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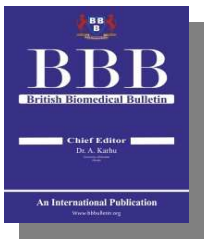

Original

Unusual Variant of Papillary Thyroid Carcinoma: Cribriform Morular Variant: A Clue to Underlying Intestinal Polyposis

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A B S T R A C T

Cribriform-morular variant of papillary thyroid carcinoma (CMV of PTC) is a distinctive histological variant of thyroid cancer, which on histopathological examination shows presence of cribriform, follicular, papillary, trabecular pattern and presence of squamous morules. These tumors are known to be associated with familial adenomatous polyposis (FAP), but can also arise sporadically in non-FAP patients. We report a case of CMV of PTC in a 35 year old female for its rarity, which alerted us to an underlying intestinal polyposis. The diagnosis of this variant should alert to the possibility of an underlying intestinal polyposis and be investigated for.

Introduction

Several histological variants of papillary thyroid carcinoma including follicular, tall cell, columnar, hurthle cell variant etc are described. CMV-PTC is a rare, under-recognised variant with distinct histological features. This variant of PTC can be associated with an underlying intestinal polyposis which may manifest before, with or after a diagnosis of PTC. Awareness of this variant of PTC is important, to alert the clinician of this association.

Case Report

Patient history

A 46 year old woman complained of gradually enlarging, painless swelling in the neck since 8 months. No family history of goiter or any endocrine disorder was noted. She gave no history suggestive of hyper or hypofunctioning of thyroid.

Physical examination

On clinical examination, thyroid was diffusely enlarged with multiple nodules. There were associated enlarged left cervical lymph nodes. The results of thyroid function tests were normal. Fine needle aspiration cytology performed showed features suspicious for papillary thyroid carcinoma. Patient underwent complete thyroidectomy and lymph node dissection and the specimen was sent for histopathological evaluation.

Histopathological examination

On gross examination, normal thyroid was replaced by multiple variably sized nodules with a grey white appearance and focal papillary excrescences (Fig. 1). Microscopic examination revealed follicles, with focal cribriform pattern lined by follicular cells exhibiting nuclear clearing with grooves and occasional pseudo-inclusions (Fig. 2). Also seen were whorls and morules of squamoid cells (Fig. 3) suggesting a diagnosis of CMV-variant of PTC. All the 4 lymph nodes dissected showed evidence of metastases. The staging was pT2N1 with complete resection. Complementary radioactive iodine therapy was given for 8 months in combination with inhibitory hormone therapy.

In view of increased association of this variant of PTC with FAP, endoscopic evaluation was suggested. There was no history suggestive of FAP in the family. Patient was advised colonoscopy which revealed presence of 3 polyps, largest measuring 0.8 cms. Biopsy of the polyp showed tubular adenomatous polyp with mild dysplasia.

Discussion

CMV of PTC is an uncommon histological variant of PTC that is commonly encountered in young females. Harach *et al* first described this variant as a peculiar form of thyroid carcinoma that can be associated with underlying familial adenomatous polyposis of the colon[1]. Subsequently, sporadic variant of this tumor was described[2]. This variant of PTC accounts for approximately 0.1%- 0.2% of all PTC. However this variant of PTC has a high prevalence of up to 12% in patients having underlying FAP. Patients with FAP have a very high risk of developing thyroid carcinoma than general population. The CMV of PTC has a high female predominance and most commonly affects young women, with a mean age at diagnosis being 28 years (range 12- 53 years). It may precede the diagnosis of FAP in many cases.

The characteristic histological features of CMV-PTC include presence of cribriform, follicular, papillary, trabecular, solid and spindle cell growth patterns with squamoid differentiation, forming morules. Colloid is usually scant within the follicular lumina. The peculiar nuclear clearing within

the morules is thought to be caused by biotin accumulation in the tumor. The tumor cells possess chromatin rich nuclei usually showing nuclear grooves, with occasional intranuclear cytoplasmic pseudoinclusions, unlike a classical PTC. The presence of cribriform pattern and squamous morules help in identifying this tumor as a distinct variant of PTC. This variant of PTC can be differentiated from high grade aggressive thyroid neoplasm, by the absence of nuclear atypia, mitosis and necrosis.

