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## Case Report

## Case report: Diffuse metastatic infiltration of the thyroid by esophageal adenocarcinoma mimicking non-neoplastic thyroid disease

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## ABSTRACT

We report a patient who suffered from esophageal cancer that metastasized to the thyroid. There are only a handful of cases of esophageal cancer with metastases to the thyroid reported in the literature. To our knowledge, this is the first with a diffusely infiltrative pattern (the others were focal masses/nodules). This diffusely infiltrative pattern of metastatic disease is important for radiologists to be aware of because it is particularly difficult to detect and is not characteristically neoplastic by pattern. A diffuse parenchymal abnormality that is bilaterally symmetric is more commonly associated with non-neoplastic diffuse thyroid disease, such as autoimmune thyroid diseases (eg, Graves' disease). As such, in addition to the more common non-neoplastic differential diagnoses associated with diffuse thyroid disease, a diffuse thyroid parenchymal abnormality in a patient with a history of esophageal carcinoma should raise the question of diffuse metastatic infiltration.

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### Case report

In October 2015, a 64-year-old man who had been diagnosed with esophageal adenocarcinoma 1 month earlier presented to the emergency department and was subsequently admitted with failure to thrive, severe malnutrition, generalized weakness, and acute kidney injury. He complained of intermittent, sharp chest pain across his chest, intermittent right-sided back pain, intermittent sweats, and right lower extremity weakness. The physical exam was remarkable for palpable

cervical lymphadenopathy. Aside from the recent diagnosis of esophageal adenocarcinoma, his past medical history was negative, and his only medications were a daily prophylactic baby aspirin and a multivitamin. He had no history of surgery and no significant family medical history. He was a longtime ex-smoker of unknown pack years.

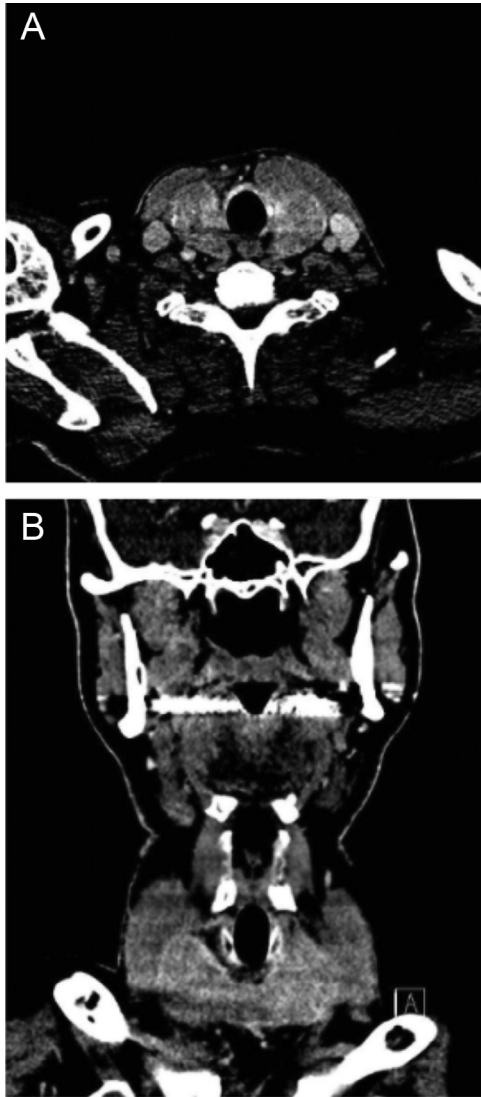
A noncontrast CT of the brain was ordered as part of the workup for his right lower extremity weakness, and this revealed multiple focal brain lesions highly suspicious for metastatic disease. On follow-up MRI of the brain, extensive metastatic disease was confirmed, and the dominant mass was

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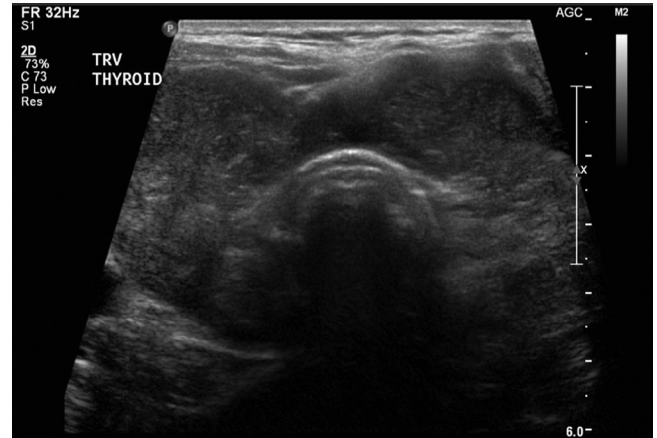
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**Fig. 1 – Axial (A) and coronal (B) images from a contrast-enhanced computed tomography of the neck show a diffuse enlargement of the thyroid gland with parenchymal heterogeneity but no focal mass.**

located in the high medial left frontal-parietal junction region, measured  $16.8 \times 16.2$  mm, and neurofunctionally correlated with his right lower extremity weakness. In total, there were 8 metastatic lesions found in the brain. Additionally, on the most inferior slice or the caudalmost slice on the CT of the brain, there was an enlarged left retropharyngeal lymph node that measured up to 15 mm.

