

A Case of Late Metastasis of a Renal Cell Carcinoma to a Multinodular Goitre

Dear Editor,

We describe a 75-year-old Chinese female with comorbidities of diabetes mellitus, hypertension and paroxysmal atrial fibrillation. She has a history of renal cell carcinoma (RCC) of her left kidney diagnosed in March 1995 when she presented with haematuria and suprapubic pain. The RCC was staged as (T1N0M0) and treated with a successful radical nephrectomy in March 1995. Histologically, it was a renal cell carcinoma measuring 4 x 3 cm, of clear cell type with admixed granular cells. Tumour was confined to the kidney and there was no capsular or vascular invasion by tumour. No lymphadenopathy or liver metastases were noted.

She was on long-term follow-up for her RCC in the urology clinic and referred to our clinic in 2008 for a large multinodular goitre (MNG), which she had for the past 40 years. She had no clinical evidence of metastatic disease when she first presented to our clinic.

Despite her large long-standing goitre, she did not complain of compressive symptoms of pain, dysphagia, hoarseness of voice or shortness of breath. She had no

symptoms of thyroid dysfunction nor did she notice a rapid increase in size of her goitre. Clinical examination revealed a large, firm MNG, with the left lobe enlarged more than the right. There was no clinical evidence of compression of neighbouring structures, retrosternal extension or malignancy. There were no enlarged cervical lymph nodes.

Previous fine needle aspiration cytology (FNAC) performed in 2005 was inconclusive. She did not undergo a repeat FNAC, or a radionuclide scan of her thyroid. A computed tomography (CT) scan of her neck was performed (Fig. 1A).

She underwent an uncomplicated total thyroidectomy in November 2008. Intraoperatively, a very large and vascular goitre with the left lobe enlarged more than the right lobe was noted. The resected specimen weighed a total of 311 g.

Intraoperative frozen section was reported as multinodular goitre with foci of clear cell lesions. Differential diagnosis included metastatic renal carcinoma and primary thyroid tumour (paraganglioma, follicular lesion with clear cells and medullary carcinoma). Grossly, multiple yellowish nodules were seen in the resected specimen, the largest

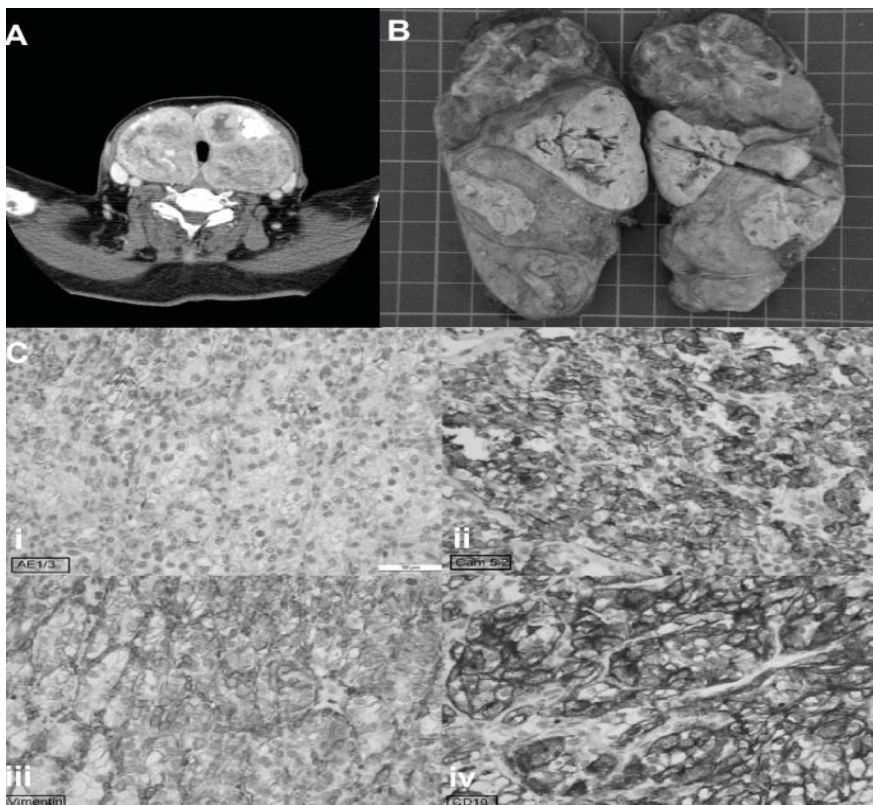


Fig. 1. Computed tomography (CT) scan of the neck. Fig. 1A showed a MNG with heterogenous attenuation and calcifications within, associated with significant concentric tracheal narrowing and displacement of the neck vessels peripherally. There was no significant retrosternal extension or cervical lymph node enlargement. Grossly, the total thyroidectomy specimen. Fig. 1B showed several well-circumscribed foci of yellowish tumour characteristic of metastatic RCC. Various immunohistochemical stains. Fig. 1C to confirm the renal origin. i) Focal cytoplasmic staining to pancytokeratin AE1/3. ii) Diffuse and strong cytoplasmic staining to low molecular weight cytokeratin cam 5.2. iii) Diffuse cytoplasmic staining to vimentin. iv) Diffuse cytoplasmic staining to CD10, 20X.