Immunohistochemical features of this tumor include positive staining with thyroid transcription factor-1, cytokeratins 7 and 19, vimentin, estrogen and progesterone receptors, bcl-2, E-cadherin and galectin-3[3]. Molecular genetics reveal activation of the WNT pathway, with accumulation of beta-catenin in this variant. The presence of genetic alterations in *APC*/beta-catenin pathway, *RET/PTC-1* and *RET-PTC-3* rearrangements are supportive of categorizing this variant as a subtype of papillary thyroid carcinoma. This tumor is usually encapsulated or locally advanced tumors without distant spread at the time of diagnosis. Treatment involves total/near total thyroidectomy with or without radioiodine therapy. CMV- PTC usually has a good prognosis, but there are few reports of this tumor behaving aggressively[4].

Because this type of papillary thyroid carcinoma can develop before familial adenomatous polyposis becomes clinically manifest, the recognition of its particular histological features should raise suspicion to the presence of underlying FAP, whenever a diagnosis of CMV-PTC is diagnosed[5].

Conclusion

As CMV-PTC can occur before the colonic manifestations are apparent, hence recognition of this variant is important so that the patient can be assessed for the presence of associated colonic disease status as well as undergo genetic and familial counseling.

Consent

A retrospective report of a rare case and the patient's identity is not revealed. No clinical photographs are used in the case report.

Abbreviations

- CMV of PTC- Cribriform-morular variant of papillary thyroid carcinoma.
- FAP-Familial adenomatous polyposis.

Competing interests

Authors declare no competing interests.

Acknowledgement

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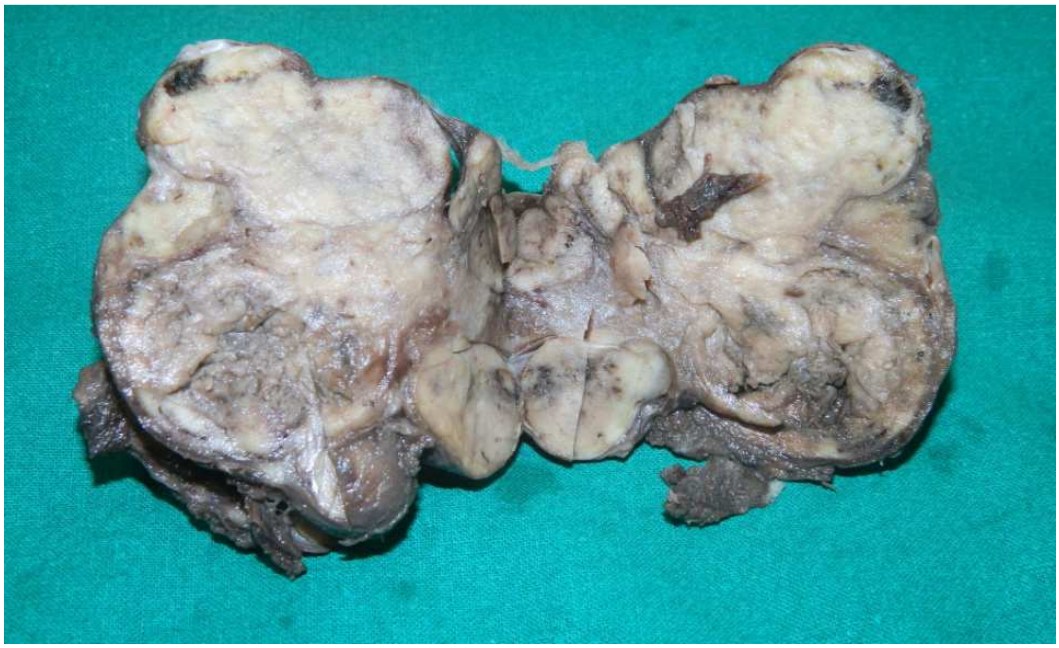

Figure 1. Gross of thyroidectomy showing multiple thyroid nodules with grey white areas and fine papillary, excrescences

