Unusual association of diseases/symptoms

A 95-year-old woman with leucocytosis and eosinophilia: anaplastic carcinoma in an ectopic thyroid

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Summary

A 95-year-old woman had been treated over the past 8 years for progressive dysphagia. When her condition worsened, blood tests revealed the presence of leucocytosis and eosinophilia in the absence of anaemia or thrombocytopenia. Within 11 days of diagnosis, the patient died of respiratory failure. Necropsy showed normal thyroid tissue and an absence of infectious disease. However, an upper mediastinal tumour was found and was histopathologically diagnosed as a neoplastic transformation of the ectopic thyroid. Only 1% of endothoracic goitres present as ectopic or autonomous goitre with no parenchymal or vascular connection to the thyroid gland. This case represents a very rare situation in which a leukemoid reaction and peripheral hypereosinophilia were observed as a manifestation of an anaplastic thyroid carcinoma in an ectopic mass.

BACKGROUND

While an ectopic thyroid is a frequent condition, discontinuity to the thyroid is rare and anaplastic transformation of an ectopic mass is even rarer. The detection of leucocytosis and eosinophilia in a peripheral blood sample indicates, in most cases, the presence of infectious or medullary diseases. However, a search of the medical literature showed no reported cases of leucocytosis (or leukemoid reaction) with hypereosinophilia associated with anaplastic transformation of an ectopic thyroid. Therefore, this rare condition must be included in the differential diagnostic list of leucocytosis and hypereosinophilia.

CASE PRESENTATION

A 95-year-old widowed Brazilian woman was admitted to the Brasília University Hospital due to a recent stop in eating. The patient had a 8-year history of progressive dysphagia with solid food that had worsened in the last year to include difficulty in swallowing liquids. Although the patient had lost weight, her appetite was preserved. She had no history of cervical or thoracic pain, fever, nausea, vomiting, haematemesis or dyspnoea, and had been treated for hypothyroidism with levothyroxine for 6 years. She presented with memory impairment for the last 5 years, which had got worse following a cerebral ischaemic event. Moreover, the patient did not present with hypertension, diabetes, medication abuse or have a family history of cancer. Upon hospital admission, physical examination showed

she was afebrile, lean and dehydrated. Her blood pressure was 100/60 mm Hg, her pulse was 90 bpm and her respirations were 27 per minute. Collateral circulation in the anterior thorax was detected, and her cardiac evaluation disclosed a diminished heart sound and isolated ventricular extrasystoles without any murmurs. Her breath sounds were found to be decreased bilaterally without any wheezing or crackles and her abdomen was unremarkable. Examination of the thyroid found it to be impalpable with no goitre or nodule detected. Eight days after her admission, the patient developed respiratory failure and died 3 days later.

INVESTIGATIONS

CT studies of the chest and neck revealed a large mediastinal mass, with tracheal, bronchus, oesophagus and superior vena cava compression (with a stricture that appeared to be 8 mm in diameter). No clear definition of its aetiology could be determined (figure 1). An oesophagogastrroduodenoscopy examination showed an extrinsic stricture in the proximal oesophagus (20 cm below the dental arch) and Chagas' disease serology was negative. Table 1 shows the haematological values on admission, which included calcium levels of 8.7 mg/dl, sodium 141 mmol/litre, potassium 3.7 mmol/litre, urea 91 mg/dl, creatinine 1.3 mg/dl, an erythrocyte sedimentation rate of 42 mm/h and a glucose level of 118 mg/dl.

Figure 1 CT studies of the patient's chest and neck revealed a large mediastinal mass.

Table 1 Haematological laboratory values on admission and 9th hospital day

Variable	Value (admission)	Value (9th hospital day)
Haematocrit (%)	42.9	41.8
Haemoglobin (g/dl)	14.1	14.1
White cell count (per mm ³)	26100	35800
Differential count (%)		
Neutrophils	58	51
Band forms	16	20
Lymphocytes	15	05
Reactive lymphocytes	03	02
Eosinophils	08	17
Platelet count (per mm ³)	255000	239000

OUTCOME AND FOLLOW-UP

Autopsy results included the detection of a tumour in the superior mediastinum with unclear margins that measured approximately 12 × 8 × 5 cm. It was found to be invasive into the structures of the region, extending to the vena cava, posterior tracheal region and bronchus. The oesophagus was the most affected organ, with invasion of the wall and ulceration. However, the thyroid capsule was found to be intact having no continuity with the tumour. Histopathological analysis identified a malignant, solid neoplasm composed of dyshesive anaplastic cells with abundant eosinophilic cytoplasm and undefined borders showing plasmacytoid and spindle-shaped cells (figure 2). The nuclei of the cells were pleomorphic, and nucleoli were large and irregular (figure 3). High mitotic activity and some atypical mitotic cells were observed, in addition to areas of extensive necrosis, especially in the middle of the neoplasm. Examination of the peripheral area of the neoplasm identified the presence of ectopic thyroid tissue as well as a focus of classic papillary carcinoma (figure 4).

