

Thyroid Hemiagenesis and Papillary Carcinoma: A Rare Association

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ABSTRACT

Hemiagenesis is the least frequent thyroid congenital anomaly. We report the case of a primary hypothyroidism due to thyroid hemiagenesis in a patient for whom, later on, a papillary carcinoma of the contralateral lobe was diagnosed. A child with known left lobe thyroid agenesis was found to have a 12 mm nodule in the right thyroid lobe during routine follow-up. Needle biopsy demonstrated the nodule to represent a papillary thyroid cancer and total thyroidectomy and lymphadenectomy of the central compartment was undertaken. Such event represents an extremely rare occurrence since there are only five other reports in literature that deal with a papillary carcinoma in a patient with thyroid hemiagenesis.

Keywords: Thyroid, Hemiagenesis, Thyroid cancer.

CASE PRESENTATION

A female newborn, diagnosed with hypothyroidism through neonatal screening had L-thyroxine substitution instituted in the first few days of life. A scintigraphic examination of the thyroid demonstrated a thyroid hemiagenesis with the presence of right lobe and isthmus and the absence of the left lobe. Over the years, the patient remained in good physical conditions and was complying well with the therapy. She had a regular growth rhythm and normal pubertal spurt. The timing of menarche was 12 years. During routine follow-up, she underwent a thyroid ultrasonography and computed tomography of the neck at 17 years that showed the presence of a 12 mm apical solid nodule on the right lobe characterized by the presence of internal microcalcifications and a marked peri- and intra-lesional vascularization. A fine needle aspiration biopsy of the nodule reported the presence of malignant cells with marked nuclear abnormalities, likely to represent a papillary carcinoma.

The patient did not have a history of irradiation of the cervical region or exposure to other factors. At the time of diagnosis of thyroid carcinoma, she was euthyroid ((TSH-1,450 μ UI/ml (n.v. 0.3-4.2)) and Tg was 10.9 ng/ml (n.v. 0-50), without any alteration of serum antithyroid antibodies (TPOAbs, TgAbs) concentration.

Surgical intervention was planned. In preparation of surgery, she underwent an X-ray of the neck and thorax that confirmed the absence of tracheal deviation/compression; also the clinical examination of the oral cavity, pharynx and larynx did not reveal any anomaly.

A standard cervicotomy was performed. During exploration, both the right and left parathyroid glands were visualized in their anatomical site and the right laryngeal nerve was identified and preserved. Then, the removal of the right lobe and isthmus was carried out (Fig. 1). As recommended by the American Thyroid Association,^{1,13} total thyroidectomy and lymphadenectomy of the central compartment-section was performed (Fig. 2). Moreover, prelaryngeal, pretracheal, laterotracheal and mediastinal anterosuperior lymph nodes were explored and excised.¹³

The final histological examination confirmed the presence of papillary carcinoma (classical variant). Moreover, among the removed 16 lymph nodes, 1 had micrometastasis.

DISCUSSION

Thyroid hemiagenesis is a rare anomaly due to an altered embryological development of one of the lobes of the gland. It has a three-fold greater incidence in women than in men and the lobe that is more frequently affected by agenesis is the left one.^{4,5}

The thyroid is embryologically derived by the ventral pocket of the median line of the floor of the pharynx. Afterwards, the pocket tends to separate from the pharyngeal wall and moves from the caudal direction up to the front wall of the trachea. This occurs in the second trimester of intrauterine life. During an altered descent of the thyroid several types of malformations of the gland may occur: lingual thyroid ectopia, which is the most frequent anomaly (1 on 3000 born alive); mediastinal ectopia; presence of a cysts/fistula of the thyroglossal duct;

ectopic thyroid nodules. Hemiagenesis of the thyroid is by far the rarest malformation among the others, but the exact incidence is not known.

The embryological reason for hemiagenesis is not yet known. According to some sources, the anomaly is a defect of the descent of the gland. More specifically, the thyroid can not develop laterally on the left side or on the right, therefore the original form of the gland does not become bilobed.

Since there is a familiarity in the development of such process, authors have even identified some of the genes that could be responsible for it (TTF-1, TTF-2, PAX-8 and HOXA-3). TTF-1 and Pax-8, thyroid specific transcription factors, play a decisive role in the determination and maintenance of cellular phenotype activating thyroglobulin (Tg), thyroperoxidase (TPO), thyrotropin receptor (TSH-R) and the sodium/iodide symporter (NIS) gene transcription.² Cases of thyroid dysgenesis causing congenital hypothyroidism are related with mutations of Pax 8.³ Moreover, in differentiated thyroid carcinomas (papillary and follicular) there are low levels of expressions of these transcription factors. There is a correlation between the

degree of thyroid tumor dedifferentiation and the loss of thyroid-specific transcription factors,⁸ TTF-1 and Pax-8 are not expressed in transformed thyroid cells and this lack of expression is associated with the absence of Tg, TPO, TSH-R7. This is related with the loss of differentiated thyroid phenotype, typical of thyroid cancer cells.²

Another theory that has been described, though less credited than the previous one, is that the cause is, the absence of the vascularization on the side of the agenesis.

It is important to discuss also the possibility of identifying or not, the parathyroid glands on the side of the thyroid agenesis. Embryologically, parathyroids originate from the fourth (the two superior glands) and from the third (the two inferior glands) pharyngeal cavity; therefore they have a different origin from the thyroid. However, in patients with thyroid hemiagenesis, it is not always possible to identify all the parathyroid glands in their anatomical position. Unfortunately, in literature there are not definite data about the site of parathyroid glands in case of thyroid hemiagenesis; therefore, when a total thyroidectomy is required, it is important for the surgeon to attempt in all cases to preserve the parathyroid glands on the side of the affected lobe in order to avoid permanent hypoparathyroidism in the patient.

In our experience, preservation of both the right and left parathyroid glands during the surgical treatment avoids alteration of serum calcium in postoperative period.¹³

The most interesting element to point out in this case is the association between thyroid hemiagenesis and the diagnosis of a papillary carcinoma on the side of the existent lobe. This occurrence represents an event in by itself. In the literature, five cases of such association have been reported, they were detailed by Khatri et al,⁶ Ashok Shaha¹² Pizzini and Papi⁹ Berni Canani et al¹⁰ and Yong Sang Lee.¹¹ In the case report by Pizzini and Papi, the association between thyroid hemiagenesis and other benign/malignant diseases of the thyroid are broadly reported.



Fig.1: Evidence of hemiagenesis: on the right the thyroid lobe, on the left the windpipe



Fig. 2: Thyroid specimen

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