

Surgery of Thyroid Nodule in Children: our experience about 36 patients

Chirurgie des Nodules Thyroïdiens chez L'enfant: notre expérience à propos de 36 patients

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ABSTRACT

Aim: Study the characteristics of thyroid nodules in children, to assess the rate of malignancy and follow their evolution.

Method: We carried out a retrospective study involving children under 16 years old, operated on for thyroid nodules in the ENT department of the Rabta hospital between years 2000 and 2020.

Results: We operated 36 patients. Eleven of them had malignant tumors. Malignancy rate was about 30.5%. Median age was 15, of which 80.5% were adolescents. Female represented 80% of our population. Malignancy was significantly higher in male (71.4% of males had malignant tumor versus 20.7% of female; $p=0.018$).

On Ultra Sonography (US), hypoechoic and unwell limited characters were significantly more observed in malignancy (respectively $p=0.037$ and $p=0.041$).

At the histological study, all malignant tumors were papillary carcinomas. Metastatic lymph nodes were present at diagnosis in 63.6% of cases.

Post operative complication rate was relatively low with 15.4% of transient hypoparathyroidism and no laryngeal nerve damage. From the children operated on for benign tumors, 38% needed substitutive therapy. Two of the eighteen followed needed thyroid surgery at 4 and 6 years postoperatively.

For malignant tumors, the median follow-up was about 19 months. Three of the eight patients followed (37.5%), had lymph node recurrence. These three children had lateral lymph node metastatic involvement at diagnosis.

Conclusion: Cancers among operated thyroid nodules in children under 16 years old are highly frequent. Male gender, irregular limits and hypoechoic character of the nodule on US are correlated to malignancy. Fine needle aspiration should be a routine exam in children.

Key words: thyroid nodule, Children, Surgery, Radio iodine, Outcome

RÉSUMÉ

Objectifs: Etudier la fréquence des cancers parmi les nodules thyroïdiens et leurs caractéristiques et évaluer les suites opératoires chez les enfants et adolescents opérés de nodules thyroïdiens.

Méthodes: Etude rétrospective colligeant les dossiers d'enfants âgés de moins de 16 ans opérés pour nodule(s) thyroïdiens(s) au service ORL de la Rabta entre 2000 et 2020.

Résultats: L'étude a concerné 36 patients. Parmi les nodules opérés, 11 étaient des cancers, soit un taux de malignité de 30,5%. La médiane de l'âge était de 15 ans, et 80,5% étaient des adolescents (enfants âgés de plus de 11 ans) Le sexe féminin représente 80% de notre population. La malignité était significativement plus fréquente parmi les garçons (71,4% des garçons avaient des cancers versus 20,7% des filles; $p=0,018$).

A l'échographie, l'hypoéchogénéicité et les limites irrégulières étaient corrélées à la malignité (respectivement $p=0,037$ and $p=0,041$). L'étude étant rétrospective

A l'histologie, tous les cancers étaient des carcinomes papillaires. Les métastases ganglionnaires étaient présentes au moment du diagnostic dans 60,6% des cas.

Les complications étaient rares avec 15,4% d'hypoparathyroïdie transitoire et aucun cas de paralysie récurrentielle. Parmi les enfants opérés pour nodules bénin, 38% ont nécessité un traitement hormonal (il s'agit de 4 lobectomies et de 3 thyroïdectomies totales), Deux des 18 patients suivis, ont eu une totalisation à 4 et 6 ans post opératoire.

Pour les nodules malins, la médiane de suivi était de 19 mois. Trois parmi les 8 patients suivis (37,5%) ont eu une récurrence ganglionnaire. Ces trois derniers avaient des métastases ganglionnaires au moment du diagnostic.

Conclusion: Le taux de cancer parmi les nodules de l'enfant est élevé. La chirurgie occasionne peu de complications. La cytoponction échoguidée devrait être un élément clé du bilan pré-opératoire.

Mots Clés: Nodule thyroïdien, Enfant, Chirurgie, Iode radio actif, Résultats

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INTRODUCTION

The thyroid nodule among children is much rarer than within the adult population. Malignancy is more frequent in pediatric population and it poses a problem of therapeutic management concerning the extent of surgery and the additional treatment with radioactive iodine.

