SURGICAL TREATMENT OF THYROID NODULES IN CHILDREN

TRAITEMENT CHIRURGICAL DES NODULES THYROÏDIENS CHEZ L'ENFANT

S. Ayadi[1], G. Yousfi[1], I. Akrout [1], N. Salem[1], F. Chaltout[2], M.Mnejja[1], B.Hammami[1], K. Chtourou[2], I. Charfeddine[1]

[1] ENT department and research Laboratory LR23ES01, Habib Bourguiba University Hospital, University of Sfax, Sfax, Tunisia.

[2] Department of Nuclear Medicine, Habib Bourguiba University Hospital, University of Sfax, Sfax, Tunisia.

ABSTRACT:

Introduction: Thyroid nodules (TN) are rare in children but carry a higher risk of malignancy (20–25%). Their management requires a multidisciplinary approach. This study aims to describe the specific features of surgical management of pediatric thyroid nodules.

Methods: A retrospective study including patients under the age of 18 who underwent surgical management for TN in the ENT and Head & Neck Surgery Department of Habib Bourguiba Hospital in Sfax, Tunisia, between 2010 and 2023. Our study aimed to describe the specific features of the surgical management of thyroid nodules in children and adolescents.

Results: Our study included 26 patients. The mean age at diagnosis was 15.4 years [8–18 years], with a sex ratio (M/F) of 0.44. Anterior neck swelling was the presenting symptom in 22 patients (84%). On cervical ultrasound, TN were classified as EU-TIRADS 5 in 30 % of cases, EU-TIRADS 4 in 12%, and EU-TIRADS 3 in the remaining cases. All patients underwent surgical treatment: lobectomy with isthmectomy in 53% of cases and total thyroidectomy as first-line surgery in 47% of cases. A central neck dissection associated with bilateral functional cervical lymph node dissection was performed in 12 % of cases. Final histological examination revealed benign nodules in 20 cases (76%) and malignant lesions in 6 cases (24%). These included 1 case of thyroid lymphoma (4%) and 5 cases (20%) of differentiated thyroid carcinoma. All patients with differentiated thyroid carcinoma received radioactive iodine (RAI) therapy combined with suppressive hormone therapy. The mean number of RAI treatments was 3 [1–9]. Postoperative recurrent laryngeal nerve palsy was observed in 2 patients (8%). The mean follow-up period was 25 months [6–120 months]. No deaths were reported.

Conclusion: TN in children and adolescents, although less common than in adults, require thorough evaluation due to a higher risk of malignancy. Close monitoring and multidisciplinary management contribute to optimizing prognosis and outcomes.

Keywords: Thyroid nodule, Child, Thyroidectomy

RÉSUMÉ:

Introduction: Les nodules thyroïdiens (NT) sont rares chez l'enfant, mais associés à un risque élevé de malignité (20–25 %). Leur prise en charge est multidisciplinaire. L'objectif de notre étude est décrire les particularités de la prise en charge chirurgicale des nodules thyroïdiens chez l'enfant et l'adolescents.

Matériels et méthodes: Étude rétrospective et descriptive ayant inclus les patients âgés de moins de 18 ans pris en charge chirurgicalement pour des NT, au service d'ORL et CCF du CHU Habib Bourguiba de Sfax, entre 2010 et 2023.

Résultats: Notre étude portait sur 26 patients. L'âge moyen du diagnostic était de 15,4 ans [8-18 ans], avec un sex-ratio (H/F) égal à 0,44. À l'échographie cervicale, les NT étaient classés EUTIRADS 5 dans 8 cas (30 %), EUTIRADS 4 dans 3 cas (12 %), et EUTIRADS 3 dans le reste des cas. Tous les patients ont bénéficié d'un traitement chirurgical: une loboisthmectomie dans 11 (43 %) et une thyroïdectomie totale d'emblée dans 15 cas (57 %). Un curage médiastino-récurrentiel associé à un curage cervical fonctionnel bilatéral était pratiqué dans 3 cas (12 %). À l'examen histologique définitif, des nodules étaient bénins dans 20 cas (76 %) et malins dans 6 cas (24 %). Il s'agissait d'un lymphome thyroïdien dans 1 cas (4 %) et d'un carcinome différencié de la thyroïde dans 5 cas (20 %). Un traitement par IRA thérapie associé à une hormonothérapie suppressive a été reçu par tous les patients atteints de carcinomes différenciés de la thyroïde. Le nombre moyen de cures d'iode était de 3 cures [1-9 cures]. Une paralysie récurrentielle postopératoire était objectivée chez 2 patients (8 %). Le recul moyen était de 25 mois [6-120 mois]. Aucun cas de décès n'a été observé.

