Case Report

Familial Adenomatous Polyposis-Associated Papillary Thyroid Cancer

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Abstract

Papillary thyroid carcinoma (PTC) associated with familial adenomatous polyposis (FAP) is rare. It is usually associated with the cribriform-morular variant of PTC, with unusual patterns on detailed histology examination. This variant is known to have a good prognosis. Papillary thyroid carcinoma associated with FAP commonly occurs in females in their 30s and rarely in the elderly. We report a case of a 69-year-old female presenting with thyroid swelling and a history of FAP.

Keywords: *familial adenomatous polyposis, papillary thyroid carcinoma*

Introduction

Familial adenomatous polyposis (FAP) is an autosomal dominant disease caused by mutation of the adenomatous polyposis coli (APC) gene. It is characterised by the presence of more than 100 colonic polyps with extra-colonic manifestations in the soft tissue (lipoma, fibroma, sebaceous cyst, desmoid tumours) and eye lesions (congenital hypertrophy of the retinal pigment epithelium) (1,2). Association of papillary thyroid cancers with FAP is rare. Recent advances in prophylactic colectomy have decreased colorectal-associated mortality; however, long-term follow-up has shown that there is significant morbidity due to extra-colonic associated malignancies such as thyroid cancer (1). We report a case of a 69-year-old female with FAP who had undergone panproctocolectomy 10 years previously and was presenting with papillary thyroid cancer and an abdominal desmoid tumour.

Case Report

A 69-year-old woman presented to our surgical outpatient clinic with progressively increasing anterior neck swelling for 6 months. There was no evidence of upper airway obstruction, hoarseness, dysphagia or symptoms of superior vena cava obstruction. She was clinically euthyroid.

She had a history of lower gastrointestinal bleed 9 years previously. It was associated with loss of weight and appetite. Colonoscopy revealed multiple polyps throughout the colon that proved to be tubular lesions with severe dysplasia on histological examination. There was a strong family history of colorectal cancer affecting 5 of her 10 siblings.

She underwent a total colectomy with abdominal perineum resection at the age of 59 years, as intraoperatively there were more than 100 polyps in the colon up to 3 cm from the anal verge distally. Histopathological examination showed these polyps were high-grade tubulo-villous adenomas. She had an uneventful recovery and has been on regular follow-up at our colorectal clinic.

Nine years later she complained of anterior neck swelling. This swelling increased in size progressively over a period of 6 months with no constitutional symptoms. On examination, there was a hard thyroid swelling involving both lobes and measuring 10 cm x 10 cm, with no palpable lymphadenopathy. Clinically, she was euthyroid. There was also a palpable abdominal mass measuring 12 cm x 12 cm at the left iliac fossa.

A contrasted computer-tomography scan of the neck and abdomen was performed. The findings consisted of a well-defined heterogeneous enhancing mass involving both thyroid lobes extending retrosternally with a necrotic centre. There were multiple subcentimetre cervical lymph nodes at level 1–3 bilaterally. A large

heterogeneous mass with solid and cystic components was also seen at the lower abdominal compartment, consistent with a desmoid tumour. No lesions were seen in the pancreas.

Oesophago-gastroduodenoscopy (OGD) examination showed multiple benign-looking polyps in the stomach and duodenum, which were histologically confirmed as tubular adenomas. Fine needle aspiration cytology of the thyroid mass was performed.

Cytological examination of the thyroid yielded a cellular sample with malignant thyroid follicular epithelial cells in monolayer sheets and small groups. The malignant cells showed fine vesicular nuclei with a powdery chromatin pattern. Many nuclear grooves and creases were visible. However, intranuclear pseudoinclusion was hardly seen. The cytological features were consistent with papillary carcinoma of the thyroid.

