



THE ROLE OF ULTRASOUND SCREENING FOR THYROID CANCER IN PATIENTS WITH FAMILIAL ADENOMATOUS POLYPOSIS SYNDROME

Endocrinology

Maria Mohammed Fariduddin*	Department Of Endocrinology, State University Of New York- Upstate Medical University, Syracuse, New York, USA. *Corresponding Author
Ifeoma Egbuonu	Department Of Endocrinology, State University Of New York- Upstate Medical University, Syracuse, New York, USA.
Natalia Iorio	Department Of Gastroenterology, State University Of New York- Upstate Medical University, Syracuse, New York, USA
Divey Manocha	Department Of Gastroenterology, State University Of New York- Upstate Medical University, Syracuse, New York, USA
Nidhi Bansal	Department Of Endocrinology, State University Of New York- Upstate Medical University, Syracuse, New York, USA.

ABSTRACT

Familial adenomatous polyposis (FAP) is an inherited disease that is characterised by multiple recurrent cancers of the colon (large intestine). Thyroid nodules and thyroid cancer are among the few extraintestinal manifestations of FAP, with a prevalence of 35-80% and 3-12% respectively. The incidence of thyroid cancer is higher in FAP patients than in the general population. However, routine thyroid cancer screening is not consistently performed by most practitioners when managing patients with FAP. We sought to assess the frequency of thyroid cancer screening among patients with FAP and the prevalence of thyroid cancer among these patients. We performed a retrospective chart review of all adult patients with FAP, between January 2000 and December 2016 at our center. 51 patients were identified with a confirmed diagnosis of FAP based on colonoscopy and pathology criteria. Of the 51 patients with FAP syndrome, only 14 patients had thyroid ultrasound performed, and 3 patients were found to have thyroid cancer. With limited data, our analysis showed a reduced prevalence of thyroid cancer of 5% when compared to historical data. Most adult FAP patients did not get thyroid cancer screening and this could be due to lack of awareness in medical providers on the increased incidence of thyroid cancer and FAP. Every clinician managing FAP patients should be educated on the increased risk of thyroid cancer in FAP and the role of thyroid ultrasound screening for early detection of thyroid cancer.

KEYWORDS

Thyroid Cancer, Ultrasound, Familial Adenomatous Polyposis

INTRODUCTION

Familial adenomatous polyposis (FAP) is an inherited genetic disorder caused by germline mutation of *Adenomatous Polyposis Coli* (APC) gene on chromosome 5q21-q22 [1] and is inherited in an autosomal dominant pattern, where even one copy of a mutated gene from one parent is enough to cause the syndrome. It is characterized by the development of hundreds and thousands of colorectal polyps with definitive malignant progression if left untreated. Focus of management of FAP is on initiating colonoscopies early in life for screening for colon cancer, as well as timing the colectomy (surgery to remove the colon) before manifestation of the malignancies. Extraintestinal manifestations of FAP include both benign and malignant lesions. Congenital hypertrophy of the retinal pigment epithelium, Desmoid tumors, epidermoid cyst gastric adenomas are a few of the common benign lesions seen with FAP. [2] Extraintestinal malignancies associated with FAP are usually seen in the thyroid gland, adrenal gland and brain. The incidence of thyroid nodules in patients with FAP is about 80% and about 12% of those are found to be malignant [3]. They are seen more commonly in women with mean age of 28 years. [3] The most common histology is the papillary type with cribriform morula variant seen in a third of these cancers. [3]

Microscopic appearance of these tumors shows areas of cribriform architecture and sometimes spindle shaped cell component with whorled architecture. These pathologic findings can mimic an aggressive neoplasm but lack of nuclear atypia, mitosis, and necrosis help in differentiating malignant from benign nodules. [4] It is important to recognize these unusual morphological aspects because thyroid cancer may be the first manifestation of FAP. At the current time, the guidelines focus on recognizing colon cancer in patients with FAP, and though there are recommendations on screening for thyroid cancer in patients with FAP, incidence of thyroid cancer does not match with the frequency of neck ultrasounds performed. [5] With our study we sought to identify the role of ultrasound screening to detect thyroid cancer in patients with FAP.