We suggest to study the characteristics of operated thyroid nodules in children, the frequency of cancers discovered among them, and to assess the postoperative follow-up.

MATERIAL AND METHODS

We carried out a retrospective study involving 36 children operated on for thyroid nodules in the ENT department of the Rabta hospital between years 2000 to 2020.

Included were children aged 16 and below, with confirmed benign or malignant tumors diagnosed on histological examination. We excluded patients over 16 years old and patients operated on for Hashimoto's pseudo-nodular thyroiditis. The 2017 TNM classification was adopted for cancer classification.

For each patient, we specified the data from physical examination, biology results, ultra sonography (US), surgery, frozen section biopsy, histological finding, and follow-up. TIRADS classification started in our institution in 2014 and the criteria for suspected malignancy were not all mentioned on the US report, so very few patients had an assessment of the risk of malignancy according to TIRADS classification.

For quantitative variables, we studied distribution of data by coefficients of asymmetry, kurtosis and by tests of normality. We described these variables by the means and standard deviation if it was a normal distribution and by the medians and the interquartile intervals if it was not.

To analyze association between two qualitative variables, we used Pearson chi² test if application conditions were verified and the Fisher if not. To analyze association between a qualitative and a quantitative variable, we used Mann Whitney test. We retained the significance level for $p \leq 5\%$.

RESULTS

Among the 36 children operated, 11 had malignant tumors (30.5% of malignancy). Median age was 15 [5-16 years old], of which 80.5% were adolescents (aged over eleven). When comparing children to adolescents, age wasn't correlated to malignancy ($p=0.986$).

Eighty per cent of our population was girls. Malignancy was significantly higher in boys (71.4% of boys had malignant tumor versus 20.7% of girls; $p=0.018$). Sex ratio in benign tumors was 0.08 versus 0.83 in malignant ones.

The nodules were mainly discovered by basal cervical swelling. In 3 cases, it was discovered during

exploration for cervical lymphadenopathy. In one case, it was an incidental US finding.

On examination, the median diameter was 30 mm. Nodules were mostly firm, mobile and painless, excepted two who were hard and fixed, corresponding to malignant tumor. Cervical lymph nodes were present in 3 children. They were homolateral to the thyroid nodule in 2 cases and bilateral in the other one. Their size was between 10 and 20 mm, and they were hard in two cases.

Nasofibroscopy was performed in 31 children, and showed normal laryngeal mobility in all cases.

On US, the nodules averaged 31 mm. In 25 cases, patients had only one nodule, five others had 2 nodules, and the rest ($n=6$) had multinodular thyroid. Most of malignant nodules had one criteria of malignancy, of which: two were highly hypoechoic, three had calcifications, and two had irregular limits. Moreover, among malignant nodules, one was hyperechoic. Hypoechoic and unwell limited characters were significantly more observed in malignancy (respectively $p=0.037$ and $p=0.041$). In 5 children, US showed enlarged suspicious lymph nodes, of which three were found on examination, and 2 on US. In malignancy, metastatic lymph nodes were suspected pre operatively in 45.5% of cases.

Among the 25 benign nodules, only three children had total thyroidectomy. The rest had a lobectomy. Among the eleven malignant thyroids four underwent total thyroidectomy with bilateral prophylactic central lymph node dissection at once, for malignant frozen section biopsy. Two children underwent a two stage total thyroidectomy with unilateral prophylactic central lymph node dissection for malignancy discovered on histology.

Four children had a total thyroidectomy with central and lateral functional lymph node dissection: they had suspicious lymph nodes homolateral to the nodule on US, and frozen section biopsy confirmed malignancy. One child had bilateral central and lateral functional lymph node dissection because he had bilateral suspicious lymph nodes on US, and frozen section biopsy was in favor of poorly differentiated carcinoma. At the histological study, the 11 cases of malignant tumor were papillary carcinoma.