Conclusion: Les NT chez l'enfant et l'adolescent, bien que plus rares que chez l'adulte, nécessitent une évaluation rigoureuse en raison d'un risque de malignité plus élevé. Un suivi étroit et une prise en charge multidisciplinaire assurent un bon pronostic.

Mots clés: Nodule thyroïdien, Enfant, Thyroïdectomie

Auteur correspondant: Sirine Ayadi
E-mail: sirine_ayadi@medecinesfax.org

INTRODUCTION:

Thyroid nodules (TN) are relatively uncommon in children, with an estimated prevalence ranging from 0.2% to 5% [1]. As in adults, the majority of TN are benign. However, the risk of malignancy in children is significantly higher than in adults. It is estimated at 20% to 25%, compared to 5% in adults [1,2]. Therefore, the management of these TN requires a multidisciplinary approach, involving paediatricians, otolaryngologists, and radiologists. Surgical management of thyroid nodules in children is reserved for cases of suspected malignancy or when signs of compression or aesthetic issues.

Our study aimed to describe the specific features of surgical management of thyroid nodules in children and adolescents.

METHODS:

We have conducted a descriptive and retrospective study in the otolaryngology department of Habib Bourguiba Hospital in Sfax over 14 years, from January 2010 to December 2023. We included patients under the age of 18 who underwent surgery in our department for a thyroid nodule. A minimum postoperative follow-up of six months between the date of surgery and the date of the last update was required for the patient to be included in our study.

For each patient, we collected medical history, physical examination, paraclinical data, detailed surgical treatment, extemporaneous examination, and definitive histological results. We noted adjuvant treatment received if necessary, and monitoring and treatment modalities for recurrences. Statistical analysis of the data was performed using SPSS version 27 software. Qualitative variables were expressed as percentages and numbers. Quantitative variables were estimated as means and standard deviations or as medians and extremes.

RESULTS:

Our study included 26 patients. The mean age at diagnosis was 15 years and 4 months [range 8–18 years] (Table I). Only 2 patients were younger than 12 years (8%). Five patients (20%) had a family history of thyroid surgery for benign TN, and three patients (12%) had a personal history of thyroid dysfunction (Table I). Anterior cervical mass was the most common reason for consultation, observed in 22 patients (84%) (Table I). Physical examination revealed a thyroid nodule in 25 patients (96%) and cervical lymphadenopathy in 7 patients (28%), affecting level IIb in 20% of cases, level III in 8% of cases, and level Vb in 4% of cases (Table I). Preoperative indirect laryngoscopy was normal in all cases. No patients had signs of clinical dysthyroidism. Thyroid function tests were normal in 25 patients (96%). Mild hyperthyroidism was noted in only one patient.

Table I: Epidemiological and Clinical Characteristics

Characteristic	Number	Percentage
Age	15 years and 4 months [8–18]	----
Sex (male/female)	26 patients (8/18)	0.44%
Personal history: Hypothyroidism Hyperthyroidism Adenectomy	 2 patients 1 patient 1 patient	 8% 4% 4%
Family history: Hyperthyroidism + benign thyroid nodule	 1 patient	 4%
Benign thyroid nodules without dysthyroidism	4 patients	16%
Clinical presentation: Thyroid nodule High dysphagia to solids Cervical lymphadenopathy	 22 patients 4 patients 4 patients	 84% 16% 16%
Physical examination: Thyroid nodule Cervical lymphadenopathy - Level IIb Cervical lymphadenopathy - Level III Cervical lymphadenopathy - Level Vb Cervical lymphadenopathy - Other	 25 patients 7 patients 5 patients 2 patients 1 patient	 96% 28% 20% 8% 4%

Preoperative cervical ultrasound showed a single NT in 15 patients (57%) and multinodular goitre in 11 patients (43%). The average size of the nodules was 34.2 mm [20-60 mm]. They were classified as EUTIRADS III in 58% of cases, EUTIRADS IV in 12% of cases, and EUTIRADS V in 30% of cases. Fine needle aspiration biopsy of the thyroid nodule was performed in 4 patients (16%). The cytological study was classified as Bethesda I in one patient (4%), Bethesda III in two patients (8%) (atypia of undetermined significance), and Bethesda V (suspicious for malignancy) in one patient (4%).

