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Case report

Coexistence of anaplastic and papillary thyroid carcinomas and diagnostic pitfalls of fine needle aspiration

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Anaplastic thyroid carcinoma is a highly aggressive thyroid cancer with a dismal prognosis. We report a case of anaplastic thyroid carcinoma coexisting with papillary carcinoma. This is an extremely rare occurrence and is considered to have negative prognostic significance.

Key words: Anaplastic thyroid carcinoma, papillary carcinoma, fine needle aspiration.

INTRODUCTION

Anaplastic thyroid carcinoma (ATC) is a rare type of thyroid cancer (Gilliland et al., 1997). It ranks among the most lethal of all human malignancies (Demeter et al., 1991) and represents over half of thyroid cancer-related deaths (McIver et al., 2001), although the vast majority of thyroid cancers are well-differentiated and carries an excellent prognosis (Sniezek and Holtel, 2003). Papillary carcinomas of the thyroid are the most common well-differentiated malignant growth affecting the thyroid, currently representing 60 to 65% of malignant thyroid neoplasm. Although the aetiology of this neoplasm is unknown, they are thought to be related to neck irradiation (Mack and Preston-Martin, 1998), adenoma transformation, and Hashimoto thyroiditis (Ming-Lang et al., 2008). Papillary carcinomas are usually purely papillary but occasionally have areas of histologically different neoplasm, most commonly follicular. Overall, these carcinomas represent an indolent group of neoplasm and have an excellent prognosis. The occurrence of an anaplastic area in a papillary carcinoma represents the dedifferentiation of the primary neoplasm (Wiseman et al., 2003; Tan et al., 1995). The purpose of this presentation is to discuss an unusual clinical case of a coexisting anaplastic and papillary carcinoma of the thyroid. This case most likely represents anaplastic transformation in a pre-existing papillary carcinoma (Int J Health Science, 2009). The limitations of diagnosing this entity by FNAB as well as some clinical suggestions are discussed.

CASE REPORT

A 54 year old Kuwaiti lady presented dysphagia and chocking with food of three months duration. She has had a neck swelling which was increasing in size progressively and noticed a change in her voice over the same time period. She was previously healthy with no history of thyroid disease. On clinical examination she had a left lobe thyroid swelling which was hard in consistency. She had multiple hard and fixed cervical lymph nodes. Ultrasound showed a large 3.5 × 3.1 cm heterogeneous irregular mass with areas of calcification. The isthmus and right lobe were normal. She had extensive left lower cervical lymph nodes. Fine needle biopsy done in a tertiary referral centre revealed papillary thyroid carcinoma (Figure 1). Given her clinical course and presentation that did not correspond to the aggressive behaviour of the tumour, a search for a different diagnosis was pursued.

Computed tomography of her neck showed the same heterogeneous hypo dense lesion with retrosternal extension compressing and displacing the trachea and

