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Case report

Is it possible to determine the origin of cyst in empty thyroid bed in patient with lingual thyroid?

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Key words

lingual thyroid • cyst in empty thyroid bed • Tc-99m-pertechnetate scintigraphy • iodine-131 scintigraphy • SPECT/CT

Summary

Some patients with ectopic thyroid gland or athyreotic patients have one or more cysts in empty thyroid bed. The origin of these cysts is uncertain. We present the patient with lingual thyroid gland and small cyst in empty thyroid bed featuring the diagnostic algorithm used and discussing the possible etiologic scenarios.

Introduction

An ectopic thyroid tissue refers to all cases in which the thyroid gland tissue is present at a location other than its usual pretracheal position in the lower neck. It is an uncommon embryological anomaly resulting from no or abnormal migration of the thyroid cells from their origin in the floor of the primitive pharynx to its usual cervical location. Lingual thyroid, located at the base of the tongue in the midline, is the most commonly found ectopic thyroid tissue and accounts for 90% of the reported cases although ectopic thyroid tissue may be found anywhere along the path of descent of the developing thyroid primordium, such as sublingual, cervical, mediastinal, intratoracal and subdiaphragmatic location. In most cases the ectopic thyroid is the only functioning thyroid tissue [1].

The presence of cysts in cervical thyroid area have been described in patients with ectopic thyroid tissue or in athyreotic patients [2-3]. Etiology of this additional developmental anomaly is uncertain. They might be due to the persistence of the ultimobranchial bodies as a cystic structure or part of the thyroid-forming material, which may migrate along the normal pathway of the usual course of the thyroglossal duct, giving rise to cell residues within the empty thyroid area.

We report one such patient with lingual thyroid and cyst in empty thyroid bed and attempt to elucidate the origin of this cyst.

Case report

An asymptomatic 32-year-old woman was referred to our outpatient clinic for further investigation after her routine laboratory data showed evidence of subclinical hypothyroidism: T3 was 1,3 nmol/L (normal range = 1,3-3,6nmol/L), T4 was 72 nmol/L (normal range = 58-161 nmol/L) and TSH was 10,5 mIU/L (normal range = 0,3-3,16m IU/L). On clinical examination the thyroid gland was not palpable in its usual cervical location and there was no other palpable mass on the neck. Ultrasonography revealed empty thyroid bed with small cyst on the right side that measured 7 x 6 x 7 mm (Fig. 1A- transverse and 1B- longitudinal sonogram). Detailed ultrasound examination of other cervical regions didn't disclose any additional abnormality but coronal and sagittal view through the floor of the mouth, revealed hypoechogenic echostructure at the base of the tongue that measured 26x24x15 mm (Fig. 1C-coronal and 1D-sagittal sonogram). To confirm that this hypoechogenic structure corresponded to lingual thyroid, patient was referred to Tc-99m-pertechnetate scintigraphy (Fig. 2A-anterior and B-right lateral view),

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Fig. 1. Cyst in empty thyroid bed and lingual thyroid. Transverse **(A)** and longitudinal sonogram **(B)** shows cyst on the right side in empty thyroid bed measuring 7x6x7 mm. Posterior coronal and midline sagittal sonogram from the submental region through the mouth floor **(C and D)** shows spherically hypoechogenic mass at the base of the tongue that measures 26x24x15 mm and corresponds to the lingual thyroid.