Twenty-five patients (96%) underwent thyroid surgery in a single operation. This consisted of a lobectomy (LI) in 15 patients and a total thyroidectomy (TT) in 11 patients (Table II). Cervical lymph node dissection was performed in conjunction with thyroid surgery in 4 patients (16%) (Table III).

Table II: Extent of thyroidectomy during the first stage of surgery

Thyroid procedure	Number	Percentage	Indications	Extemporaneous examination results
LI*	15	58%	Unilateral thyroid nodule	• Hodgkin's lymphoma: 1 patient • Benign thyroid nodule: 13 patients • Awaiting final histology: 1 patient
TT**	9 1 1	35% 4% 4%	Bilateral thyroid nodules Unilateral thyroid nodule Lymph node metastasis of papillary carcinoma	Papillary carcinoma (PC***): 1 patient Benign: 8 patients Papillary carcinoma

LI*: Lobectomy with isthmectomy, TT**: Total thyroidectomy, PC***: Papillary carcinoma

Table III: Extent of lymph node dissection during the first stage of surgery

Lymph node procedure	Number	Percentage	Indications
Central neck dissection (CND)*	1	4%	• Non-conclusive extemporaneous examination (EE***) with nodule classified as EU-TIRADS 5
Bilateral CND* + Bilateral selective lateral neck dissection (SLND**) (Levels IIa, III, IV)	3	12%	• EE**: papillary carcinoma (suspected ipsilateral lymphadenopathy on ultrasound)

CND*: Central neck dissection (CND)*; SLND**: Selective Lateral Neck Dissection; EE***: Extemporaneous examination

The definitive pathological examination concluded that 77% of the NT were benign: benign multinodular goiter in 16 cases (60%), a vesicular adenoma in one patient (4%), and lymphocytic thyroiditis in three patients (12%). Malignancy of the thyroid nodule was confirmed in 6 patients (24%), with papillary thyroid carcinoma in 4 cases (16%), vesicular thyroid carcinoma in 1 case (4%), and Hodgkin's lymphoma in 1 case (4%). A second surgical procedure was performed in one patient (4%): the diagnosis of a 3 cm vesicular carcinoma of the right lobe of the thyroid with vascular invasion was confirmed by definitive pathological examination. The second operation was performed within six weeks of the first surgery: the patient underwent left total thyroidectomy with left CND.

Patients with differentiated thyroid carcinomas were classified according to the 2017 AJCC TNM classification (Table IV).

Table IV: Distribution of patients with differentiated thyroid carcinoma according to TNM classification (AJCC 2017)

pTNM Classification	Histological Type	Type of Surgery	Number	Percentage
T1aN0M0	Papillary carcinoma (PC****)	Total thyroidectomy (TT*)	1	20%
T2N0M0	Vesicular carcinoma (VC°)	TT* + Contralateral CND (Lobectomy with benign extemporaneous examination)	1	20%
T3N1bM0	Papillary carcinoma (PC****)	TT* + Bilateral CND ** + Bilateral selective lateral neck dissection (SNLD***)	3	60%

PC****: Papillary carcinoma ; VC°: vesicular carcinoma; TT*: Total thyroidectomy; CND**: Central Neck Dissection; SLND***: Selective Lateral Neck Dissection

