CLINICAL VIGNETTE

Diffuse Sclerosing Variant of Papillary Thyroid Carcinoma – A Rare and Aggressive Variant

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Introduction

Papillary thyroid carcinoma is the most frequent type of thyroid carcinoma. It is divided into many variants with variable clinicopathological characteristics and biological behaviors.[1] Most variants, especially classic papillary thyroid carcinoma, are indolent and the 5 years' survival of patients is reported to be 95-98%.[2] However, diffuse sclerosing variant of papillary thyroid cancer is rare and more aggressive than classic papillary thyroid cancer. The aim of this case report is to present a case of diffuse sclerosing variant papillary thyroid cancer.

Case Presentation

A 25-year-old woman with hypothyroidism secondary to Hashimoto's thyroiditis for more than 6 years, undifferentiated connective tissue disorder and vitiligo presented for evaluation of goiter. She was in her usual state of health until four months prior to the office visit when she noticed increasing neck swelling, worsening dysphagia, and intermittent hoarseness of the voice. Ultrasound of the thyroid four months ago showed a goiter with diffuse heterogeneous background and increased blood flow, without nodule or calcification or abnormal cervical lymph nodes. She had no prior radiation exposure. She was adopted and her adopted mother died from papillary thyroid cancer. She takes thyroxine 100 mcg/day with normal TSH of 2.4 U/ml. Her thyroid exam showed symmetrically enlarged lobes, without discrete nodules, calcification and no palpable cervical lymph nodes.

A repeat thyroid ultrasound showed similar sized goiter with diffuse heterogeneous background without any nodule or abnormal cervical lymph node or calcification (right lobe is 1.7 cm x 1.9 cm x 5.3 cm, left lobe is 1.9 cm x 1.8 cm x 4.8 cm and isthmus is 1.0 cm).

Due to worsening compressive symptoms, patient underwent total thyroidectomy. The surgical pathology showed right lobe papillary thyroid cancer, diffuse sclerosing variant. The cancer size was at least 2.0 cm with lymph vascular invasion but had no extra thyroidal extension.

Patient underwent 104.9mCi of Iodine-131 therapy. The post treatment scan showed excellent response to therapy (< 1% uptake in the thyroid bed). She had been taking levothyroxine 175 mcg daily after the surgery.

Discussion

Diffuse sclerosing variant of the papillary thyroid cancer (DSVPTC) was first described in 1985.[3] It is reported to account for about 0.7 to 6.6% of all papillary thyroid carcinomas. Higher prevalence of DSVPTC was noted in pediatric patients and in patients affected by irradiation. DSVPTC tends to occur more frequently in women and patients in the third decade of life.[4]

Most patients present with diffuse goiter and are clinical euthyroid but can be hypothyroid or hyperthyroid. Most patients have cervical lymph node metastasis at the time of the diagnosis.[5] Lung metastasis[6] and cerebral metastasis at presentation have also been reported.[7] Distant metastases may present in up to 5% of the cases.[4] DSVPTC can present as numerous diffuse microcalcifications in Hashimoto's thyroiditis [8] or can mimic benign Riedel's thyroiditis.[9]

The ultra-sonographic appearance of the DSVPTC may show diffusely altered thyroid parenchyma with a snow-storm appearance and generally firm enlarged thyroid lobes with diffusely prominent microcalcifications and psammoma bodies.[8] DSVPTC can involve the thyroid gland extensively without forming a dominant mass.[4]

If there is suspicious nodule on the thyroid ultrasound, a fine needle aspiration biopsy is the most valuable diagnostic procedure for pre-discrimination of the benign and malignant nodules. Bethesda classification is a valuable guide for fine needle aspiration reports and highly predictive for diagnosing aggressive variants of papillary thyroid carcinoma.[10]

DSVPTC is characterized by histologic features such as numerous psammoma bodies; extensive lymphocytic infiltration; squamous metaplasia; diffuse fibrosis; calcification and absence of string colloids together with the characteristic cytoarchitectural pattern of classic papillary carcinoma. The diagnosis of DSVPTC is challenging because it may be mistaken clinically for benign disease, particular thyroiditis. A diagnosis of DSVPTC should be considered when above mentioned ultrasound feature and histological features are present.[11]

The molecular profile of DSVPTC is different from classic papillary thyroid cancer. The immunohistochemical studies of DSVPTC showed different expression pattern of epithelial

membrane antigens; galectin 3, cell adhesion molecules, p53 and p63 when compared to classic papillary thyroid carcinoma.[4] Genetic analysis shows a different pattern of genetic mutation, activation of RET/PTC rearrange as the major genetic alteration in DSVPTC. RET/PTC3 rearrangement is associated with advanced stage at diagnosis and poor clinical outcomes.[12] The occurrence of thyroid cancer oncogenes BRAF and RAS mutations are uncommon events when compared to classic papillary thyroid cancer.[4]

Many studies showed DSVPTC is very aggressive and has a less favorable outcome than classic papillary thyroid cancer.[13] A meta-analysis showed DSVPTC has higher rate of cancer multifocality, vascular invasion, extrathyroidal extension, lymph node metastasis, distant metastasis and is likely to recur. It has worsened overall survival compared to classic papillary thyroid cancer and should be considered as high-risk papillary thyroid cancer.[14] Another study showed the recurrent rate within first 5 years is high and requires a careful ongoing surveillance, similar to the follow up of high risk papillary thyroid cancer patients.[15]

The treatment is total thyroidectomy with lymph node excision followed by radioiodine therapy due to the aggressive biological behavior of DSVPTC.[16]

Summary

DSVPTC has different clinical, pathological, and molecular profiles when compared to classic papillary thyroid cancer and requires more aggressive treatment and close monitoring. They may be mistaken for benign disease particularly thyroiditis. In this case, the clinical presentation, biochemical, and initial radiological findings were all indicative of benign pathology. It is important to consider this rare cancer when evaluating a young patient with goiter or Reidel's thyroiditis or Hashimoto's thyroiditis.

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