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Warthin-Like Papillary Carcinoma of Thyroid in A Background of Hashimoto's Thyroiditis: A Rare Case Report With Review of Literature

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ABSTRACT

Warthin –like papillary carcinoma is a rare and recently described variant of papillary carcinoma of thyroid .This uncommon variant has a striking resemblance to Warthins tumor of the salivary gland and is characterized by multiple papillary fronds lined by oncocytic neoplastic cells with optically clear nuclei and dense lymphocytic infiltrate in the papillary core. We hereby present a case of Warthin- like carcinoma of the thyroid in a 40 year old female with thyromegaly since six months . Thyroid hormonal levels were normal with raised antibody titres suggesting the possibility of Hashimoto's thyroiditis. Computed tomography of the neck showed a cystic lesion measuring 2.6x2.1cms. FNAC showed features of papillary carcinoma thyroid with oncocytic clusters.Total thyroidectomy specimen on histomorphology showed Warthins variant of papillary carcinoma set in a background of Hashimoto's thyroiditis.. This entity has to be borne in mind as it carries a good prognosis and long term follow up is mandatory to assess the biological behaviour.

KEYWORDS : Papillary carcinoma, Hashimoto's thyroiditis,Warthin-like .

INTRODUCTION:

Warthin like papillary carcinoma of the thyroid carries a striking resemblance to Warthins tumor of the salivary gland with papillae lined by oncocytic malignant cells having abundant cytoplasm and nuclear features as that of the papillary carcinoma of thyroid in a lymphocytic stroma.This variant has to be differentiated from other variants of papillary carcinoma ,Hurthle cell carcinoma and Hashimoto's thyroiditis.Biological behaviour of this rare variant is similar to that of the conventional type of papillary carcinoma of thyroid and carries a favourable prognosis.

CASE REPORT:

A 40 year old female presented with thyromegaly since 6 months, and pain since 3 weeks. There was no family history or any risk factors for thyroid cancer.Physical examination showed a nodular mass involving the left lobe of thyroid which measured 2 x 2 cms. There was no evidence of lymphadenopathy. Routine laboratory tests revealed normal thyroid levels and raised antibody titres suggesting the possibility of Hashimoto's thyroiditis. She underwent a computed tomography of the neck which showed a cystic lesion measuring 2.6x2.1cms. FNAC(fig1a&b) revealed a cellular smear showing multiple papillary fronds with crowding, overlapping and anatomical bordering of neoplastic cells which had moderate amount of cytoplasm and round to oval nuclei with some showing nuclear inclusions. Focal area showed cells with abundant cytoplasm and round to oval nuclei.A diagnosis of papillary carcinoma of thyroid was offered. Patient underwent total thyroidectomy and the specimen(fig 2)was received in 4 pieces, largest measuring 4x3x1cm and smallest measuring 1x1x0.5cm. External surface of all the pieces were nodular and cut section showed grey white illdefined ,firm areas with surrounding normal thyroid parenchyma. (Figure 1a&b,2 about here)

Histomorphology(fig 3,4,5) revealed a malignant neoplasm arranged in papillae lined by oxphilic cells enclosing nodules of lymphocytic stroma. The neoplastic cells had granular eosinophilic cytoplasm, round to oval optically clear nuclei with few cells showing nuclear inclusions. Adjacent thyroid parenchyma showed features of Hashimoto's thyroiditis. Postoperative period was uneventful and radioablative treatment was given 2 months later.Patient was normal with no evidence of recurrence on follow up.(figure3,4,5 about here)

DISCUSSION:

Warthin- like papillary carcinoma of thyroid is a rare variant and less than 100 cases have been documented in English literature to date (1). Apel et al was the first to report this uncommon variant of papillary carcinoma thyroid in the year 1995 and called it as "Papillary Hurthle cell carcinoma of the thyroid with lymphocytic stroma – Warthin –like tumor of the thyroid (1).This tumor accounts for 1% to 11% of all papillary carcinomas(2). Major morphological variants of thyroid malignancies according to the current WHO system are follicular, macrofollicular,clear cell,tall cell,columnarcell,clear cell,solid,oncocytic,cribriform and diffuse sclerosing types(3). Warthin-like papillary carcinoma is considered to be a hybrid variant of tall cell and oncocytic variant according to Vera –Sempere et al(4). The age group most commonly affected is between 20 and 85 years with female predeliction.Warthin-like carcinoma is most common in the fourth decade with the mean age of presentation being 44.9yrs in a retrospective study of 16 cases conducted by Jun HH in the year 2014(5). Clinical presentation is as that of the conventional papillary carcinoma. Harmone levels depend on the severity of thyroiditis,while USG and CT findings are similar as in classical papillary carcinoma . Our case was a 40 year old female with normal thyroid harmones and raised antibody titres.

Yousef et al and Baloach et al were the first to describe the cytological picture of Warthins –like variant (6,7). These tumors show a bimodal population of papillary clusters of follicular epithelial cells having nuclear clearing,grooving, intranuclear pseudoinclusions, oncocytes with round nuclei ,coarse chromatin and prominent nucleoli in a background of small and large lymphocytes.It can mimic like follicular adenoma or carcinoma with oncocytic change, if ground glass nuclei and papillary fragments are absent.