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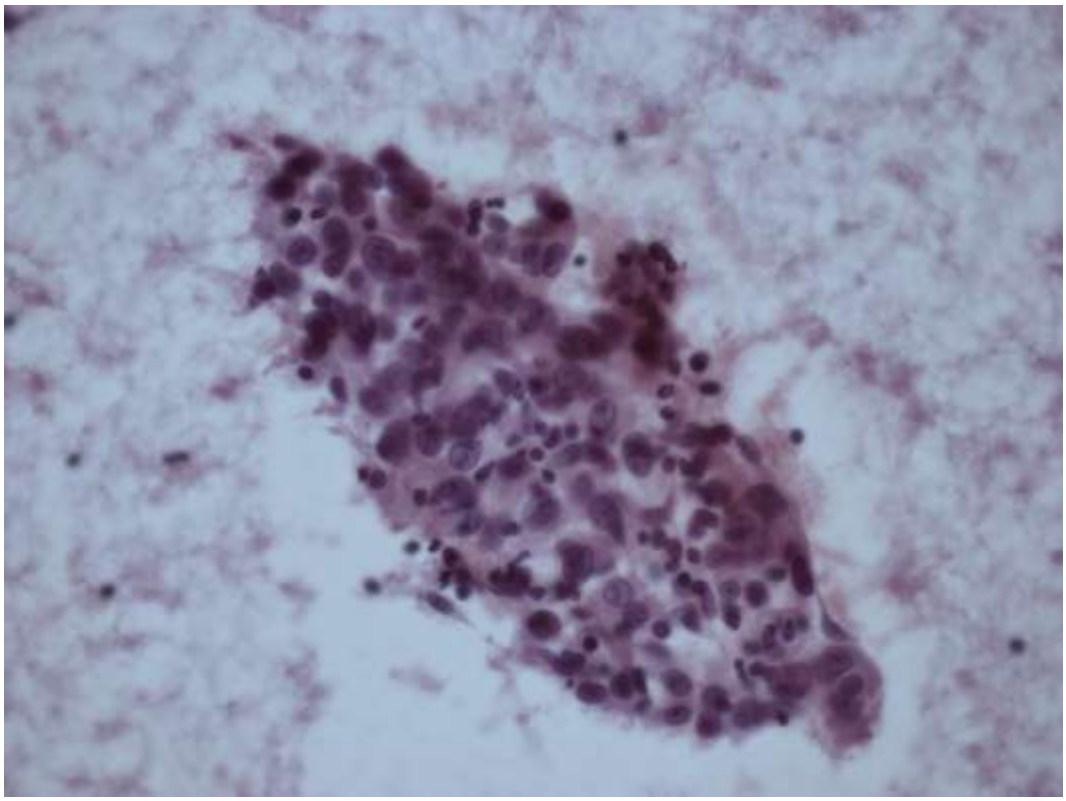

Figure 1. FNAC shows clusters cells with round to oval nuclei consistent with papillary carcinoma.

esophagus with displacement of the common carotid artery and left internal jugular vein. Cut images of the chest showed multiple nodules in both upper lung fields. No mediastinal lymph nodes seen. Core biopsy was arranged which revealed an undifferentiated anaplastic thyroid carcinoma (Figure 2). Immunohistochemical staining done and cells were epithelial membrane antigen (EMA) and vimentin positive and negative for LCA,, CD20, CD3,CK and cacitonin. Tracheostomy and feeding jejunostomy were arranged with plans for palliative radiotherapy and chemotherapy. Surgery was not performed due to rapid deterioration in patient condition and she passed away almost 6 months after initial presentation.

DISCUSSION

Anaplastic thyroid carcinomas are undifferentiated tumors of the thyroid. In marked contrast to differentiated thyroid carcinomas, anaplastic carcinomas are extremely aggressive, they rank among the most lethal of all known human malignancies, and remain almost uniformly fatal with a disease-specific mortality approaching 100% (McIver et al., 2001; Ain, 1999). Its lethality is evidenced by a 5-year survival rate of 3.6% and a median survival of 4 months. The annual incidence of anaplastic carcinoma is about two per million persons (McIver et al., 2001; Sniezek and Holtel, 2003), and accounts for only 2 to 5% of all thyroid cancers. Patients with anaplastic carcinoma are older than those with differentiated carcinoma; the mean age at diagnosis is 65 years, and fewer than 10% are younger than 50 years. Sixty to 70% of tumors occur in women (McIver et al., 2001; Wiseman et al., 2003). Rapid growth of a thyroid mass, frequently in a pre-existing goitre, is the most common manifestation; the diagnosis should be considered and expeditiously pursued in all patients who were present with this finding, since early recognition of the disease is essential to allow prompt initiation of therapy (Akaishi et al., 2011). Regional or distant spread is apparent at the time of initial diagnosis in 90% of cases. The lungs are the most common site of distant metastases, being involved in up to 90% of patients with distant disease (Carcangiu et al., 1985; Venkatesh et al., 1990). These metastases are usually intrapulmonary mass lesions, but pleural involvement can occur. Approximately 5 to 15% of patients have bone metastases. Five percent have brain metastases, and a few have metastases to the skin, liver, kidneys, pancreas, heart, and adrenal glands (Tan et al., 1995; Carcangiu et al., 1985). Rare patients have no detectable thyroid tumour at the time of diagnosis, presenting with metastatic disease (Aldinger et al., 1978).