Postoperatively, the average length of hospital stay was 2.7 days [2-5 days]. In the immediate postoperative period, the most frequent postoperative complication was transient hypocalcemia, which occurred in 6 patients (23%). Transient dysphonia was reported in 2 patients (8%). There were no cases of postoperative dyspnea. Recurrent paralysis, confirmed by indirect laryngoscopy, was observed in 2 patients (8%). In one case, this involved unilateral immobility of the vocal cord (4%), and in the other, laryngeal diplegia in the paramedian position (4%). Six months after surgery, patients with recurrent paralysis had recovered vocal cord mobility, and no cases of permanent hypoparathyroidism were observed. LT4 hormone therapy was initiated after total thyroidectomy in 12 patients. It was used as a suppressive therapy in 5 patients (20%) with differentiated thyroid carcinoma (DTC) (Table IV) and as a replacement therapy in the other patients. The patient with Hodgkin's lymphoma underwent two courses of chemotherapy. Adjuvant treatment with I131 was indicated in all children with differentiated carcinoma, with an average of 3 courses [1-9 courses] (Table V). The average time between surgery and the first course was 5 months [1–15 months]. The dose per course was 100 mCi. The first post-therapeutic whole-body scan (WBS) showed a white isotopic map in one patient (4%), cervical uptake related to residual lateral lymph nodes in four patients (16%), and upper mediastinal uptake related to residual thymus in one patient (4%). Thyroglobulin (Tg) levels measured under stimulation were above 100 ng/mL in one patient (corresponding to lateral cervical lymph node fixation and mediastinal fixation at WBS) and below 10 ng/mL in the other patients. Anti-thyroglobulin antibodies were negative in these patients. A complete clinical and biological response was observed in two patients (40%). An indeterminate biological response was noted in two patients (40%), with stimulated Tg between 1 and 10 ng/mL and no uptake at the last WBS. Finally, one case was classified as an incomplete response due to persistent lymph node uptake in level V at the WBS during the ninth course of I-131, associated with a gradual increase in Tg levels. This patient underwent selective lymph node dissection in level V, with a post-operative drop in Tg levels.

For patients who had undergone lobectomy and presented with benign nodules at surgery, the appearance of thyroid nodules on the remaining lobe was observed in one patient. There were three nodules, the most significant measuring 23 mm and classified as EUTIRADS 3. A total thyroidectomy was performed on this patient after 4 years, due to their refusal to continue follow-up care. No postoperative complications were observed: no hypocalcemia, dysphonia, or postoperative dyspnea. The final pathological examination concluded that the nodule on the remaining lobe was benign.

During the follow-up, no cases of death or distant metastasis were noted. The average follow-up period for our patients was 25 months [6 months-10 years] with a survival rate of 100%.

Table V: Management of thyroid carcinomas

	Histological Type	pTNM Classification	First WBS Uptake*	Number of I-131 Treatments	Last WBS Uptake*	Thyroglobulin (Tg) Level (Last Value) **	Surgical Reintervention
Patient 1	Vesicular carcinoma (FC°)	T2N0M0	Cervical uptake	2	None	<0	None
Patient 2	Papillary carcinoma (PC****)	T1aN0M0	Cervical + mediastinal uptake (thymus)	2	None	4.1 ng/ml	None
Patient 3	Papillary carcinoma (PC****)	T3N1bM0	Left paramedian cervical uptake	3	None	5.5 ng/ml	None
Patient 4	Papillary carcinoma (PC****)	T3N1bM0	No uptake	1	None	<0	None
Patient 5	Papillary carcinoma (PC****)	T3N1bM0	Cervical uptake	9	Cervical	145 ng/ml	Adenectomy

WBS*: Whole-body scan; Tg**: Thyroglobulin; VC° = vesicular carcinoma (FC); PC****: Papillary carcinoma (PC)

DISCUSSION:

Over 14 years, 26 patients were identified (≈2 per year), with a mean age of 15 years and 4 months and a female predominance. EU-TIRADS V nodules were observed in 31%, and suspicious lymphadenopathy in 16%. Lobectomy was performed in 57% and total thyroidectomy in 43% of cases. Postoperative complications included transient recurrent laryngeal nerve paralysis (8%) and transient hypocalcemia (23%). Histopathology confirmed differentiated carcinoma in 20%, Hodgkin's lymphoma in 4%, and lymph node involvement in 12%. Hormone therapy was replacement in 27% and suppressive in 20%. One case of lymph node recurrence (papillary carcinoma) was treated surgically. The 2-year survival rate was 100%.