measuring 4.5 x 3.5 cm (Fig. 1B). Final histology was reported as metastatic renal cell carcinoma, clear cell type, Fuhrman nuclear grade 2 to 3. Immunohistochemistry of the malignant clear cells exhibited focal moderate cytoplasmic expression of AE1/3, Vimentin and strong expression of CD10 (Fig. 1C). S-100 and TTF-1 were negative which excluded possibilities of paraganglioma or primary thyroid neoplasm. Staging investigations revealed no evidence of metastatic disease.

Metastases of RCC to the thyroid gland without involvement of other organs is rare but is an important consideration in the long-term follow-up of patients with previously resected RCCs. Wychulis et al¹ found the incidence of metastases to thyroid from all forms of malignancy to be (0.07%) (14 of 20,262 patients). The clinical course of renal cell carcinoma is often one of slow progression with late development of distant metastases. Tumours that most frequently produce thyroid metastases found at autopsy are, in descending order: melanoma (39%), breast carcinoma (21%), renal cell carcinoma (12%).² In cases that present clinically, RCC is responsible for the majority of cases.^{1,3}

Green et al⁴ reported in a study of 36 cases, that the average age at presentation of metastases to the thyroid from RCC was 59 years (range, 35 to 88). Also, metastatic lesions most commonly occurred years after the primary lesion was treated. Metastatic tumour presented more than 10 years after the primary was treated in 13 of 43 (30.2%) patients. Heffess et al⁵ reported in a study of 36 cases, that development of clinical thyroid gland metastases occurred at an average of 9.4 years after resection of primary RCC. Thirty of 36 patients presented with a solitary thyroid nodule while 3 patients had multifocal or bilateral disease.

Differential diagnoses include primary clear cell carcinoma of the thyroid (including papillary carcinoma, follicular carcinoma and follicular adenoma), metastatic clear cell carcinoma of the lung and metastatic acinic cell carcinoma of the salivary glands.

Imaging modalities such as ultrasonography, CT and magnetic resonance imaging (MRI), cannot differentiate between a primary and a secondary thyroid neoplasm. Radioscintigraphic imaging using iodine-131 or technetium-99m is inconclusive as both primary and secondary lesions appear as a cold nodule with decreased uptake focally, or as multiple discrete defects.

Metastatic RCC has distinctive architectural, cytologic, histologic and immunohistochemical features which allow it to be distinguished from a primary thyroid neoplasm. FNAC is useful in the diagnosis of metastatic RCC to the thyroid. Clusters of cells with sharp borders, abundant clear cytoplasm, and large, oval, moderately hyperchromatic

nuclei with visible nucleoli should raise the suspicion of a metastatic renal cell carcinoma. Our patient had thyroid gland enlargement due to both her metastatic RCC and MNG. In such patients, attempts at diagnosis with FNAC may yield a false-negative result if a benign nodule was sampled.

Histologically, RCC is characterised by its content of glycogen and lipid. Immunohistochemical staining shows that metastatic RCC cells show focal positivity of keratin but no staining for thyroglobulin or thyroid transcription factor-1 (TTF-1). Metastatic RCCs often stain positive for CD10 and some may also stain positive for vimentin. Immunostaining for RCC marker would also be useful in this case but we found the history of previous RCC and strong staining for CD10 to be suffice for diagnosis of metastatic RCC.

Our case illustrates that RCC metastatic to the thyroid may masquerade as a primary thyroid neoplasm and must be suspected in patients with a history of RCC. Lifelong follow-up of patients with previously resected RCCs is necessary as metastatic RCC may present many years after the patient has undergone a presumably curative radical nephrectomy. During follow-up, we should pay particular attention to patients with a known benign cause of thyroid enlargement such as MNG, as the clinical suspicion of a concurrent malignant process may be reduced. Thyroidectomy with resection of the metastasis may improve survival and can potentially be curative if the metastasis is solely to the thyroid with no other organ involvement.⁵

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