INTRODUCTION

Familial adenomatous polyposis (FAP) is an autosomal dominant disorder in which hundred to thousands of colorectal polyps develop by early adulthood. The genetic mutation implicated in FAP is the APC gene, and patients uniformly develop colorectal cancer. There is a known association between FAP and thyroid cancer, with 1–2% of FAP patients developing thyroid malignancy. Harsach et al. further characterized the thyroid cancer found in FAP patients as non-papillary, non-follicular histologic origin, deeming it a truly unique malignancy.

The cribriform morular variant (CMV) of papillary thyroid carcinoma (PTC) was first described in 1999 by Camasse–Tejeiro and Chan. In their original series of four patients with this tumor, all of whom had no medical or family history of FAP but with analogous histologic features as those tumors found in FAP patients, they hypothesized that CMV-PTC was, in fact, the sporadic counterpart of the FAP-associated thyroid malignancy. CMV was thus classified as a subtype of PTC because of the presence of RET/PTC in a significant proportion of cases, which is a feature exclusive to PTC. We present two patients at our institution with a diagnosis of CMV-PTC, and briefly review the literature on this unique pathologic entity.

METHODS

This study was approved by the Institutional Review Board of the University of California, Los Angeles. We performed a retrospective chart review of two patients who underwent total thyroidectomy for biopsy-proven papillary thyroid cancer at a tertiary academic medical center between January 1, 1995 and December 31, 2015. Patient characteristics and clinical outcomes were reviewed.

RESULTS

Case 1

The patient is a 52 year old female who presented to the head and neck surgery clinic with a slow-growing, painless, right sided neck mass overlying the thyroid region over the last 3 months. Associated symptoms include very mild dysphagia, a constant sore throat, and voice changes (specifically, decreased vocal range). She reports no dyspnea or shortness of breath, but the mass results in compressive symptoms which prompts her to lay on her right side. Her past medical history is significant for diabetes. She denied smoking or alcohol use.

On exam, she has a firm 4 cm right-sided thyroid mass. Magnetic resonance (MR) imaging of the neck demonstrated a 4 x 6 cm right thyroid mass (Figure 1), and an FNA biopsy suggested a diagnosis of follicular neoplasm. She underwent a total thyroidectomy and tolerated it well without complications. A component of the mass extended inferiorly into the anterior mediastinum, but gross total resection was achieved. Path returned as CMV-PTC (Figures 2 and 3), measuring 6.5 cm in size, with multifocal extracapsular, vascular, and extrathyroidal extension.

She underwent radioactive iodine treatment, but developed a recurrent right sided thyroid mass 1 year later. Computed tomography (CT) of the neck demonstrated recurrence in the right thyroid bed. She underwent reoperation with sacrifice of the right recurrent laryngeal nerve due to tumor encasement. Path was once again consistent with CMV-PTC. She has since been referred for external beam radiation.

Case 2

The patient is a 23 year old female who presents to the head and neck surgery clinic for a 1 month history of a right neck mass over the thyroid area. She is otherwise asymptomatic. Thyroid ultrasound demonstrated a 5 cm mass within the right thyroid gland. FNA biopsy revealed papillary thyroid carcinoma, possible tall cell variant.

She underwent total thyroidectomy with central neck dissection. Path returned as CMV-PTC within the right thyroid lobe, measuring 4.7 cm in size, with lymphovascular invasion. No lymph nodes were positive for carcinoma. She has since been referred for radioactive iodine therapy.

DISCUSSION

Though grossly similar to traditional PTC, the distinct appearance of the tumor on histopathologic analysis. The tumor typically contains areas of cribriform and morular patterns, but the distinguishing feature is positive staining for both intracytoplasmic and intranuclear beta-catenin (as compared to only intracytoplasmic staining in non-CMV PTC). This is thought to be a result of the APC mutation which causes beta-catenin to accumulate within the nuclei as well.

In a series of 12 patients of FAP patients with PTC, the overall survival was favorable, estimated to be 90% at 5 years and 77% at 20 years. The study also observed that the disease tended to occur in young females and have multicentric and/or bilateral foci. Both cases in this series involved female patients, of which one is in her early twenties. Another study found that the risk of thyroid cancer is as high as 6% in FAP patients, which prompted the recommendation of thyroid cancer screening.

In summary, the cribriform morular variant of PTC is a rare but aggressive thyroid malignancy, though not to the degree of other PTC variants such as tall cell. Optimal treatment parallels that of standard thyroid malignancies, in which surgical extirpation remains the gold standard. Due to its histologic similarities to FAP-associated thyroid cancer, referral for gastroenterology evaluation is recommended.

REFERENCES