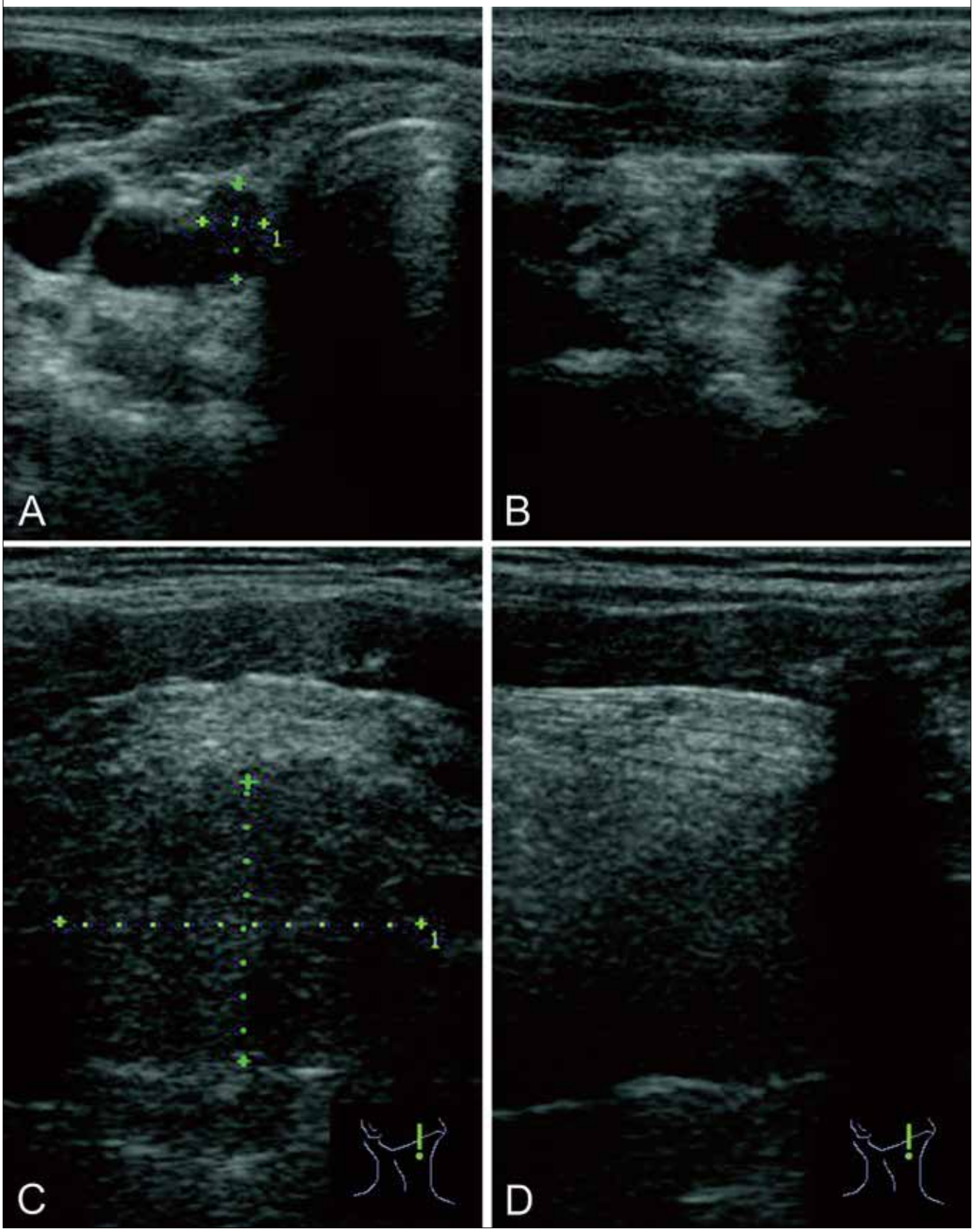