The patient underwent total thyroidectomy and right lateral and central neck dissection. Intraoperative findings were a large hard right thyroid lobe measuring 8 cm x 7 cm x 4 cm, while the left thyroid lobe appeared completely normal (Figure 1). Even though the cervical lymph nodes were not enlarged bilaterally on the CT scan, the right cervical lymph nodes appeared enlarged at level III and IV during surgery and we proceeded with central and right lateral neck dissection. Histopathological examination of the right thyroid lobe showed an encapsulated tumour composed of malignant thyroid cells in solid sheet, cribriform pattern and papillary architecture (Figure 2). The malignant cells showed nuclear grooving with occasional intranuclear pseudoinclusion and squamous morule formation (Figure 3). The final histological diagnosis was cribriform-morular variant of papillary thyroid carcinoma of the right thyroid lobe. The left thyroid lobe was free of malignant infiltration. Further, there was no evidence of cervical lymph node metastases in any of the examined lymph nodes.

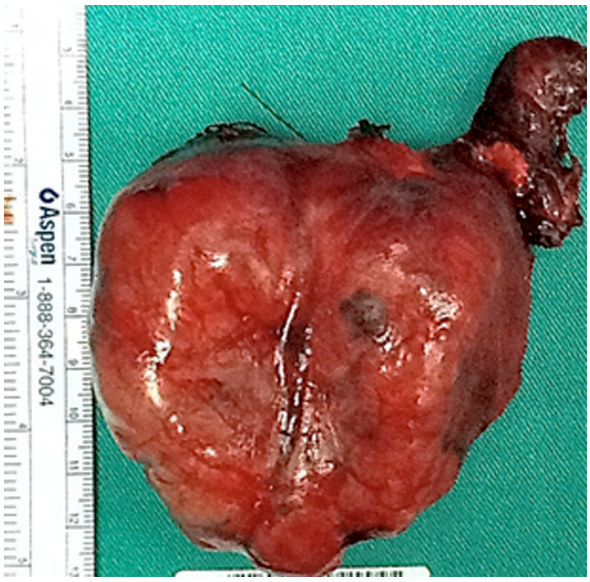

Figure 1: Gross specimen of an enlarged right thyroid lobe and a normal left thyroid lobe.

The post-operative period was uneventful. Subsequently, the patient was sent for radioactive iodine treatment followed by thyroxine suppressive therapy and yearly thyroglobulin monitoring.

Discussion

Papillary thyroid carcinomas are frequently sporadic and are associated with rearrangement of rearranged during transfection (RET) proto-oncogene in 25% to 40% of all cases. FAP is also known to have an association with extra-colonic malignancies, namely pancreatic and thyroid carcinoma (2). Papillary thyroid carcinoma is known to be associated with FAP, an autosomal dominant disease that is characterised by the presence of hundreds of polyps along the gastrointestinal tract. Familial adenomatous polyposis coli is caused by a germline mutation of the APC gene located at chromosome 5q21 (3). The APC gene encodes a protein complex (APC protein) that functions as a tumour suppressor by its interaction with beta-catenin (4). The combination of the APC gene and beta catenin is responsible for cellular proliferation, migration and metastasis. Mutation of the APC gene results in abnormal cellular proliferation, which leads to tumorigenesis.

Papillary thyroid carcinoma (PTC) in FAP patients was first reported by Crailin in 1949, but the association between the two was not fully appreciated until Kashiwagi et al. reported two sisters with PTC and FAP (5). The incidence of papillary thyroid carcinoma associated with FAP ranges between 0.6% and 1.2%. It usually occurs within 17 years of the initial FAP diagnosis, which was the case for our patient, who was diagnosed with papillary thyroid carcinoma 10 years after the initial diagnosis of FAP (6). Although the relative risk of thyroid cancer is 7.6% in cases of FAP, the absolute risk of developing thyroid cancer is only 2%. For this reason, most centres do not recommend routine neck ultrasound screening of FAP patients. While FAP-associated papillary thyroid carcinoma is most common

