Hurthle cell adenoma as an incidental finding in Hashimoto’s thyroiditis - case report and short review of literature

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Citation

Abstract
Several thyroid neoplasms are known to arise in thyroid glands with preexisting thyroiditis. Apart from the well documented occurrence of follicular and papillary carcinomas, Hurthle cell neoplasms (both adenomas and carcinomas) are often detected in these cases. We present the case of a female patient who was diagnosed on histopathology as having Hashimoto’s thyroiditis with a Hurthle cell adenoma, along with a short discussion of recent developments pertaining to Hurthle cell neoplasms.

INTRODUCTION
The association of autoimmune thyroiditis especially Hashimoto’s thyroiditis with thyroid neoplasms has often been reported and detailed research has been carried out in this area. We now have extensive literature pertaining to the pathogenesis of these lesions. Hurthle cell neoplasms are also known to arise in a background of thyroiditis, though the frequency is much less in comparison to the occurrence of follicular/papillary carcinomas. As with follicular neoplasms, it is often difficult to differentiate a benign Hurthle cell adenoma from a carcinoma on cytology, hence surgery is advisable where there is a suspicion. We would like to discuss here a case of Hurthle cell adenoma arising in Hashimoto’s thyroiditis, along with recent research regarding the molecular basis of Hurthle cell neoplasms.

CASE REPORT
A 35 year old female presented with a swelling in the right side of the neck for the past 1 year, with progressive increase in size. There was no associated pain, hoarseness of voice or loss of weight. There were no features of hypo/hyperthyroidism. The patient had not received any irradiation to the head and neck region in the past. Clinical examination revealed a mass measuring 3 x 3 cms. It was mobile, firm, non-tender, non-pulsatile and moved on deglutition. The margins were well defined. Ultrasonography revealed a large, solitary, heterogeneous nodule in the right lobe of the thyroid.

Fine needle aspiration cytology (FNAC) was performed by non-aspiration technique. The material obtained consisted of scant, thick colloid and small clusters of follicular cells along with a prominent superimposed lymphocytic infiltrate. In addition, numerous oxyphil cells were observed with dense eosinophilic cytoplasm and anisokaryosis. Marked nuclear atypia was noticed in several cells. Antibodies to thyroid peroxidase were found to be raised (472 IU/L). In light of the above observations, a provisional diagnosis of Hashimoto’s thyroiditis with the possibility of a Hurthle cell neoplasm was made.

The patient underwent thyroidectomy. The post-operative tissue specimen received for histopathological examination was a single encapsulated nodular mass, around 4 cms in diameter. It was firm to hard in consistency. The cut section was tan-brown in colour, solid with multiple, variably sized nodules and a central hemorrhagic area. Microscopic examination showed a diffuse lymphocytic infiltrate with formation of many lymphoid follicles, thyroid follicles were reduced and atrophic (Fig.1). A large focal encapsulated area was composed of clusters and sheets of oxyphil cells which were round to oval in shape, with abundant granular cytoplasm and enlarged hyperchromatic nuclei (Fig.2,3). A few had prominent nucleoli. There was no evidence of capsular or vascular invasion. The final histopathological diagnosis was of Hashimoto’s thyroiditis with Hurthle cell adenoma.
**DISCUSSION**
Hashimoto’s thyroiditis is a well known cause of hypothyroidism and is characterized by autoimmune destruction of the thyroid gland. Antibodies against various thyroid antigens are present, especially anti-TSH (thyroid stimulating hormone) receptor antibody, anti-thyroglobulin and anti-thyroid peroxidase antibody. It is commonly seen in the 5th and 6th decade and is ten times more prevalent in females than in males. Various synonyms for Hashimoto’s thyroiditis include diffuse lymphocytic thyroiditis, goitrous autoimmune thyroiditis and struma lymphomatosa.

Most of the patients are either euthyroid or present with features of mild hypothyroidism with a mild to moderately enlarged, painless thyroid gland. It is associated with various thyroid neoplasms- follicular adenoma, follicular carcinoma, papillary carcinoma, medullary carcinoma, lymphomas, Hurthle cell adenoma and Hurthle cell carcinoma.