Prophylactic central dissection was metastatic in 33.33% of cases. Malignant tumors were associated to lymphocytic thyroiditis in 3 cases, but difference with benign tumors wasn't statistically significant ($p=0.154$).

Metastatic lymph nodes were present at diagnosis in 63.6% of cases (7 of 11). Table I summarizes the histological findings.

**Table I: histological findings in malignant tumors.**

Thyroid histology	Lymphnode dissection histology			TNM Classification
	Central compartment		Lateral compartment	
	Safe	Metastatic	Metastatic	
TPC 30mm	X			pT2 N0
TPC 40mm	X			pT3a N0
TPC infiltrating peri thyroid tissues (2 foci: 50 mm and microcarcinoma)		X	X	pT3b N1b
TPC 15 mm		X	X	pT2 N1b
TPC 40 mm (vesicular form) + invasive insular part		X	X	pT3b N1b
TPC 25 mm infiltrating peri thyroid tissues (vesicular form)		X	X	pT3b N1b
TPC 10 mm infiltrating peri thyroid tissues (vesicular form)		X	X	pT3b N1b
TPC 13 mm + LT		X		pT1b N1a
TPC 30mm+ vascular embolism + LT	X			pT2 N0
TPC 30 mm (2 stages TT)		X		pT2 N1a
TPC 20 mm (vesicular form) + LT (2 stages TT)	X			pT2 N0

TPC: thyroid papillary carcinoma. LT: lymphocytary thyroiditis. TT: total thyroidectomy

Ten patients were lost to follow up immediately after surgery. For the 26 other children, we have a mean overall follow-up of one year, with a median of 23,3 months.

All of the immediate continuations were simple. Thereafter, transient hypoparathyroidism was noted in four children (15.4%), of which three had central lymph node dissection. Only one child operated on for benign thyroid had hypoparathyroidism. No one of the patients had vocal cord paralysis.

From the 25 children operated for benign tumors, eighteen were followed-up. Seven (38%) needed substitutive therapy, of which four had a loboisthmeomy. Two needed thyroid surgery at 4 and 6 years postoperatively for recurrent nodule (they had one or two micro nodules preserved at first surgery).

For malignant tumors follow-up, some biology and US data are missing. Three of the eleven children were immediately lost to follow-up. The median follow-up was about 19 months.

The eight patients followed received radio-iodine treatment with intense central cervical fixation at first therapy and no distant metastasis. Three of the eight children (37.5%) had lymph node recurrence. These three children had lateral lymph node metastatic involvement at diagnosis. Ganglionic recurrence occurred on the area of first functional neck dissection.

The first child had a clean mapping at 6 months of the cure and thyroglobulin was normal at 3 years.

The second had a clean mapping at 18 months (post-operative) but thyroglobulin was checked only at three months post-operative.

In the third case, scintigraphy was clean at six months after radio iodine, and thyroglobulin checked one-year post-operative and was normal.

In the fourth case, no scintigraphic or biological controls

were available after the 100mCi first radio-iodine treatment. For the fifth patient, the mapping was clean at 6 months post-operative, but thyroglobulin rate rose to 79 ng/ml, so a second radio iodine therapy of 100 mCi was administered with clean mapping and normal thyroglobulin at three years.

The sixth child fixed at the first post-operative mapping in lymph nodes areas that were suspicious on US; then he had picking nodes and had another radio iodine cure. The seventh had 2 clean radio iodine scintigraphy and ascending thyroglobulin rate; we found suspicious lymph nodes on US and he was eligible to US guided lymph node fine needle aspiration before surgery, but didn't represent. The eighth one fixed on several lymphnodes areas at second post-operative radio iodine scintigraphy. These lymph nodes were suspicious on US. Moreover, thyroglobulin rate was high. He had another lymph node dissection for lymph node recurrence, and a third radio iodine therapy; the last scintigraphy was clean, with normal thyroglobulin.

DISCUSSION

Through our study, we could assess the rate of malignancy in children (30.5%), and follow their evolution. However, the retrospective nature of the study meant that some data was missing.

We observed that thyroid nodule in children is rare: thirty-six children operated in 20 years versus more than 200 adults per year operated in our institute.

