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Clear Cells Carcinoma of Thyroid: Difficult Diagnosis and Rare Case

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Abstract

Clear cell carcinoma of the thyroid is rare. We report a case observed in a 17-year-old woman with a nodule in the left lobe of the thyroid. Cervical ultrasound showed a single nodule of the left lobe of the thyroid, measuring 28 × 14 × 21 mm with microcalcifications, classified TIRADS 4. Pathological and immunohistochemical examination of the excisional specimen concluded with clear cell carcinoma. The epidemiological and histological aspects were discussed.

Keywords

Clear Cells, Carcinoma, Histology, Thyroid

1. Introduction

Clear cell carcinoma of the thyroid is a rare tumor and is classified as a variant of follicular carcinoma according to the WHO [1]. On routine morphological examination, it is very difficult to distinguish it from metastasis from renal cell carcinoma or from parathyroid tumor or other types of clear cell carcinoma. The mechanism of transformation of follicular cells into clear cells can be attributed to the dilation of mitochondria or an accumulation of glycogen or lipid or colloid vacuole in intra-cellular. An immunohistochemical examination is necessary to decide the diagnosis. We report a case of clear cell carcinoma of the thyroid in order to describe, through a review of the literature, the clinical, morphological and immunohistochemical aspects of this pathology.

2. Observation

It was a 17-year-old young woman, with no particular personal history, present-

ing with swelling of the neck, hence her consultation at the hospital. Clinical examination did not find cervical compression syndrome or laryngotracheal invasion. The thyroid gland was flexible, unindurated, and mobile in relation to the superficial and deep plane. The patient did not present any sign of clinico-biological dysthyroidism but slight hypocalcemia at 1.96 mmol/l. Cervical ultrasound revealed a thyroid nodule in the left lobe, measuring 28 × 14 × 21 mm with microcalcifications classified TIRADS 4 (**Figure 1**), and infracentimetric lymphadenopathy. The right thyroid lobe was normal. The kidney ultrasound did not show any abnormality. A left thyroid loboisthmectomy was performed. The parathyroid gland was structurally normal at the time of surgery. On gross examination, the left loboishmectomy patch measured 5 × 2.5 × 1.5 cm, showing on section a whitish, shiny, well-defined nodule of 3 × 2 cm. Histological examination showed tumor proliferation of solid or vesicular or papillary architecture with slender conjunctival vascular axes, lined by large cells, with clear or granular cytoplasm, with hyperchromatic nuclei, not very atypical (**Figure 2**). Papillary atypia has not been seen. The entire tumor population was stained with CKAE1/AE3, EMA, CK7, Vimentin and TTF1. CD10 was negative (**Figure 3**). The Ki67 tumor proliferation index was evaluated at 30%. The immunohistochemical profile was in favor of primary clear cell vesicular carcinoma of the thyroid. Radiation therapy was administered and the patient is currently progressing well.

3. Discussion

The clear cell carcinoma variant of the thyroid is a rare entity. To our knowledge, this is the first case described in Madagascar. In a series by Segal K *et al.*, it represents only 0.52% of thyroid cancers over a period of 30 years [2]. In contrast to oxyphilic or squamous metaplasias which are most often seen in non-neoplastic lesions of the thyroid, transformation into clear cells can only be

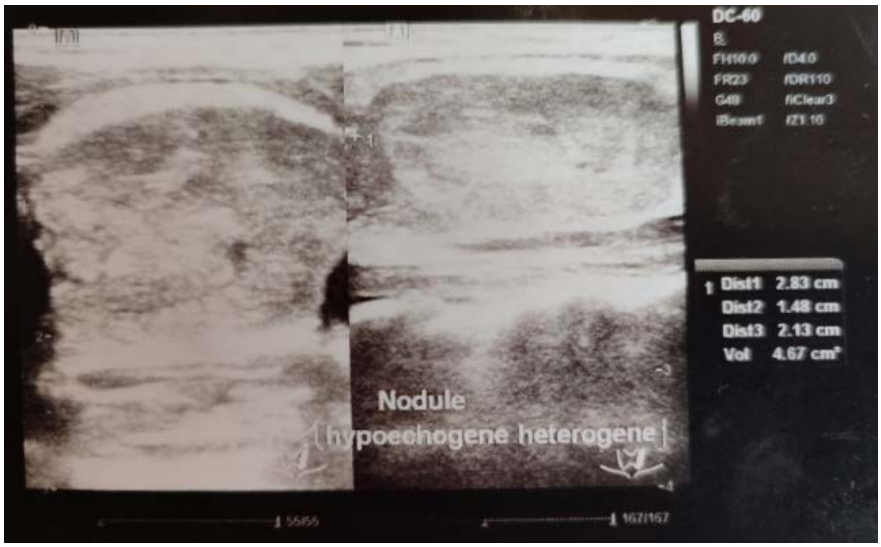

Figure 1. Thyroid ultrasound showing heterogeneous hypoechoic nodule. Source: OSTIE.

