Clinics in Surgery

Case Presentation
Published: 11 Oct, 2017

Cribriform Morular Variant of Papillary Thyroid Cancer: An Indication for Colonoscopy and Genetic Testing?

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Abstract

Papillary thyroid cancer is a common diagnosis in young patients that generally confers an excellent long term prognosis. Several variants exist which confer important clinical implications. The Cribriform Morular Variant of Papillary Thyroid Cancer (CMV-PTC) is a rare variant that is sometimes associated with Familial Adenomatous Polyposis (FAP). Here we describe an additional case of this rare subtype and review of the literature, focusing on the frequency of association with FAP and recommendations for subsequent management, including consideration for colonoscopy and genetic testing. CMV-PTC is associated with FAP in approximately 39% of cases in reports in the literature, however cases that are not associated with FAP are likely under reported and thus the true estimation of CMV-PTC in FAP positive and negative cohorts is likely unknown. CMV-PTC is often diagnosed significantly earlier than colon cancer in patients with FAP and represents an opportunity for early detection colon cancer. Given the reports of non-FAP colon polyps in patients with CMV-PTC, colonoscopy should be performed when the diagnosis of CMV-PTC is rendered with consideration for genetic testing as well depending on family history and patient preferences in a shared decision making framework.

Introduction

Papillary thyroid cancer is a common diagnosis in young patients that generally confers an excellent long term prognosis. Several variants exist which confer important clinical implications. The cribriform morular variant of papillary thyroid cancer is a rare variant that is sometimes associated with familial adenomatous polyposis (FAP). CMV-PTC is associated with FAP in up to 39% of cases in reports in the literature, however cases that are not associated with FAP are likely underreported and thus the true estimation of CMV-PTC in FAP positive and negative cohorts is likely unknown. Here, we describe an additional case of this rare subtype and review of the literature, focusing on the frequency of association with FAP and recommendations for subsequent management, including consideration for colonoscopy and genetic testing.

Case Presentation

A 28-year-old female was noted to have a palpable thyroid nodule on a routine physical exam. She had no symptoms of thyroid dysfunction and specifically denied any neck pain, dysphagia, dyspnea or hoarseness. Her medical history was otherwise unremarkable and she took no medications. She had a family history of an aunt with breast cancer and her grandfather had prostate cancer. She denied a family history of thyroid or colon cancer. The patient's physical exam was normal with the exception of a firm right sided thyroid mass. There was no palpable cervical lymphadenopathy and her voice was normal. Thyroid function tests were normal as well. An ultrasound revealed a right sided, complex, mixed solid and cystic nodule measuring 2.1 cm × 1.8 cm × 1.6 cm. No cervical lymphadenopathy was noted on ultrasound. The nodule was biopsied via ultrasound guided FNA and a diagnosis of papillary thyroid carcinoma was made. An uncomplicated total thyroidectomy was performed. No lymphadenopathy was noted intraoperatively in the central neck. The pathology report demonstrated a 1.8 cm × 1.9 cm papillary thyroid carcinoma, cribriform morular variant (Figure 1-3), with negative margins, no angiolymphatic or perineural invasion, and no extrathyroidal extension. Immunohistochemical stain for beta catenin was applied with valid controls and exhibited both nuclear and cytoplasmic staining (Figure 4 and 5). In recognition of the association of the cribriform morular variant of papillary thyroid cancer, the patient was referred postoperatively for screening colonoscopy, which was negative for polyps. She declined genetic

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Received Date: *09 Mar 2016*
Accepted Date: *20 Apr 2017*
Published Date: *11 Oct 2017*

Citation:
Coleman G, Roman R, Newbrough B, Milan S. Cribriform Morular Variant of Papillary Thyroid Cancer: An Indication for Colonoscopy and Genetic Testing?. Clin Surg. 2017; 2: 1669.

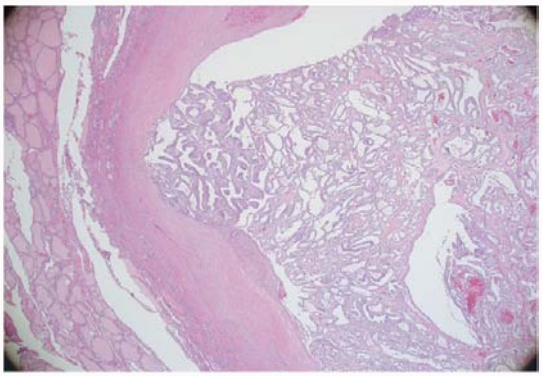

Figure 1: Image is a low power view featuring normal thyroid tissue at left side of picture; papillary carcinoma (mid and right side of screen) featuring conventional (papillary architecture) and cribriform pattern showing empty follicular structures (40X).

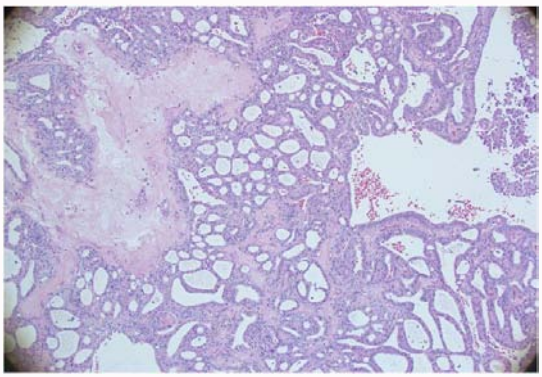

Figure 2: Cribriform are.as (back to back empty follicles) medium power (100X).