In addition, papillary projections and nuclear pseudoinclusions were present in 4 of the 12 histological slides analysed. Furthermore, in this region, immunohistochemical staining revealed expression of thyroglobulin (Tg), cytokeratin AE1/AE3 and epithelial membrane antigen. In contrast, the anaplastic area showed no Tg and AE1/AE3 expression yet epithelial membrane antigen expression was still detected (figure 5). These results confirm the epithelial nature of the neoplasm. Strong staining for a mutagenic form of the p53 oncoprotein was also observed suggesting that this genetic mutation was involved in the oncogenesis that had occurred.¹ Upon complete histological examination of the thyroid gland no changes or diagnostic evidence of malignancy were detected.

DISCUSSION

Ectopic thyroid is the most common anomaly of thyroid histogenesis and can develop along the thyroglossal duct tract. However, it can also present, although less frequently, in the mediastinum, lymph nodes, tracheal or oesophageal wall. Ectopic thyroid is susceptible to the same diseases that affect the thyroid gland, but malignant transformation is rare.² For example, only 1% of endothoracic goitres present as ectopic or autonomous goitre and usually there is no parenchymal connection with the thyroid gland.³ In addition, most patients with retrosternal goitres have a cervical mass and experience dyspnoea, dysphonia, dysphagia, pericardial effusion and superior vena cava syndrome.⁴

The peak incidence of anaplastic carcinoma occurs in old age around the seventh decade; more than 60% of cases involve patients 65 years and older.⁵ Anaplastic thyroid carcinoma can present as a long-standing differentiated carcinoma that suddenly becomes fulminant after an interval of several years. In a retrospective study of 84 patients with anaplastic carcinoma, 21% had been diagnosed with differentiated thyroid carcinoma, and 37% reported having

Figure 2 H&E staining of anaplastic thyroid carcinoma sections detected a solid neoplasm that was composed of plasmacytoid, dyshesive cells. ($\times 100$)

Figure 3 H&E staining of anaplastic thyroid carcinoma sections detected pleomorphic nuclei, irregular borders and prominent nucleoli. ($\times 400$)

Figure 4 H&E staining of ectopic thyroid tissue sections identified the presence of a foci typical of papillary carcinoma. ($\times 40$)

Figure 5 Immunoreactivity of epithelial membrane antigen detected in the anaplastic carcinoma.

a goitre that was dormant for a long time and then underwent a sudden burst in growth.⁶ In the present case, the origin of the anaplastic tumour on the ectopic gland is clearly shown to be from a previous papillary carcinoma. Unfortunately, anaplastic carcinoma is associated with a very poor

patient prognosis as it is one of the most aggressive thyroid cancers.⁷

Metastatic spread is common in anaplastic tumours with 75% of patients already having distant metastases detected at the time of diagnosis. Frequently these tumours

metastasise to the lungs, bones, mediastinum and peritoneum.⁸ In this case, the patient did not have detectable metastases. Advanced age, male gender and dyspnoea at the time of diagnosis are associated with a worse prognosis.⁹

The presence of leucocytosis and eosinophilia in the patient's peripheral blood was of relevant clinical interest in this case especially in the absence of detectable infection. In fact, previous studies have reported the occurrence of thyroid carcinoma concomitant with leukemoid reaction and hypereosinophilia, but none was located in an ectopic mass.¹⁰ Moreover, the haematopoietic growth factors produced by tumoural tissue can cause eosinophilia and neutrophilia associated with non-lymphohaematopoietic malignant diseases, such as differentiated thyroid carcinoma^{11–13} and anaplastic carcinoma.^{10 14–17} Furthermore, paraneoplastic leucocytosis is usually associated with granulocyte-colony-stimulating factor-producing tumours such as anaplastic thyroid carcinoma.¹⁵ Therefore, the present case was unique in its presentation of leucocytosis and hypereosinophilia as a manifestation of anaplastic carcinoma in an ectopic thyroid.

Learning points

- ▶ This rare condition must be included in the differential diagnostic of leucocytosis and hypereosinophilia especially when infection and bone marrow proliferative diseases are ruled out.
- ▶ An ectopic thyroid should be followed for the possibility of neoplastic transformation.
- ▶ Ectopic goitre without thyroid involvement is rare.

Competing interests None.

Patient consent Obtained.

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