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CLINICAL STUDY

Thyroid diseases in children and adolescents

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Abstract: *Background*: Thyroid nodules are relatively rare in children and adolescents and have a prevalence between 0.2 %–1.8 %. They are more often malignant in children than in adults and thus an early diagnosis is extremely important.
Objective: The aim of the study was to analyze the group of pediatric patients with nodular thyroid diseases.
Methods: The authors processed the documentation of 66 pediatric patients with nodular thyroid disease who have been surgically treated at the Clinic of Otorhinolaryngology and Head and Neck Surgery, JFM CU and MFH in Martin during 2003–2007.
Results: Family history was positive in 32 patients (48.5 %). Twenty-three patients (35 %) had hyperfunction thyroid disease. Euthyroid status was found in 43 patients (65 %). Ultrasonography examination was performed in all patients. Percutaneous aspiration biopsy was performed in 38 patients (58 %) and peroperative histology in 40 patients (61 %). Technecium (Tc)99m-scintigraphy was performed in 4 patients (6 %). CT and MRI examination of the neck and upper mediastinum was indicated in one child. All patients were surgically treated with classical approach after achieving euthyroid stage. Total thyroidectomy was performed in 24 patients, hemithyroidectomy in 41 patients and isthmectomy was done in one patient. No severe postoperative complications were present.
Conclusion: Thyroid diseases are the second most frequent endocrinopathy in children and adolescents with girls being more frequently affected. It is multidisciplinary problem requiring cooperation of specialists in different fields of medicine. In patients with thyroid diseases not responding to conservative treatment or with clinical signs of mechanical syndrom surgery is a causal therapy *(Tab. 3, Ref. 20).* Full Text (Free, PDF) *www.bmj.sk.*
Key words: thyroid gland, goiter, child, adolescent, malignant, thyroidectomy.

Thyroid nodules are relatively rare in children and adolescents and have a prevalence between 0.2 %–1.8 % (1), whereas in adults it is around 4–7 % (2). In very young children incidence rates are practically negligible (3). In contrast to prevalence, thyroid nodules are more often malignant in childhood than in adulthood. In children 26 % of thyroid nodules are malignant, while in adults the corresponding value is 5–10 % (2). Risk factors for developing thyroid nodules in children are female sex, postpubertal age, previous or co-existing thyroid disease, previous irradiation of the neck and a family history of thyroid disease (4). In cases of conservative treatment failure, progressive goiter enlargement, mechanical syndrome, unclear cytology and malignant thyroid tumor surgical treatment is indicated.

The aim of the study was to analyze the group of the hospitalized and surgically treated pediatric patients at the Clinic of Otorhinolaryngology and Head and Neck Surgery, Jessenius Faculty of Medicine, Comenius University (JFM CU) and Martin Faculty Hospital (MFH) in Martin during 2003–2007 with nodular thyroid disease, to evaluate the possibilities for diagnosis, indications for surgery and postoperative complications.

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Methods

Sixty-six pediatric patients (10 males, 56 females) with thyroid gland diseases who underwent surgery between 2003–2007 at the Clinic of Otorhinolaryngology and Head and Neck Surgery, JFM CU and MFH in Martin were retrospectively analyzed. Cooperation with National Institute of Endocrinology in Lubochna and ambulatory endocrinologists yielded in selection of this group of patients. The data on patient's history, diagnostic procedures, treatment and complications were acquired from medical records. Data on age and calcemia are shown as mean± standard deviation.

Results

General description of the patient group

Average age of boys was 14± 3 and of girls 15± 3 years. Youngest boy and girl were 4 and 7 years old. Family history was positive in 32 patients (48.5 %). Twenty-three patients (35 %) had hyperfunction thyroid disease related to diffuse autoimmune thyrotoxic goiter – morbus Graves-Basedow (21 patients) or thyroid

Tab. 1. Clinical signs in patients with euthyroid disease (n=43).

Symptom	n	%
Palpable resistance	43	100
Growth progression	14	33
Mechanical syndrom	7	16
Pain	2	4.7

Tab. 2. Clinical signs in patients with hyperthyroid disease (n=23).

Symptom	n	%
Exophtalmus	14	60
Cephalea	3	13
Heat intolerance, sweating	10	43.5
Palpitations	3	13
Tremor	6	26
Diarrhoe	2	8.7
Weight loss	6	26
Nervousness	2	8.7
Tiredness	5	22
Increased appetite	1	4.3
Tachycardia	5	22
Insomnia	1	4.3
Hair loss	4	17
Mechanical syndrome	1	4.3

adenoma (2 patients). Euthyroid status was found in 43 patients (65 %) with diagnosis of polynodosal struma (2 patients), left sided nodosal struma (22 patients), right sided nodosal struma (17 patients), struma isthmica (1 patient) or papillary cancer (1 patient). Clinical signs of both eu- and hyperthyroid diseases are shown in Tables 1 and 2.