METHODS

We performed a retrospective chart analysis of adult patients with ICD 9 and ICD 10 diagnostic code for FAP between January 2000 and

December 2016 at SUNY Upstate University Hospital and affiliated clinics in Syracuse, NY. We collected demographic data, colonoscopy/histopathology reports, thyroid sonogram imaging and available cytopathology results. We confirmed diagnosis of FAP with available colonoscopy, pathology and/or genetic reports.

RESULTS

5570 charts were reviewed and 51 patients were identified with biopsy and genetically proven FAP. Of the 51 patients 26 (51%) were women with a mean age of 38 years (+/-16 years). No documentation of palpable clinical nodules in the thyroid gland in these patients. Only 14 of these patients had neck ultrasound performed for screening and 10 of them were found to have thyroid nodules, size ranging from 0.3-2.0 cm. All the patients identified with thyroid nodules were females. 8 out of the 10 patients underwent Fine needle aspiration and biopsy, and 3 of them were found to have thyroid cancer. They were asymptomatic without any palpable thyroid nodules. All of the 3 patients had papillary thyroid carcinoma and underwent total thyroidectomy.

DISCUSSION

The historical incidence of thyroid nodules in patients with FAP is 80% with 12% being malignant. [3] Our single institution review showed a 8% of thyroid nodules in patients with FAP to be malignant. It is usually seen in the first 17 years of diagnosis of the initial FAP diagnosis. Cribriform variant of papillary carcinoma is seen in majority of patients with FAP who develop this cancer. [4] Cribriform variant represents about 01-0.2% of all papillary thyroid cancer and is associated with the mutation of APC and B catenin gene. [4] Diagnosis of Cribriform variant of papillary thyroid cancer in a patient with no diagnosis of FAP is an indication for a screening colonoscopy regardless of patient's age or symptoms as well as a genetic test of the APC gene sequencing given its high association with FAP. [4] Patients with FAP undergo routine screening with endoscopies and colonoscopies but thyroid cancer screening is not routinely performed despite being recommended in the guidelines. This is very likely due to a combination of physician unawareness and patient noncompliance. Treatment of familial thyroid cancer is similar to any thyroid cancer and options include total thyroidectomy, radioactive iodine and lifelong suppressive doses of oral levothyroxine to maintain a low

TSH. The Cribiform variant usually has good prognosis with low recurrence rate.[4]

CONCLUSION

Ultrasound screening is recommended for screening for thyroid carcinoma in patients with FAP, however it is not routinely performed. It may be due to lack of awareness among practitioners about the increased incidence of thyroid cancer in FAP patients. Patient education is also important as we found from our analysis that there were many patients who did not undergo the screening ultrasound despite being recommended by their physicians. Every clinician managing FAP and patients with the disease should be educated on the increased risk of thyroid cancer in FAP and the role of thyroid ultrasound screening for early detection of thyroid cancer.

Statement of Ethics

The study was approved by Internal Review Board (IRB) at Upstate University Hospital. Since the study was a retrospective review that did not involve disclosing patient sensitive information an ethics committee approval was not required by the IRB.

Disclosure Statement

The authors have no conflicts of interest to declare.

Funding Sources

None

REFERENCES

1. Burt RW, DiSario JA, Cannon-Albright L. (1995) Genetics of colon cancer: Impact of inheritance on colon cancer risk. *Annu Rev Med.* 46:371–9.
2. Slowik V, Attard T, Dai H, Shah R, Septer S. (2015). Desmoid tumors complicating familial adenomatous polyposis: a meta-analysis mutation spectrum of affected individuals. *BMC Gastroenterol* 15: 84 10.1186/s12876-015-0306-2
3. Jarrar AM, Milas M, Mitchell J, et al. (2011) Screening for thyroid cancer in patients with familial adenomatous polyposis. *Ann Surg.* 253:515–521.
4. Perea Del Pozo E, Ramirez Plaza C, Padillo Ruiz J, Martos Martinez JM. (2015) Cribiform variant of papillary thyroid cancer and familial adenomatous polyposis. *Int J Surg Case Rep.* 16:192–194. doi:10.1016/j.ijscr.2015.08.013
5. Greenhill C. (2011) Cancer: screening for thyroid cancer in patients with FAP is worthwhile. *Nat Rev Endocrinol.* Apr;7(4):186.