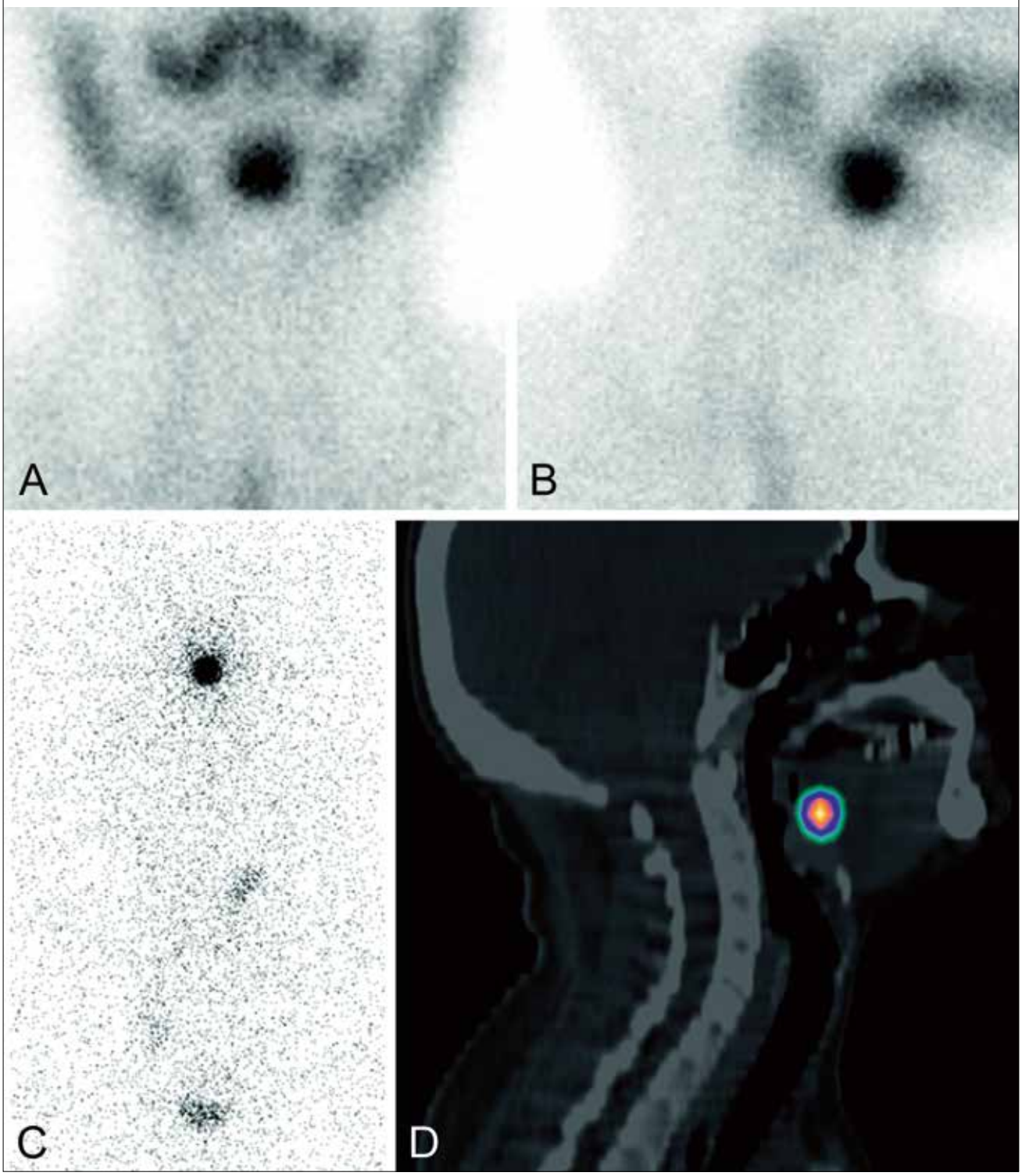