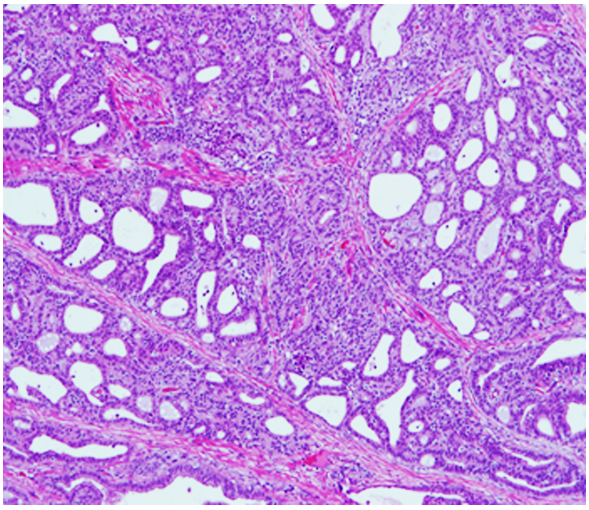

Figure 2: Section shows malignant cells in cribriform pattern (H&E, X10).

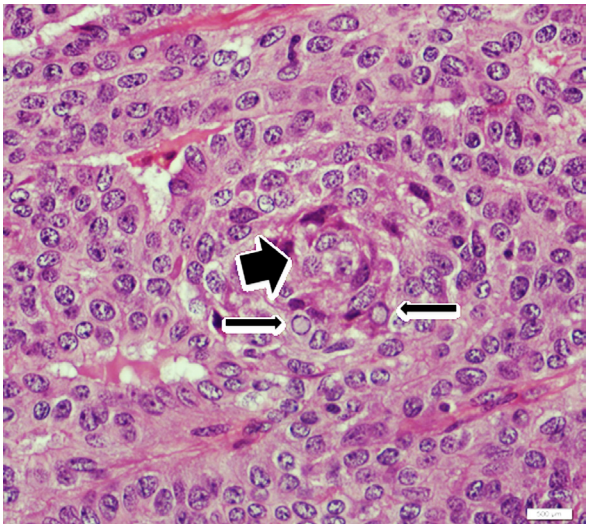

Figure 3: Squamous morules with intranuclearpseudoinclusion and nuclear grooving (H&E, X40).

in females (94%) under 30 years old (80%), our patient was diagnosed with PTC at 69 years of age. Histologically, the tumor has predominant classic papillary architecture (2).

Concomitant classical papillary and cribriform pattern has been noted in most of the detailed histological examinations of cases reported in the literature (6,7). The malignant cells have round to oval nuclei with nuclear grooving, occasional nuclear clearing and intranuclear pseudoinclusion-like structures. There were occasional squamous morules seen in our case, which are commonly observed in PTC associated with FAP (8). Rohaizak et al. reviewed four cases of PTC associated with FAP in young female patients with similar histological patterns (1). The cribriform-morular variant shows a better prognosis than other variants of papillary thyroid carcinoma (7,8,9). Most of the reported cases had no disease recurrence either in the lymph nodes or in the thyroid remnant, even though initially a few of the cases had cervical nodal involvement (8,9). There was one case of patient with an atypical cribriform-morular variant who died 17 months after surgery (10). However, this was probably due to the presence of a poorly differentiated component and poor neuroendocrine differentiation.

Treatment of familial thyroid carcinoma is similar to treatment for usual thyroid carcinoma. Furthermore, multifocality or multicentricity of malignant nodules in a thyroid gland points to total or near total thyroidectomy for managing PTC associated with FAP. In most of the cases reported in the literature, treatment of PTC associated with FAP has been similar to treatment of common papillary thyroid carcinoma, which involves surgery, radioactive iodine administration and lifelong suppressive doses of oral thyroxine. In our patient, we performed central and lateral neck dissection because of a large tumor (more than 4 cm) and presence of suspicious lymph nodes. However, we felt that due to the indolent nature of the tumour, extensive lymph node dissection was not necessary: clinically, there was no obvious lymph node involvement detected by palpation or radiological examination.

In summary, a high index of suspicion for papillary thyroid carcinoma should be considered in FAP patients presenting with thyroid swelling, with the cribriform-morular variant being the most common. This variant is associated with a good prognosis, and total thyroidectomy is still the preferred choice of surgery in all cases.

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Conflict of Interest

None.

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Authors' Contributions

Conception and design: SNAS, NAN, RM, NMI, NHML
Drafting of the article and critical revision of the article for important intellectual content: SNAS, NMI

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