Hurthle cell tumors represent less than 5% of all thyroid tumors. These are composed predominantly of Hurthle cells, which are thyroglobulin producing, mitochondria-rich thyroid epithelial cells. They are also known as Askanazy cells/oxyphil cells, and are an associated finding in various benign thyroid conditions like Hashimoto’s thyroiditis, non-specific chronic thyroiditis, long standing hyperthyroidism, nodular goiter and thyroid neoplasms where they represent oncocytic metaplasia. A diagnosis of a Hurthle cell neoplasm can be made only if 75% or more of the tumour...
cells are Hurthle cells.\textsuperscript{a}

The majority of these tumors are benign and are labeled as Hurthle cell adenomas, but up to 40\% are malignant.\textsuperscript{7} Documentation of the presence of capsular/vascular invasion or lymphatic spread is necessary for the diagnosis of Hurthle cell carcinoma.\textsuperscript{a} However, some of these tumors exhibit few features of invasion but lack unequivocal signs of malignancy and patients have remained well on follow up. Such tumors are considered atypical Hurthle cell adenomas or Hurthle cell tumors of uncertain malignant potential.\textsuperscript{a}

The molecular basis of Hurthle cell proliferation has been extensively studied and several interesting insights are now available. Persistent autoimmune cell response may lead to oxyphil cell hyperplasia in autoimmune thyroiditis.\textsuperscript{a} In addition; the mitochondrial DNA common deletion (mtDNA CD) has been identified in cases of Hashimoto’s thyroiditis with oxyphil cells, pointing to the possible role of genetic defects in the respiratory chain in development of oxyphil cell change in these cases.\textsuperscript{8}

The 4,977 base pair deletion (mtDNA CD) has been detected in Hurthle cell tumors as well, and in one series, up to 16\% deletion frequency was detected in every Hurthle cell tumor.\textsuperscript{a} This is again suggestive of a possible association between Hurthle cell tumors and germline polymorphisms of ATPase-6 (Adenosine triphosphatase-6).\textsuperscript{a} It is thought that the decreased efficiency of mt DNA replication could have an etiopathogenetic role in the development of Hurthle cell tumors. The increased mitochondrial content maybe a compensatory process arising from defective energy productions of the cell.\textsuperscript{a}

A very interesting and relevant observation was put forward by Katoh et al, who stated that oxyphilia in thyroid tumors may be a primary development, due to somatic mutations, or a secondary phenomenon linked to oxidative damage or environmental aggression.\textsuperscript{10} In other words, somatic mutations lead to oxyphil cell tumors (true oxyphil tumors) while in other thyroid neoplasms, the change is a consequence of the accompanying inflammatory cells.\textsuperscript{a}

More recent research has brought attention to ‘Genes associated with Retinoid-1 Interferon induced Mortality (GRIM)’\textsuperscript{,11} One specific gene, GRIM-19, is a 552 base pair gene and it encodes a 16 kDa protein. GRIM-19 is a dual function gene, associated with both interferon/retinoic acid induced cell death and mitochondrial metabolism.\textsuperscript{11} It is linked to Hurthle cell tumors through somatic and germline mutations.\textsuperscript{12} In fact, the GRIM-19 mutation is the first nuclear mutation specifically linked to Hurthle cell tumors.\textsuperscript{12}

It is often difficult to differentiate a benign from a malignant Hurthle cell neoplasm on aspiration cytology. Moreover, a diagnosis of malignancy can be confirmed only on histopathology through detection of capsular/vascular invasion or lymphatic spread. Statistically significant features on cytology that indicate a neoplastic process include a high proportion (>90\%) of Hurthle cells, cellular discohesiveness, nuclear pleomorphism, large nucleoli and lack of accompanying inflammatory cells.\textsuperscript{13}

Hurthle cell carcinoma behaves in a more aggressive fashion as compared to other well differentiated thyroid neoplasms. It is therefore advisable to perform a thyroidectomy in all suspicious cases of thyroid nodules, with special reference to Hurthle cell associated lesions. Moreover, a careful follow up is also essential in all cases of nodular goitre/thyroid nodule.

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