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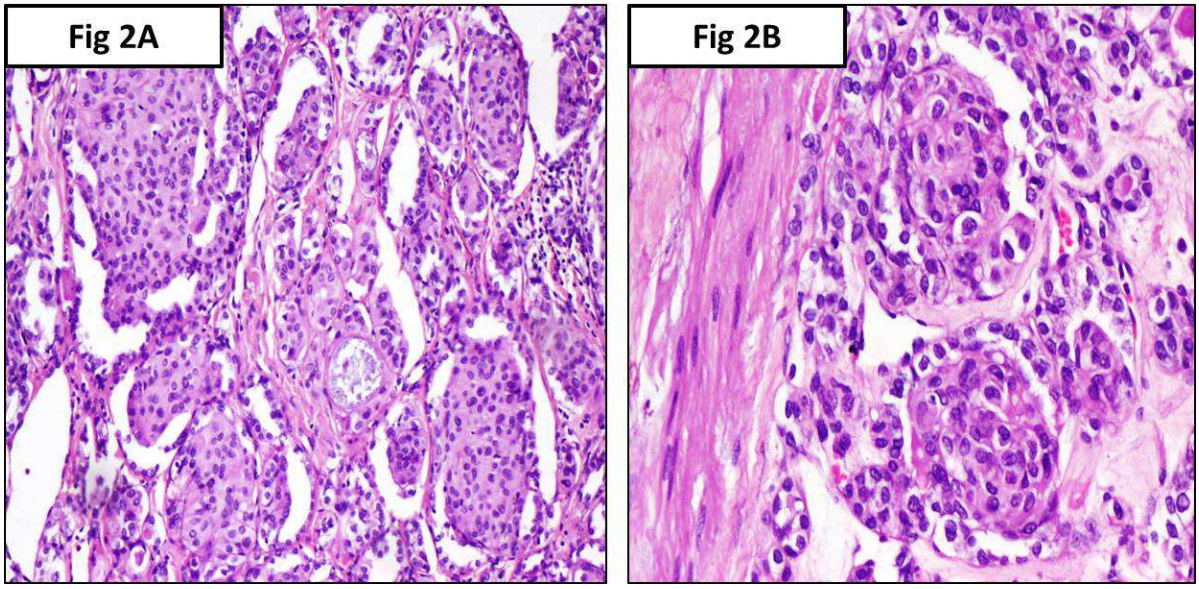

Figure 2. Image on left and right shows numerous whorled squamous morules within the follicles H&E, at 100X and 200X respectively

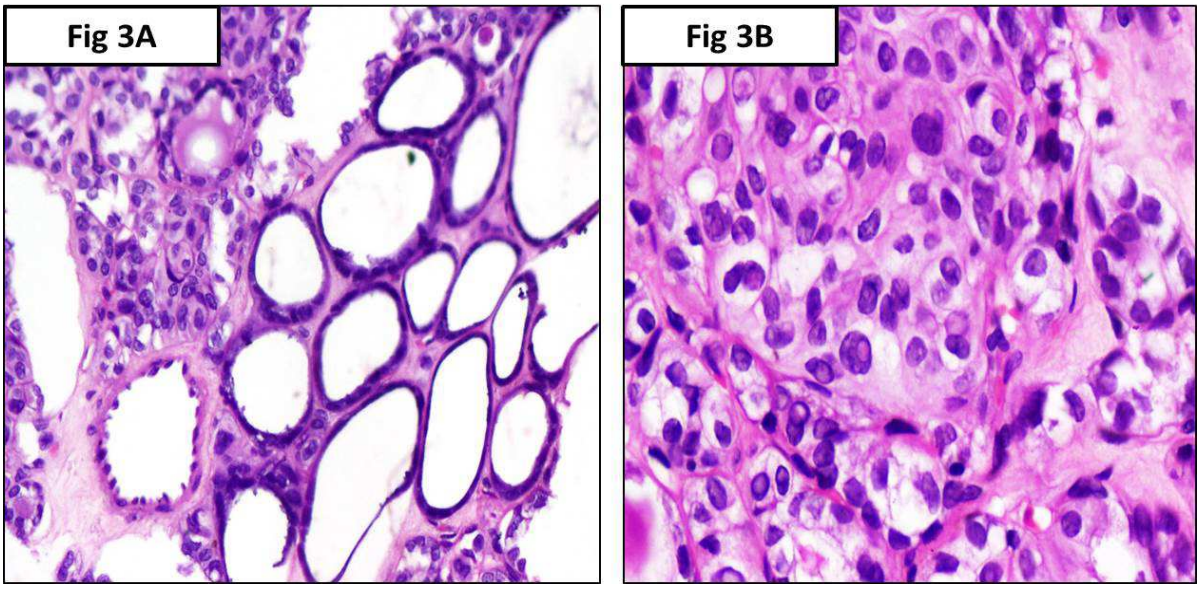

Figure 3. Image on left shows cribriform appearance of the dilated follicles and on right shows intranuclear inclusions and clearing typical of papillary carcinoma of thyroid, H&E, 200X