We opted for a population under the age of 16, referring to the recommendations of the French ENT Society of 2011 which identify this age as the lower threshold for the presumption of malignancy [1]. We found a peak of frequency of thyroid nodules in adolescence (more than 11 years old) that is confirmed by several studies [2- 5]. Our study population counted 80% of girls; however, malignancy was more observed in boys (71.4% of tumors in boys was malignant vs 20.7% in girls). Many authors noticed that male gender is a presumptive factor for malignancy [1,5-7].

Clinically, goiter was more often mono or pauci-nodular (83.3%). Preoperatively, suspicious adenopathies (clinically or on US) were present on the lateral sector in 5 patients from 11, meaning in 45.5% of cases versus 31% in Alnajar cohort [8].

No one of our patient had thyroid fine needle aspiration (FNA). This last one is a routine exploration of thyroid nodules in children [3-5,9,10]. No ultrasound appearance has a sufficiently high negative predictive value to be predictive of benignity [8]. Gupta and Al Nofal agree that the indications for fine needle aspiration should be broader in children than in adults [5,10]. Thus all our patients were eligible for a preoperative FNA.

TSH has for some years been recognized as a biological sign of malignancy [7,9,11]. Indeed, Mussa et al proved that malignancy rate increased linearly with the TSH level and this within the normal range, with a threshold value of 2.8 mU/L [7].

The type of surgical procedure depends on the extension



of nodular lesions. In case of malignant frozen section examination or malignant cytology, total thyroidectomy is recommended [4,11,12]. Bilateral central dissection, prophylactic or not, is systematically recommended [4,11,12]. Lateral dissection is indicated in cases of cytologically proven lateral lymph node metastases [4,11].

The complication rate after surgery is relatively low with 15.4% of transient hypoparathyroidism and no laryngeal nerve damage.

In literature, complication frequencies depend on studies. Definitive hypoparathyroidism frequency is around 2.5 and 14% [2,11-14]. Low post-operative (day 1) calcemia < 1.6 mmol/L [20] or iPTH < 15 ng/mL [11] would be correlated with permanent forms of hypoparathyroidism. The American Thyroid Association (ATA) recommends postoperative iPTH assay [11].

For laryngeal paralysis, it fluctuates between 0 et 6% [2,11-14]. Central dissection is associated with more parathyroid and inferior laryngeal nerve involvement [13]. Monitoring of inferior laryngeal nerves is recommended by some authors [4,14]. It is not likely to decrease the rate of laryngeal paralysis according to the ATA and is only useful in children under 10 years of age, in recurrent dissections and in revision surgeries [1].

In literature, malignancy fluctuates between 22 and 27.2% [2-5,8,10,15], most of it are papillary type, with a frequent lymph node involvement at diagnosis (27 to 83%) [2,3,5]. These figures matches with our results: we found 30.5% of malignancy, all of them papillary, and 63.6% of lymph node metastasis.

Eleven percent of our patients had nodular recurrence on remaining lobe at 4 and 6 years post-operative. It's

rare before 4 years old, with an estimated frequency between 3 and 28% [1].

All of our patients, with malignant tumors, received radioactive iodine treatment. It's indicated in cancer size more than 1 cm, in lymph node or distant metastasis, and if margins are infiltrated [12].

The malignant recurrence rate ranges from 10 to 39% depending on the series [10-13], in accordance with our results (37.5 % in our population).

The prognosis for differentiated thyroid cancer is good. Mortality is equal or less than 2% compared to 5.8-15% in adults [11-13]. The survival rates for 1753 cases, at 5, 15 and 30 years is > 90% [13].

CONCLUSION:

Our study highlights the high frequency of cancers among operated thyroid nodules in children under 16 years old. The rate of postoperative complications is low, making thyroid nodule surgery a harmless procedure. The study of factor statistically associated to malignancy revealed male gender, irregular limits and hypoechoic character of the nodule on US. Fine needle aspiration should be a common practice in children, even more than in adults.

Compliance with ethical standards:

retrospective study respecting anonymity for patients, no patient agreement was needed.

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