The enlarging thyroid tumor may cause neck pain and

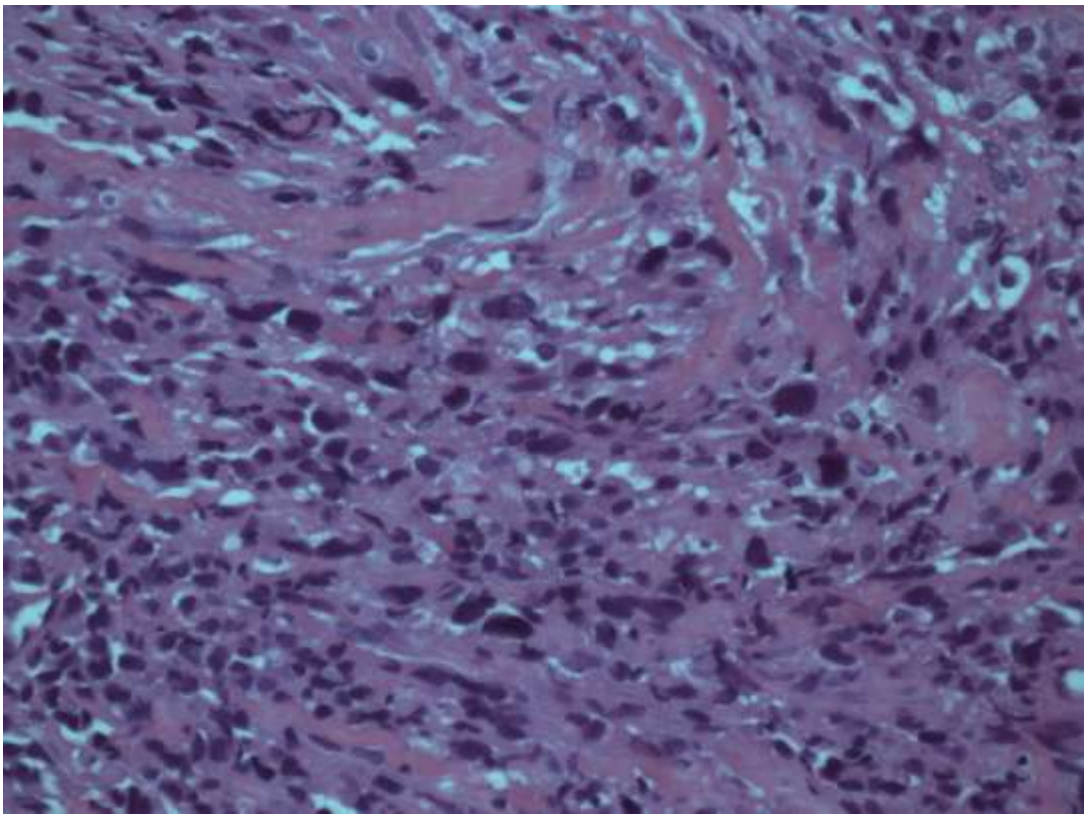

Figure 2. Core biopsy shows infiltrating atypical giant and spindle-shaped cells with pleomorphic hyperchromic nuclei and abundant cytoplasm.

tenderness, and compression, and patients may present with dyspnea, dysphagia, hoarseness, cough and sometimes haemoptysis. Less common symptoms are chest pain, bone pain, headache, confusion, or abdominal pain from metastases (Lip et al., 1992). Constitutional symptoms can occur, including anorexia, weight loss, fatigue and fever of unknown origin. Rarely, rapid growth of the tumour within the thyroid causes thyroiditis, with symptoms of hyperthyroidism and more severe neck pain and tenderness (Murakami et al., 1989; Oppenheim et al., 1983).

Most patients have normal serum thyroid hormone and thyrotropin (TSH) concentrations, except for those few patients with tumour-related thyroiditis and hyperthyroidism from presumed rapid tumour growth and concomitant tissue destruction (Murakami et al., 1989; Oppenheim et al., 1983).