Preoperative examination

The extent of the preoperative investigations was determined by endocrinologist. Ultrasonography examination was performed in all patients. Percutaneous aspiration biopsy was performed in 38 patients (58 %) and peroperative histology in 40 patients (61 %). Technecium (Tc)99m-scintigraphy was performed in 4 patients (6 %). CT and MRI examination of the neck and upper mediastinum was indicated in 1 child.

Surgical treatment

All patients were surgically treated with classical approach after achieving euthyroid stage (Tab. 3). Total thyroidectomy was performed in 21 patients for Graves-Basedow disease, in 2 patients for polynodosal bilateral struma and in one patient for papillary thyroid cancer. Hemithyroidectomy was done in 17 patients for right sided nodosal struma and in 24 patients for left sided nodosal struma. Isthmectomy was done in one patient for struma isthmica.

Postoperative course and complications

Paresis of reccurent laryngeal nerve was not seen in any patient. Antiedematous treatment was indicated in two patients because of tight preparation in the area of reccurent laryngeal nerve. Lowest plasma value of ionized calcium was 0.57 mmol/l with mean value of 1.04±0.02 mmol/l. Lowest plasma value of total calcium was 1.58 mmol/l with mean value of 2.23±0.06 mmol/l. Nine patients (13.6 %) with clinical signs of hypocalcemia (paresthesia) were treated with oral or intravenous calcium preparations. Average value of blood drainage by Redon drain was 30 ml. The drain was removed on the 1st postoperative day. In one patient revision was required due to blood loss of 300 ml.

Tab. 3. Type of surgical intervention (n=66).

Surgery	n	%
Total thyroidectomy	24	36.5
Hemithyroidectomy	41	62
Isthmectomy	1	1.5

Conservative treatment

From 43 patients with normal thyroid function, 34 (79 %) were left untreated and 9 patients (21 %) were treated with Euthyrox. From 23 patients with hyperthyroid disease, 16 (70 %) received Lugol, B6 and Carbimazol/Propycil, 4 (17 %) were treated with Lugol, B6, Carbimazol/Propycil and Trimepranol, 2 patients (8.7 %) received B6, Carbimazol/Propycil and Trimepranol and one patient (4.3 %) only B6 and Propycil.

Discussion

Many thyroid diseases present clinically as thyroid nodules. The data from two large studies (collecting cases of pediatric thyroid nodules over several decades) are showing sex distribution of 128 children as 81 % girls and 19 % boys. The mean age was 13 years (range 1–18 years) and the vast majority of patients were euthyroid (1, 5). Similar age and sex distribution was in our group of 66 pediatric patients with 84.8 % of girls and 15.2 % of boys.

Prevalence

Thyroid nodules are relatively rare in children and adolescents and have a prevalence between 0.2–1.8 % (1). The real prevalence of thyroid nodules remains unknown because in most cases they are asymptomatic and detected incidentally by parents or physicians. Thyroid nodules are more often malignant in children than in adults. Among 15–19-year-old patients, it is becoming the eight most commonly diagnosed cancer (7.5 % of all cancers) and the second most common cancer among girls in this age group (13.4 % of all female cancers) (6). Additionally, recurrence rates tend to be higher in children (7). In our group of patients only one girl (1.5 %) had diagnosis of papillary carcinoma at 14 years of age.

In high-risks groups that include children exposed to ionizing radiation or those treated with radiation for head, neck or mediastinal conditions the incidence of thyroid cancer can be much higher (7). For example, in children younger than 15 years

who were exposed to radiation from the Chernobyl accident in April 1986, the relative incidence of thyroid cancer has increased from 0.1–0.3/100 000 before the accident to 3.3–13.5/100 000 in 1990–1996 (8). Children and adolescents are much more sensitive to the effects of ionizing irradiation than adults. One explanation of this phenomenon is that thyrocytes have a very low division rate at adult age compared to younger age groups. Radiation-induced mutations are thus less likely to be transmitted to later generations of cells in higher age groups in view of the early expiration of the potency of thyrocytes to divide (9). Faggiano et al (10) revealed that small, metabolically active follicles predominate in children <12 years of age, a finding indicating that iodide transport mechanisms are more active in the thyroids of younger individuals.

Thyroid carcinoma in pediatric patients differs from that in adults with respect to its presentation and outcome. In children, it tends to present at a more advanced stage than in adults, with a higher frequency of lymph node and pulmonary metastases (11). Tumor size was larger and infiltration of thyroid capsule and node metastases were higher in patients <18 years when compared with other age groups (12). In pediatric population, papillary carcinoma is more aggressive disease. Because pediatric cancers have a better prognosis than their adult counterparts, this does not influence patient outcome. Age can be considered the most important factor in determining prognosis (12).

