Her mother had a history of TC but no known diagnosis of FAP. She underwent total thyroidectomy with histology demonstrating papillary microcarcinoma in the right thyroid lobe and isthmus, and multinodular goiter in the left thyroid lobe. Capsular invasion was present, but no extrathyroidal invasion or lymph node involvement was observed. One 49-year-old female had PTC. She underwent total thyroidectomy with histology demonstrating a 15 mm poorly differentiated PTC with marked mitotic activity (5 mitosis per 10 high-power fields), focal areas of necrosis, and capsular invasion in a background of chronic lymphocytic thyroiditis. No extrathyroidal invasion or lymph node involvement was observed. She was treated

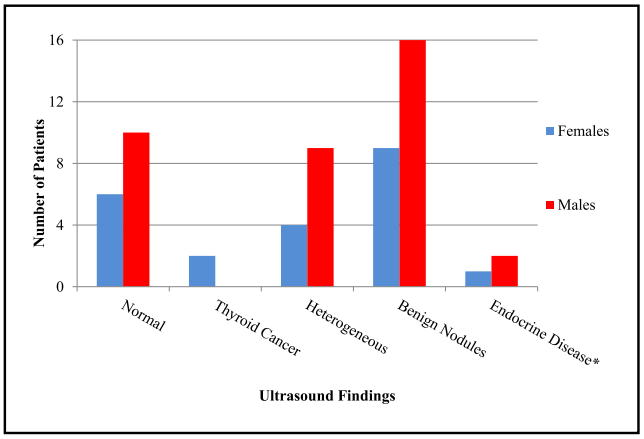

Figure 1 Thyroid ultrasound findings detected during screening program. *Endocrine disease refers to benign findings leading to the diagnosis of thyroiditis, hyperthyroidism, or goiter.