Grossly Warthin-like variant of papillary carcinomas are grayish white ,well circumscribed, measuring 0.3 to 5 cms with a mean of 2cms and are confined to the thyroid gland. Focal areas of haemorrhage and cystic degeneration can occur. Histomorphology shows papillary structures lined by oncocytic cells with optically clear nuclei with some showing nuclear pseudoinclusions and grooving with lymphocytic infiltration of the papillary core. This lymphocytic infiltration in the papillary core is due to an immunological response and its presence is important as it offers a lesser recurrence rate with favourable prognosis without further tumor progression(8). Intra tumoral and peritumoral lymphocyosis is considerd as a marker of favourable prognosis according to Matsubayashi et al(9).IN a study conducted by Fienmesser and Kawai et al, tumor associated lymphocytes has been found to play a major role in control of thyroid cancer with associated evidence of expression of HLA type II antigens by the malignant thyroid follicular epithelial cells in response to such lymphocytic infiltrate(10,11).No clinical significance of lymphocytic infiltrate in papillary carcinoma of thyroid has been reported by Gomez et al(12). Coexistent lymphocytic thyroiditis or Hashimoto's thyroiditis was seen in more than 90% cases of Warthins-like carcinoma(13). We documented coexistent Hashimoto's thyroiditis in our case too.

The histological differentials are tall cell and oncocytic variant. Tall cell variant has more than 50% cells with tall cell morphology and these cells have a height twice the width with abundant eosinophilic cytoplasm and basally placed elongated nuclei. Oncocytic variant has eosinophilic granular cytoplasm with typical nuclear features of conventional papillary carcinoma.The lymphoplamocytic infiltration seen in Warthin-like carcinoma is not evident in both the Tall cell and oncocytic variants. Papillary Hurthle cell carcinoma exhibit papillary fronds lined by oncocytic cells with nuclear features of papillary carcinoma but lack lymphocytic infiltration and association with lymphocytic thyroiditis(14,15).

Regional lymph node metstases is rare in this variant and a large case series reported by Paliogiannis showed that the presence of regional lymph node metastasis was uncommon and accounted to about 22% (16) .

immunohistochemical markers like EMA,AE1/AE3,S-100protein,galectin3, HBME-1,thyroglobulin,cyclin D1 ,TTF-1,UCHL1and CD79+, CD20+, CD3+ for the lymphocytic population, were employed for the confirmation of the diagnosis in various case series(16) Immunohistochemistry was not done in our case as the histomorphology was distinct and typical of of Warthin-like papillary carcinoma .

75% of patients with Warthin-like variant have been reported to exhibit BRAF mutations from a small series studied by Finkelstein. (17). This mutation is associated with a worst prognosis in case of classical papillary carcinoma in comparision with the Warthin –like variant which carries a good prognosis. RET rearrangement is not only seen in classical papillary carcinoma thyroid,but has been documented in the Warthin like variant,thus proving it as a variant of papillary carcinoma(18). Only two cases have been documented in literature , to have a worst prognosis,one with anaplastic feature and the other with a dedifferentiated histomorphology (19).

Surgical management is as for the conventional papillary carcinoma of the thyroid .Total thyroidectomy is the mode of treatment followed by chemotherapy.There is limited knowledge on the postoperative followup of this variant.Our case also underwent total thyroidectomy followed by 4 cycles of chemotherapy.Post operative period was uneventful and patient is disease free.

CONCLUSION:

Warthin-like variant of papillary carcinoma being distinct in its histomorphological features needs mention in the histopatholOgy case summary as it has a favourable and good prognosis and needs exclusion from other variants having an aggressive behaviour.Long term follow up of such patients is of atmost importance so as to know the biological behaviour and clinical course of such tumors.

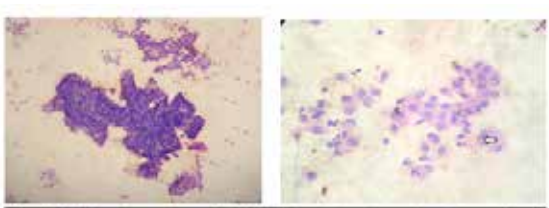

Figure1a&b: a) papillary clusters of thyroid follicular cells and oncocytic cell clusters. b) oncocytic cell clusters with intranuclear inclusions.

Figure -2 Gross –thyroid in four pieces showing ill defined grey white areas

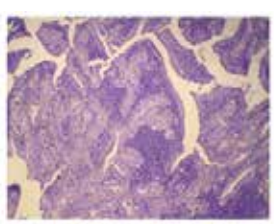

Figure-3. (10x100)Papillary fronds lined by oncocytic neoplastic cells with lymphocytic infiltrate in the papillary core.

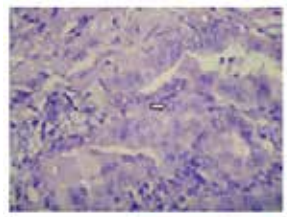

Figure-4.(4x100) Oncocytic neoplastic cells with optically clear nuclei and nuclear inclusion

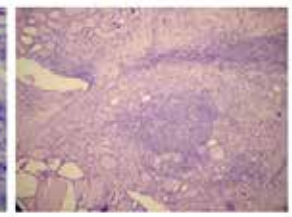

Figure-5.(10x100) Adjacent foci of Hashimoto's thyroiditis

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