Fig. 2. Scintigraphic visualization of lingual thyroid and nonvisualization of cyst in empty thyroid bed. Tc-99m-pertechnetate scintigraphy **(A-anterior, B- right lateral view)** shows focal area of abnormal radiotracer uptake in lingual region with no evidence of radiotracer uptake in the region of the normally located thyroid. Iodine-131 scintigraphy of the head, neck, thorax and abdomen **(C)** also shows only one focus of activity in the mouth projection without any activity in the usual cervical thyroid region and absence of any other ectopic activity. Small activity of excreted I-131 is visible in the stomach, bowels and bladder. Iodine-131 SPECT/CT (low dose) **(D)** localizes this ectopic thyroid tissue at the base of the tongue, confirming the existence of lingual thyroid.



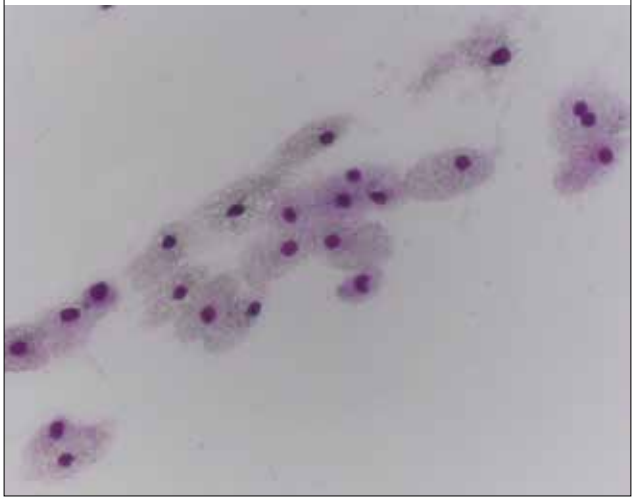
which showed the uptake of radiotracer in the mouth cavity and absence of radiotracer activity in the normal cervical thyroid region. Iodine-131 scintigraphy (Fig. 2C) of the head, neck, thorax and abdomen also showed only a single focus of activity in the mouth projection without any activity in the usual cervical thyroid region

and without any other ectopic activity. The Iodine-131 SPECT/CT (low dose) (Fig. 2D) localized this ectopic thyroid tissue at the base of the tongue, confirming the existence of lingual thyroid. The sonographycally guided fine-needle aspiration cytology of the small cyst in the thyroid bed yielded the translucent viscous content. In cytologicaly smear (Fig. 3.) there were macrophages and precipitate without follicular or parafollicular cells, but in punctate both specific markers of these cells (thyroglobulin and calcitonin) were positive. This provided the circumstantial evidences of existence of follicular and parafollicular cells in the cyst. In aspirate the thyroglobulin was 201,7 ng and calcitonin was 213,9 pg. Thyroglobulin and calcitonin in serum specimen were 2,8 ng/ml (reference value = < 40 ng/ml) and 3,5 pg/ml (reference value = < 10 pg/ml) respectively. Thyroxin therapy was prescribed and on control examination three months later TSH was normal.

Discussion

The thyroid gland has a dual embryonic origin and produces two different hormones by two different cell types: the thyroid hormones by thyroid follicular cells and calcitonin by parafollicular or C cells, respectively. The most abundant cells, thyroid follicular cells, thyrocytes also produces a thyroglobulin. Thyrocytes arise from the embryonic endoderm as a thickening in the floor of the primitive pharynx, whereas C cells precursors migrate from the neural crest bilaterally to the fourth and fifth pharyngeal pouches and become localized in the ultimobranchial bodies. Ultimobranchial bodies are a pair of transient embryonic structures derived from the fourth and fifth branchial pouches, located symmetrically on the sides of the developing neck, bearing embryonic cells from which calcitonin producing cells develops [1]. Thickening in the floor of the primitive pharynx becomes the site at which the foramen cecum develops. This thickening, the so-called median anlagen, soon forms a small outpouching that becomes the thyroid diverticulum. The thyroid then descends in front of the pharyngeal gut as a bilobed diverticulum. The thyroglossal duct maintains a connection between the descending thyroid gland and the tongue, but between the 5th and 10th embryonic weeks regresses. Continuing on its path, the thyroid gland descends anterior to the hyoid bone and the laryngeal cartilages. In the seventh week of embryonic development, the thyroid reaches its final position in front of the trachea anterior to the developing second, third and fourth tracheal rings. At that time it connects with the two lateral anlagen, the ultimobranchial bodies. In the coupling process both the thyroid anlage and the ultimobranchial bodies disappear as individual structures, and the cells contained in them disperse in the structure of the thyroid gland. Follicular cells from median anlagen continue to organize in the thyroid follicles, whereas the calcitonin producing C cells remain scatter within the interfollicular space, mostly in a parafollicular position [1]. The small cyst on the right side of the empty thyroid bed in our patient is not uncommon finding in patients with ectopic thyroid or athyreosis, but its origin is uncertain. For example, in 57 children with congenital hypothyrodism, 42 with ectopic thyroid tissue and 15 with athyreosis, cysts in empty thyroid bed were found in 39 patients (68% of cases), 29 of them with ectopic thyroid and 10 of them with athyreosis. All cysts were located in the empty thyroid area, 57% in the left and 43% in the right side, closer to the midline in all cases. Those patients had either single cyst (16 patients) or multiple cysts (23 patients) and the cysts were bilateral in 17 of the 39 patients. Most of the cysts were vertically oval or round, with a size ranging in diameter from 2-21 mm^2. The authors speculated that these cysts might be due to the persistence of the ultimobranchial bodies as a cystic structure or a part of the thyroid-forming material, which may migrate along the normal pathway of the usual course of the thyroglossal duct, giving rise to cell residues within the empty thyroid bed. The exact nature of these cysts couldn't be established by histological examination because histological verification was unjustified in these patients [2]. Pathohistology examination of four out of five autopsies specimen of cysts in thyroid bed, in the region of the upper parathyroids in patients with lingual thyroid, revealed both follicular and parafollicular-C cells. Since the ultimobranchial body derives from the fourth and fifth branchial pouches and descends with parathyroid IV to fuses with the thyroid, while parathyroid IV remains as the upper parathyroid closely applied to the thyroid lobe, and because these unusual cystic structures in these patients were found immediately adjacent to the upper parathyroid in absence of normally descended thyroglossal duct-derived tissue, the authors concluded that these structures derive from the ultimobranchial tissues and that the ultimobranchial body contributes both C cells and follicular cells of the thyroid in