Interesting is the question of relationship between juvenile autoimmune thyroiditis (JAT; morbus Graves-Basedow), cancer and thyroid nodules that was studied in a large case series of pediatric patients. The data show that thyroid nodular disease is present in 31.5 % of pediatric patients with JAT and that cancer occurs among these in at least 9.6 % of cases, with papillary carcinoma being the most common histology type. Multinodularity is more frequent than uninodularity in patients with cancer (13).

Diagnosis

The diagnostic procedure of thyroid nodules in children and adolescents is similar to that in adults. In childhood the traditional diagnostic approach to thyroid nodules consists of clinical, laboratory, and imaging evaluations. Risk factors for malignancy of thyroid nodules are a fast growth, positive family history, neck irradiation in past, hoarseness, a very firm nodule, fixation of the nodule, and cervical lymphadenopathy. Although thyroid cancer in children usually has very indolent course, even with pulmonary metastases, early diagnosis is important to identify as soon as possible patients who need to undergo surgery.

In the evaluation and management of nodular thyroid disease ultrasonography (USG) and fine needle aspiration biopsy (FNAB) are most important. Thyroid USG is the imaging method of choice for the evaluation of thyroid gland structure, and FNAB, as the most accurate test for nodule diagnosis. It has reduced the need for scanning and for thyroidectomy, thereby reducing the health-care costs significantly.

In all patients of our group USG examination was done. The ultrasonographic criteria used to identify and characterize suspicious nodules in children are controversial and not well defined (14). It is generally accepted that USG examination can be successfully used for screening and early detection of thyroid nodules in children. In nodules with maximal diameter of 15 mm and smaller, a USG examination can be useful in helping to determine which nodules can be aspirated rather than which should be followed up. Nodules larger than 15 mm are not reliably differentiated with the USG criteria examined and may require cytologic or histologic examination for definite classification (14). The most reliable criteria for thyroid cancer diagnosis in children were irregular outline, subcapsular nodule location, and type III vascularization at power Doppler ultrasonography.

FNAB is basic in the evaluation of solitary thyroid nodules, cysts, and dominant nodules within multinodular goiters, at least in adults (15). If the procedure is performed properly, it should have very low false negative and false positive rates, with accuracy ranging between 69 % and 93 % (16). On the contrary, for children few data are available. Some consider this procedure of limited usefulness in children because of its discomfort and the high rate of side-effects such as papillary endothelial hyperplasia, hemorrhage, vascular proliferation, vascular thrombosis, fibrosis, cystic change, infarction, and abscess (17). Preferably those less than 10 years of age should undergo excisional biopsy under general anesthesia instead of FNAB (18).

The important question is whether FNAB is the most useful procedure to detect malignancy, whether surgical treatment is needed, and whether this approach compares favourably with conventional clinical, laboratory, and imaging studies. The accuracy of FNAB supports its diagnostic usefulness in the management of patients with thyroid nodules and in differentiation between benign and malignant lesions (13). Normalization of TSH is mandatory prior to FNAB, because if it is elevated, it promotes goiter development and could be responsible for morphological changes in epithelial follicular cells.

Taken together, fine needle aspiration biopsy when performed properly is a safe technique even in childhood and adolescence, offering the best sensitivity, specificity and accuracy in detecting malignancy compared with conventional approaches. It is recommended as the first diagnostic test in euthyroid pediatric patients with thyroid nodules (17).

Another diagnostic approach is scintigraphy (thyroid scan). In our study Technecium (Tc)99m-scintigraphy was performed in 4 patients (6 %). Thyroid scintiscanning has long been considered the first examination on a thyroid nodule. However, in recent years it has been less frequently used in the initial routine evaluation because most benign and malignant nodules show reduced concentrations of radioisotope, whereas hyperfunctional nodules are occasionaly malignant (19). Thyroid scintiscanning is useless in detecting malignancy and should be performed only in thyrotoxic patients with thyroid nodules (19).

Therapy

The primary treatment of thyroid nodules should be surgical (18). Thyroidectomy (total or hemithyroidectomy) is the most effective treatment modality. The possible postoperative complications are disscused elsewhere (20). Among treatment op-

tions for solitary benign thyroid nodules surgery is also used for definite histologic diagnosis or nodule ablation. Conservative thyroxine treatment has some benefit, but its efficacy remains low. It may only slow growth of the nodules. Observation is related to psychological burden and cost of longterm follow-up. Laser therapy is still at experimental level (4).

Conclusion

Thyroid gland diseases are the second most frequent endocrinopathies in children and adolescents with girls being more frequently affected. It is a multidisciplinary problem requiring cooperation of specialists in different fields of medicine. In our opinion, according to other authors, in patients with thyroid gland diseases not responding to conservative treatment or in clinical signs of mechanical syndrome the surgery is a causal therapy.

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