A contrast-enhanced CT of the neck was acquired to further characterize the palpable cervical lymphadenopathy and the imaged enlarged retropharyngeal lymph node, and this showed diffuse cervical lymphadenopathy, as well as diffuse enlargement of the thyroid gland (Fig. 1). A thyroid ultrasound was subsequently obtained, which showed diffuse enlargement without mass or nodule (Fig. 2). The left lobe had measurements of  $4.6 \text{ cm} \times 1.4 \text{ cm} \times 1.3 \text{ cm}$ , and the right lobe had measurements of  $5.5 \text{ cm} \times 3.2 \text{ cm} \times 3.8 \text{ cm}$ . Thyroid function testing (thyroid-stimulating hormone and free T4) was normal.



**Fig. 2 – Ultrasound of the thyroid gland shows a diffusely enlarged and heterogeneous gland without a discrete focal mass or nodule. AGC, adaptive gain control.**

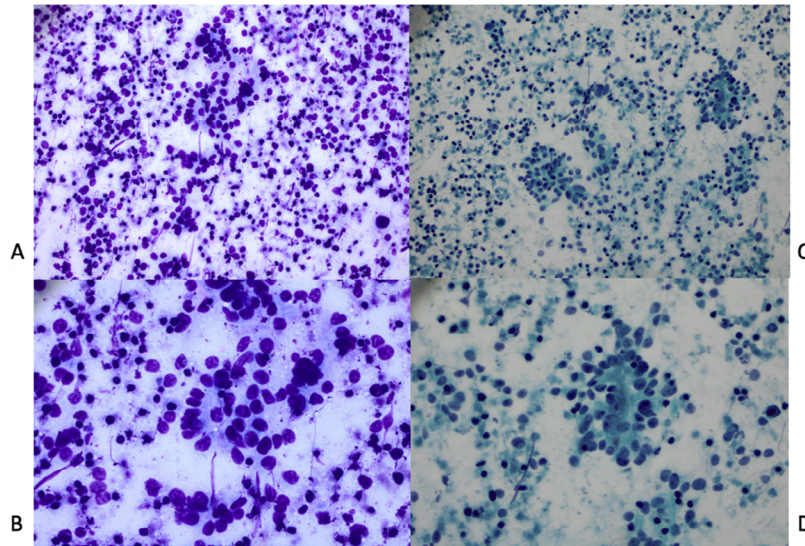
An ultrasound-guided fine needle aspiration of the right lobe of the thyroid gland yielded malignant cells in loose clusters forming glands, suggesting adenocarcinoma. Subsequent staining of the aspirate was positive for CDX2, a highly sensitive and specific marker for gastrointestinal adenocarcinoma [1], and was negative for thyroid transcription factor-1, a sensitive marker for thyroid malignancy [2]. Additionally, the tumor cells were morphologically similar to the primary esophageal adenocarcinoma (Figs. 3 and 4), and core biopsy of an enlarged right submandibular lymph node demonstrated metastatic adenocarcinoma (Fig. 5), supporting the diagnosis of esophageal adenocarcinoma metastasis to the thyroid.

After a discussion with the patient and the family regarding treatment options, chemotherapy was not pursued because of concerns of it being more harmful than beneficial, given the patient's functional status and pace of disease. The patient did not undergo targeted therapy for the metastatic disease to the thyroid. Soon after completing palliative radiotherapy to the brain and the esophagus, the patient was discharged home with hospice care.

## Discussion

In general, clinical or radiological signs of metastatic disease to the thyroid gland are uncommon. Autopsy series have shown rates of metastases to the thyroid in the range of 0.5%-24.0% in patients with cancer [3-6]. When metastasis occurs, usually it is from cancers of the lung, colon and rectum, kidney, and breast [7,8], with radiological patterns that can be classified into solitary, multiple, and diffuse types [9]. Diffuse metastases are rare. In 1 series of 78 patients with thyroid metastases, only 6% exhibited diffuse metastases compared with 27% with solitary nodules and 67% with multiple nodules [4].

To our knowledge, there have only been 6 other cases of esophageal cancer metastasis to the thyroid gland as of January 2017 [10,11]. Five out of these six cases include esophageal