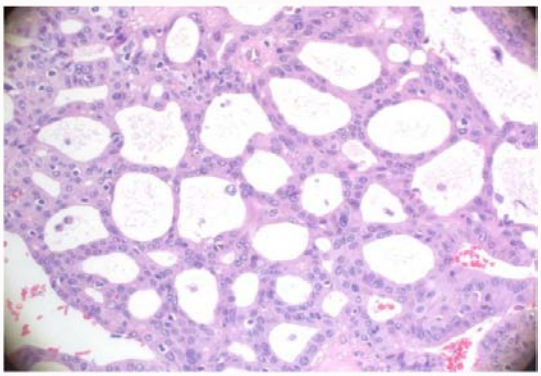

Figure 3: High power (1000x) view showing cribriform structures and empty follicles. A nuclear pseudo inclusion is highlighted by the arrow.

testing.

Discussion

Cribriform morular variant is a rare subtype of PTC with a recognized prevalence of 0.16% of all papillary thyroid cancer [1-5]. No preoperative features have been identified that particularly herald CMV-PTC [6,7]. Fine-needle aspiration cytology typically shows classic PTC features [8], although sometimes morules and spindle cells may clue the diagnosis [9]. Immunohistochemically, strong staining in the cytoplasm and immunoreactivity for b-catenin is characteristic of CMV-PTC [10,11]. BRAF mutations are often

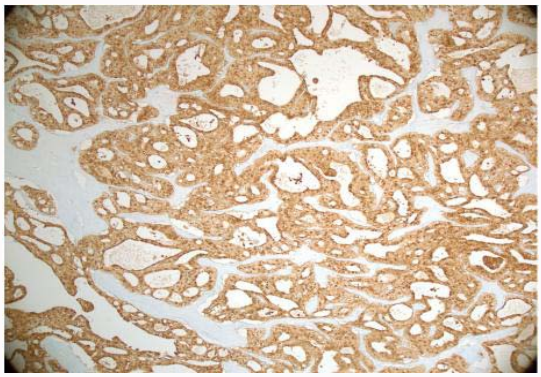

Figure 4: Medium power (200X) beta catenin: Immunohistochemical stain for beta catenin shows diffuse nuclear and cytoplasmic staining for beta-catenin confirming the diagnosis.

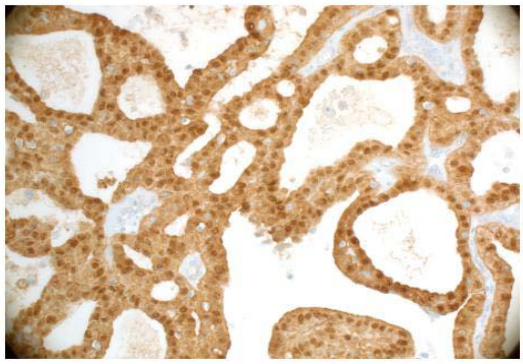

Figure 5: High power view (400X) beta catenin showing nuclear and cytoplasmic staining.

negative [11-14]. Familial adenomatous polyposis is a hereditary cancer syndrome resulting from an autosomal dominant mutation in the tumor suppressor APC gene and confers a 100% cumulative risk of developing colorectal cancer unless prophylactic colectomy is performed early. Further, up to one-third of newly diagnosed cases occur in patients without a family history of colon cancer and appear to represent either de novo germline mutations or mosaicism. The average age of colon cancer diagnosis in patients with FAP is 38-41 years. The risk of developing thyroid cancer in patients with FAP is about 2% and the age at diagnosis is earlier than that for colon cancer, with an average age of 25-33 years. One hundred and thirty-nine previous cases of CMV-PTC have been reported in the literature, and of these reported cases, approximately 39% have been found to be associated with FAP. Recognition of the association of CMV-PTC with FAP presents an opportunity for early diagnosis of this colon cancer syndrome. While CMV-PTC is often associated with FAP, sporadic CMV-PTC has also been described and is likely underreported in the published literature [15,16]. Thus so far no definitive characteristics pertaining to the thyroid are useful in predicting if CMV-PTC is FAP-associated, although two studies have noted trends toward younger age at diagnosis, multi-centricity, and bilateral tumors [5,17]. Reports of patients with CMV-PTC and non-FAP associated colon cancers also exist and further complicate the issue of whether genetic testing, colonoscopy or both, is indicated when this entity is clinically recognized [18,19].

Conclusion

The cribriform morular variant of papillary thyroid cancer is a

rare variant is often associated with Familial Adenomatous Polyposis (FAP). Clinical recognition of the potential association may serve to aid in early detection of occult FAP and colon cancer in some patients with a diagnosis of CMV-PTC. CMV-PTC is often diagnosed significantly earlier than colon cancer in patients with FAP and represents an opportunity for early detection colon cancer. Cribriform morular variant of PTC is associated with FAP in nearly 40% of cases in reports in the literature, however cases that are not associated with FAP are likely underreported and thus the true estimation of CMV-PTC in FAP positive and negative cohorts is likely unknown. Given the reports of non-FAP colon polyps in patients with CMV-PTC, colonoscopy should always be performed when the diagnosis of CMV-PTC is rendered with consideration for genetic testing as well depending on family history and patient preferences in a shared decision making framework.

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