Mini-invasive videoassisted thyroid lobectomy for neonatal hyperfunctioning adenoma related to a somatic TSHr gene mutation

Lobectomie thyroïdienne mini-invasive vidéo-assistée pour adénome néonatal hypersécrétant en présence d’une mutation du gène TSHr somatique

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Abstract

We report here a case of a paediatric hyperthyroidism due to a micro-macro-follicular thyroid adenoma in the presence of heterozygous point mutation of TSH receptor (TSHr). We describe the case from the initial diagnosis, through laboratoristic examinations and imaging techniques, until the radical surgical treatment made by a mini-cervicotomic videoassisted technique. We also explained the genetic work-up from peripheral blood and thyroid adenoma tissue.

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1. Case report

Thyroid nodules in childhood and adolescence are rare with an estimated prevalence ranging from 0.05% to 1.8%. They are usually non-functioning and they are malignant in up to 25% of cases. Only in few cases they may be solitary benign hyperfunctioning thyroid adenomas (HFTA) [1,2].

We report a case of a newborn male affected by neonatal non-autoimmune hyperthyroidism due to HFTA.

The baby was born by a natural childbirth at term. Early neonatal laboratory screening showed elevated FT4 values. After the first month FT4 appeared normal, while FT3 resulted increased with low border-line TSH level. At the second month, FT4 and FT3 values remained quite unchanged, while TSH was suppressed. No TSH receptor antibodies (TSI) were detected in the patient’s serum, while serum thyroglobuline levels resulted very high = 244 ng/mL (n.v. <55). To note that there was positive familiar history for thyroid diseases: the mother has previously submitted to a right lobectomy plus isthmectomy at the age of 24 for euthyroid follicular adenoma, a maternal aunt and the grandmother presented benign euthyroid disorders.

During the first two years of life, the baby showed a normal growth and never presented cardiac or intestinal troubles. Only in the last period, he demonstrated hyperkinesis and disturbed sleep.

The first neck ultrasonography examination at the age of 22 months showed an hypoechoic roundish area, of 16 mm in diameter, on right thyroid lobe with intranodular vascularization and regular defined margins. This ultrasound finding corresponded at 99mTc-pertechnetate thyroid scintigraphy to...
increased uptake area, with functional suppression (lack of visualization of the surrounding tissue). These data suggested the diagnosis of solitary autonomously functioning area (Plummer adenoma). Medical therapy with Metimazole was started at the age of 30 months with the lowest dosage required to achieve and maintain, without side effects, euthyroidism condition (2.5–5 mg daily).

Imaging monitoring by ultrasound, at the age of 38 months, revealed an increase of nodule dimension that showed a diameter up to 19 mm, even if no clear palpable mass was appreciable in the neck due to the deep location of the nodule.

At the age of 46 months, when the baby grew up to 15 kg weight and 96 cm height, he underwent right thyroid lobectomy removing the hyperfunctioning nodule by mini-cervicotomic videoassisted technique. No surgical complications occurred and the child was discharged in the 2nd postoperative day; cosmetic result after 1 month was evaluated as excellent. TSH value one month after surgery was 11 mU/L (0.4–4), confirmed at 3 months after surgery when 12.5 μg daily levothyroxine was administrated.

Histological specimens confirmed the suspected clinical diagnosis: an encapsulated micro-macro-follicular thyroid adenoma with features of hyperfunction, as pseudopapillary hyperplasia and colloid reabsorption.

Genetic workup from toxic thyroid adenoma tissue demonstrated an heterozygous point mutation of TSH receptor (TSHr) Exon 10 of the TSHr gene (chromosome 14q3), codon 453 with ATG (Methionine) to ACG (Threonine) substitution (endocrinology and metabolism department of Pisa’s university).

Genetic workup from peripheral blood DNA of the little child and his relatives (parents, grandmother and maternal aunt) did not demonstrate any mutation or polymorphism of the TSH receptor gene.

2. Discussion

Thyroid hyperfunctioning disorders at birth are rare and require an accurate diagnostic work up to choose the adequate treatment[3]. Despite the very young age of the patient, after first assessment (clinical, laboratory and ultrasounds evaluation), 99mTc-pertechnetate thyroid scintigraphy is mandatory, in order to evaluate the functional status of the nodule, especially in the presence of intranodal vascularization seen by ultrasound: in fact, while hyperfunctioning (“hot”) nodules are usually benign, non-functioning (“cold”) ones may be malignant in a few cases, thus requiring further assessment by fine needle aspiration biopsy (FNAB).

In our little patient, the typical scintigraphic pattern of elective radionuclide uptake on the nodule, without any other sign of uptake in the surrounding thyroid tissue, lead to initial diagnosis of Plummer adenoma, excluding the need of FNAB evaluation. On the other hand, the absence of TSI concurred to exclude any kind of auto-immune component. So we may state that the morpho-functional evaluation of thyroid nodules has the most direct effect on both addressing the correct diagnosis and the treatment.

As reported above, a medical approach by Methimazole (that has a better overall safety profile in pediatric age than propylthiouracil [4]) was started, although this kind of drug represents only a temporary palliation because hyperfunctioning nodules are unsusceptible of spontaneous remission [5], unlike auto-immune hyperthyroidism whose remission rate by drugs exceed 30% [6].

As definitive treatment for paediatric patients, especially if younger than 10 years, a low risk surgery is preferred on radiometabolic therapy with 131Iodine that can cause radio-induced thyroid malignancy and subsequent genetic damage [4]. In order to obtain an optimal result avoiding surgical complication (especially recurrent laryngeal nerve and parathyroid glands damage), the choice of an high-volume qualified center for thyroid surgery in children is recommended. In fact, due to the rarity of this disease in children, paediatric surgeons are not confident with thyroid surgery and most of the general surgeons are not habit with the small size of the patients [4,6]. In the case here reported, the definitive treatment was delayed at age of 46 months in order to obtain more favourable anthropometric conditions: videoscopic magnification of image by mini-invasive surgical approach brilliantly overcome the problem of small sizes of the surgical field, and it could help in unexpected anatomic variation (e.g. anomalous double branch origin of the inferior right thyroid artery from the common right carotid artery, a rare vascular anomaly already discovered by our group and described in other two patients [7]), thus avoiding delays in surgical therapy.

Because of the very young age of the patient, genetic work-up was performed after surgery, since particularly in children, somatic or germ mutations of TSHr gene are found to lead to hyperthyroidism. These mutations cause constitutive activation of the TSHr, responsible for cases of familial hereditary hyperthyroidism (germline mutations), cases of sporadic congenital hyperthyroidism (de novo mutations), and thyroid hyperfunctioning autonomous adenomas (somatic mutations) [8–10]. So far, there is a few literature about this issue [10,11], and very poor about pediatric age [8,9,12].

We can conclude that, although rare, TSHr gene mutations should be investigated in an infant presenting with non-autoimmune hyperthyroidism. In fact, genetic assessment might have implication on thyroidectomy extension: total thyroidectomy and aggressive approach should be considered in patients with TSHr gene germ cell mutations [13], instead of conservative approach by lobectomy, that is the procedure of choice when a somatic mutation is present and, as showed in this case report, could be even helped by mini-invasive videoassisted surgery.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