As in adults, the majority of paediatric NTs are benign [1,3]. It has been shown that 75% of NTs are benign in children. However, the risk of malignancy in paediatric NTs is 3 to 5 times higher than in adults [4]. In our series, malignant thyroid NT was noted in 24% of cases. PTC, mainly papillary carcinoma, is the most common type [5] and can be observed in children of any age. Most cases are discovered during late childhood, with a peak incidence after the age of 15 [3]. In fact, according to the latest ATA recommendations, thyroid cancer is the eighth most common cancer in the 15-19 age group and the second most common cancer in adolescent girls [6]. Exposure to ionizing radiation is a well-established risk factor for the development of papillary thyroid carcinoma, particularly for doses between 20 and 29 Gy, with a peak incidence observed 15 to 25 years after exposure [7]. The risk is even higher when exposure occurs at a young age, particularly in children under 5 years of age [7]. Hormone production disorders are also associated with a risk of developing NT [8]. Two patients in our series (8%) had congenital multinodular goiter with congenital hypothyroidism. One of the two patients had papillary thyroid carcinoma. The ultrasound criteria for suspected cancer are the same as those in adults [9], as is the 2017 Bethesda cytological classification [10]. However, it is recommended that fine needle aspiration biopsy (always ultrasound-guided) be performed for all nodules larger than 1 cm in children, for nodules that are suspicious on ultrasound, even if they are smaller than 1 cm, and for suspicious cervical lymph nodes [6]. New studies have shown a high risk of malignancy in Bethesda subgroups in children compared to adults. This risk poses a therapeutic problem, particularly in Bethesda stage III, where the risk of malignancy increases from 7.4% in adults to 14.9% in children [11], and surgery is indicated from the outset. Lymph node involvement is present in 52% to 90% of cases, depending on the series [12]. It is more common in children with papillary carcinoma than in adults [13]. According to the latest ATA 2015 recommendations [6], CND is recommended for patients with extra-thyroid extension observed pre- or intraoperatively, patients with central or lateral lymph node involvement, and patients with tumors larger than 4 cm [14]. Postoperatively, estimates of the risk of hypocalcemia and recurrent nerve injury vary widely between studies [15,16]. The risk of developing transient hypocalcemia after total thyroidectomy is high, ranging from 32% to 52% [3], depending on the study, but the risk of developing permanent hypoparathyroidism is very low (<2.5%) [3,6]. Recurrent paralysis is a rare complication: paediatric series show rates ranging from 1% to 6% [6]. It is most often transient. The surgical difficulty is mainly related to the identification of the inferior laryngeal nerve, which is thinner than in adults. During surgery, the AACE and AHNS-ES recommend monitoring the laryngeal nerve due to its small size in children. This monitoring is strongly recommended in cases of cervical lymphadenopathy or increased thyroid volume [17]. Postoperative monitoring is based, in benign cases, on clinical examination, biological data, and ultrasound (requested in cases where a thyroid nodule is present on the remaining lobe). In cases of PTC, monitoring is based on thyroglobulin (Tg) levels, anti-Tg antibodies, ultrasound, and whole-body scanning. The timing and frequency of these tests depend on the risk [6]. To destroy any thyroid residue, adjuvant treatment with radioactive iodine is the best combination in terms of survival and reducing the risk of long-term recurrence in pediatric DTC [18,19]. In our series, five patients (20%) received postoperative RAI therapy, with good results in 80% of CDT cases. Long-term follow-up is recommended, as disease recurrence may occur several decades after the initial diagnosis and treatment [20]. The prognosis for differentiated thyroid carcinomas is favorable in the vast majority of cases, both in children and adults. It is a cancer with a good prognosis, even in cases of distant metastasis [21,22]. In our series, the prognosis was favorable in all cases. In the paediatric population, the ten-year survival rate reported in all studies is excellent, ranging from 93% to 100% [21]. In studies with longer follow-up periods, the 30-year survival rate is excellent, approaching 95%.

The strength of our study lies in its coverage of 14 years. Its main limitation, however, is its retrospective design. Additionally, the inclusion of various histological types, encompassing both benign thyroid nodules and thyroid carcinomas, represents another potential limitation.

CONCLUSION:

Thyroid nodules are much less common in children and adolescents than in adults. Their incidence has been increasing in recent years due to recent screening strategies. The risk of malignancy in thyroid nodules is higher than in adults, with better overall long-term survival. However, given the rarity of this condition, it would be useful to conduct multicenter studies to better understand the paediatric profile of thyroid nodules, particularly carcinomas.

Ethics approval: Our study was granted a waiver of formal IRB approval, as it did not involve any intervention or collection of identifiable patient data.
Informed consent: Parental consent for publication of anonymized data was obtained. General institutional consent for the research use of medical records without disclosure of identifiable information was in place; hence, no additional retrospective consent was required.

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