Fig. 3. Fine needle aspiration cytology of small cyst in empty thyroid bed in patient with lingual thyroid shows only macrophages without follicular or parafollicular cells (May Grunwald Giemsa stain, magnification x 400).



man [3]. This thesis of ultimobranchial origin of follicular and parafollicular cells is supported by the reports of patients with etopic thyroid presenting as a submandibular mass without detectable thyroid tissue in the normal median position [4 5], and ectopic thyroid tissue located in the carotid space with orthotopic thyroid gland [6]. At last, the remnants of ultimobranchial bodies in normal thyroids are usually referred by pathologists as solid cell nests. It is now widely accepted that solid cell nests and so-called "mixed" follicles are indeed ultimobranchial body remnants. Solid cell nests are composed of main cells and C cells. It has been suggested that main cells might be pluripotent cells contributing to the histogenesis of C cells and follicular cells, as well as to the formation of certain thyroid tumors [7]. According to these, the cysts in thyroid bed must represent the cystic degeneration of the remnants of the ultimobranchial bodies, which contains both, follicular and parafollicular cells.

In contrast to these theses, there are evidences of existence of parafollicular cells in lingual thyroids. Pathohistology examination of six lingual thyroids confirmed coexistence of follicular and parafollicular cells [8]. The authors speculated that primordial thyroid follicular cells contains pluripotent stem cells from which the follicular and parafollicular cells can derive. According to the authors, another possibility is that some non-stem cells can transdifferentiate to calcitonin producing cells. These findings suggest that the ultimobranchial bodies are not the only source of calcitonin-producing cells in humans. The corroborated finding is the detection of medullary thyroid carcinoma in a lingual thyroid [9]. One can conclude that if only a few clusters of these multipotent cells from lingual thyroid migrate to the usual pretracheal thyroid position, and if they undergone cystic degeneration, the result may be cyst in empty thyroid bed.

Theoretically, there is also the possibility that follicular cells in cyst derived from medial anlage and parafollicular cells from lateral anlage.

Conclusions

We present the patient with two developmental anomaly of the thyroid tissue. Beside ectopic, lingual thyroid, the patient had cyst in empty thyroid bed. Although we provided circumstantial evidences of the presence of both follicular and parafollicular cells in the cyst, this does not suffice to determine the cyst origin and this issue remains the controversial one.

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