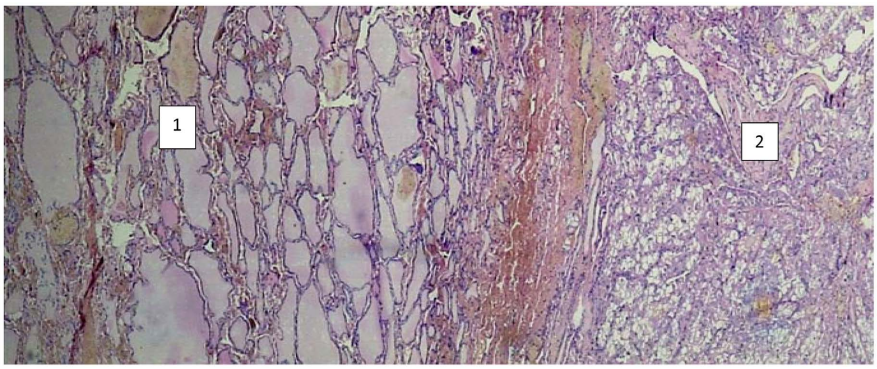

Figure 2. Thyroid parenchyma infiltrated by tumor proliferation. 1) Normal thyroid parenchyma; 2) Clear cell tumor proliferation. Haematein Eosin ×40. Source: UPFR of Pathological Anatomy and Cytology of the CHU-JRA.

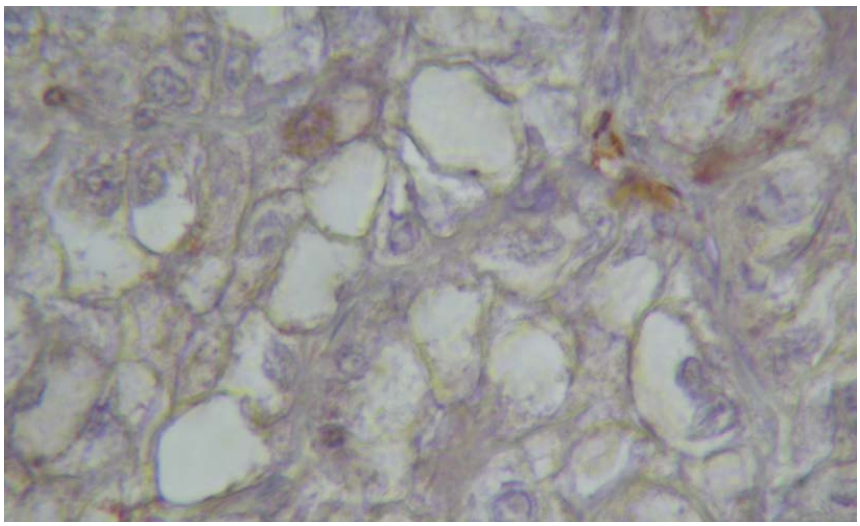

Figure 3. No expression of Immunohistochemical staining of CD 10. Source: Pathology anatomy laboratory of the Pasteur Institute of Madagascar.

observed in neoplastic lesions in this organ [3]. The mechanism of transformation of follicular cells into clear cells is not yet well understood, however, this ultrastructural change can be attributed to the dilation of mitochondria or an accumulation of glycogen or lipid or colloid vacuole in intra-cellular [4] [5]. Physiopathologically, clear cells may arise from follicular cell metaplasia or derive from pluripotent cells of endodermal origin with the capacity to donate the thyroid as well as the parathyroid; or to a selective deficit of the system involved in the biosynthesis of the peptide portion on thyroglobulin, to compensatory hypertrophy and hyperactivity of the Golgi apparatus or finally by the lack of hydrolytic enzyme necessary for the degradation of colloid vacuole [3].

On imaging, hypoechoic nodules with blurred outlines and presenting microcalcifications are cancerous in more than 50% of cases [6]. What has been observed in our case.

Macroscopic examination can already guide the diagnosis. It is a well-defined nodule or an infiltrating lobular mass, yellowish, greyish or focally whitish in

Table 1. Immunohistochemical profiles of the main differential diagnoses of clear cell carcinoma of the thyroid [8].

	Renal metastasis	Vesicular tumor	Medullary carcinoma	Parathyroid
Thyroglobulin	−	+	−	−
TTF1	−	+	+	−
CD10	+	−	−	−
Vimentin	+	+/−	+/−	+/−
Chromogranin	−	−	+	+
Parathyroid hormon	−	−	−	+
Calcitonin	−	−	+	−
EMA	+++	+	+	+

color. In our case, it was a well-encapsulated, whitish, shiny nodule developed on the upper pole of the thyroid.

Morphologically, three types of cells can be observed: cells with clear cytoplasm, cells with vacuolated cytoplasm and cells with granular cytoplasm [3]. In our case, the tumor cells mostly had a clear, granular cytoplasm.

Morphological and architectural aspects pose a problem for the differential diagnosis of parathyroid adenoma, the exceptional extent of parathyroid cancer, or more frequently metastasis of kidney cancer [7]. Faced with these differential diagnostic problems, an immunohistochemical examination should be used for diagnostic confirmation of tumor lesions with clear cells in the thyroid gland (**Table 1**) [8]. The normal appearance of the parathyroid gland seen during surgery and the positivity of TTF1 ruled out the parathyroid origin of the tumor. The absence of a kidney tumor on ultrasound as well as the negativity of CD10 made it possible to rule out its renal origin. After eliminating the main differential diagnoses, we retained the diagnosis of primary clear cell vesicular carcinoma of the thyroid.

According to a study by Cipriani *et al.*, it was not shown a significant difference in evolutionary and aggressiveness for clear cell carcinomas compared to other types of thyroid carcinoma [9].

4. Conclusion

Clear cell carcinoma is rare, morphologically posing a problem of differential diagnosis with metastasis from renal cell carcinoma or parathyroid tumor, requiring immunohistochemical examination. In developing countries like ours, it is sometimes difficult to make a diagnosis unless the patient has the means to send the case for immunohistochemical study abroad.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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