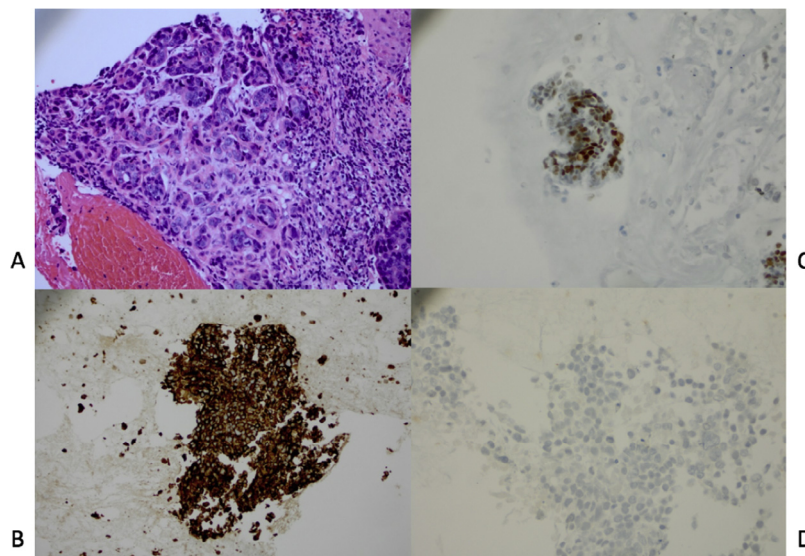
**Fig. 3 – FNA of thyroid mass (A and B DQ; C and D Pap) aspirates demonstrating a cellular smear consisting of malignant cells in loose clusters and forming glands. The tumor cells feature cytologic atypia with nuclear pleomorphism, prominent nucleoli, hyperchromasia, and necrosis. FNA, fine needle aspiration; DQ, Diff-Quik; Pap, papanicolaou.**

squamous cell carcinoma as the primary neoplasm. Other than our case, there is only 1 other case report of esophageal adenocarcinoma [12] metastatic to thyroid.

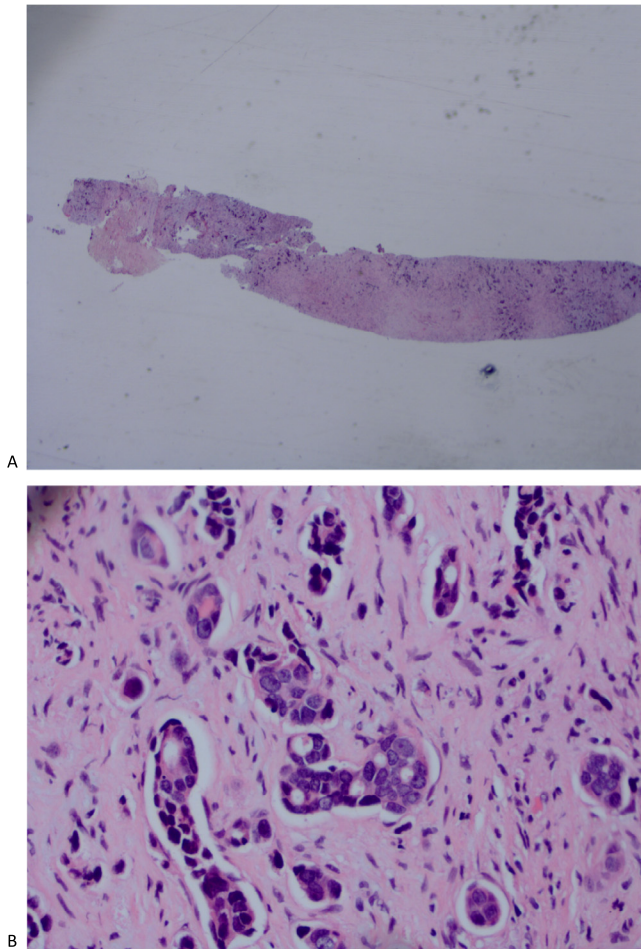
The case presented here is the only one with a diffusely infiltrative pattern (Fig. 1). The other 6 cases were metastatic deposits manifested by focal nodules as opposed to diffuse infiltration of the thyroid gland. This case of diffusely infiltrative metastasis to the thyroid gland is particularly important because the imaging features mimic those of more common, non-neoplastic diffuse thyroid diseases such as Graves' disease. If there is no history of cancer, it would be reasonable to leave metastatic infiltration out of the provided differential diagnosis

and to provide the standard differential diagnosis for an enlarged, diffusely heterogeneous thyroid gland, including Graves' disease, acute phase autoimmune thyroiditis, and acute infectious thyroiditis.

Because of the relative rarity of clinically evident metastatic disease to the thyroid gland, management is determined on a case-by-case basis. Four out of the 6 previously reported cases were treated with thyroidectomy, and the management in the other 2 cases was not reported [13]. Most patients with metastasis to the thyroid had poor outcomes; however, there is 1 reported case where the patient was without evidence of recurrence 4 years after thyroidectomy [14].



**Fig. 4 – Malignant cells are morphologically similar to the adenocarcinoma in esophagus biopsy (A). Immunohistochemical stain was performed on the cell block. Malignant cells stained positive for pancytokeratin (B) and CDX-2 (C), and negative for thyroid transcription factor-1 (D). CDX-2, caudal type homeobox 2.**



**Fig. 5 – Hematoxylin and eosin stain of ultrasound-guided right submandibular lymph node core biopsy shows a malignant glandular tissue on a background of desmoplastic reaction. (A) Low-power cross section. (B) High power showing mucinous glands and desmoplastic reaction.**

### Teaching point

Although diffuse thyroid enlargement usually reflects non-neoplastic diffuse thyroid disease such as Graves' disease, in patients with cancer (in this rare case, esophageal adenocarcinoma), diffuse metastatic infiltration of the thyroid gland should be included in the differential diagnosis.

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