Many studies showed that ATC represents a terminal "de-differentiation" of a pre-existing differentiated carcinoma. These studies lend support to the hypothesis that anaplastic carcinoma develops from more differentiated tumours as a result of one or more dedifferentiating events, possibly loss of the p53 tumour suppressor protein (Nakamura et al., 1992). 16p loss or BRAF activating mutations (Quiros et al., 2005).

Anaplastic carcinoma is generally best managed with surgery followed by a multimodality regimen of radiotherapy and chemotherapy. Most patients with ATC are incurable; however, a multimodality approach, in selected individuals, might improve local control and extend survival. Brignardello et al. (2007) showed that debulking surgery followed by adjuvant chemo radiotherapy is the only modality approach that modified survival of ATC patients (Tan et al., 1995). In our case debunking surgery could not be done because of the extent of local invasion and involvement of the trachea and oesophagus.

Several important prognostic characteristics have been identified. Patients with disease either confined to the thyroid or with only local and regional metastases survive longer than those with distant metastases (Brignardello et al., 2007). Tumour size also appears to be important, Tan et al. (1995) showed that the two-year survival was 25 versus 3 to 15% in patients with tumours less than 6 cm versus larger than 6 cm in maximum dimension (Tan et al., 1995). Other variables that may predict a worse prognosis include older age at diagnosis, male sex, and dyspnoea as a presenting symptom (Brignardello et al., 2007).

The diagnosis of anapaestic carcinoma is usually established by cytological examination of cells obtained by fine-needle aspiration biopsy or of tissue obtained by

large-needle or surgical biopsy. The relative efficacy of FNA and cutting-needle biopsy varies. Many centres have reported similar results with both methods, and many consider the techniques to be complementary (Lip et al., 1992; Murakami et al., 1989; Oppenheim et al., 1983; Akslen et al., 1991). FNA biopsy has resulted in improved diagnostic accuracy, a higher malignancy yield at the time of surgery, and significant cost reductions (Castro and Gharib, 2005). False-negative rates vary from zero to five percent, usually because of sampling error (Venkatesh et al., 1990; Oppenheim et al., 1983; Quiros et al., 2005; Brignardello et al., 2007; DeLellis, 2006; Nel et al., 1985; Radetić et al., 1984; De Crevoisier et al., 2004). For this reason, most cytopathologists require at least eight clusters of follicular cells on at least two slides (two separate passes with the needle) to consider a specimen diagnostic.

A series of 5605 aspirates reported a 2.3% false negative and 1.1% false positive rate (Nakamura et al., 1992). The overall accuracy of FNA exceeded 95%.

ATC usually does not concentrate radioiodine or express thyroglobulin. It is essential to verify the diagnosis histologically because insular thyroid cancer, lymphomas, and medullary thyroid cancer are occasionally confused with undifferentiated neoplasms. Immunohistochemical study is helpful in establishing the diagnosis. In our case the tumour was positive for epithelial (EMA) and sarcoma (Vimentin) markers, but was negative for hormonal (calcitonin and thyroglobulin) markers.

In the case of anaplastic carcinoma core biopsy is usually needed since it provides tissue for histology and analysis of tumour markers. In our case FNAC revealed papillary thyroid carcinoma, however, given the aggressiveness of tumor, core biopsy was done which confirmed anaplastic carcinoma.

We think that the initial work up of such patients should include fine needle aspiration cytology since it is a sensitive and specific test for the diagnosis of thyroid cancer, allowing definitive initial surgery and avoiding unnecessary procedures; however, when the diagnosis is inconsistent tissue biopsy should be done to further delineate the clinical issue and plan the appropriate management.

Conclusion

Anaplastic thyroid carcinoma is a rare type of thyroid cancer that is almost always rapidly fatal. It can arise de novo or from pre-existing well-differentiated thyroid cancer. The occurrence of an anaplastic area in a papillary carcinoma represents the dedifferentiation of the primary neoplasm. This is an extremely rare occurrence and is considered to have negative prognostic significance. FNAC should not mislead the physician nor affect the management approach and a further search should be pursued if indicated by the clinical behaviour of the tumour as in our case. This diagnosis must be included in the differential diagnosis of poorly differentiated tumours of the neck.

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