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Thyroid carcinoma surgery in children and adolescents – 15 years experience surgery of pediatric thyroid carcinoma

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ABSTRACT

Objectives: The purpose of this study is to evaluate the characteristics of thyroid gland surgery focusing on malignancies at the pediatric age with the main concern on treatment results and complications in extensive primary treatment.
Methods: The records of all patients 18 years and younger with surgically treated thyroid diseases in the Prague Hospital, Motol, between 1991 and 2006 were retrospectively reviewed.
Results: Thyroid surgery was performed on 148 pediatric patients (including 56 carcinomas). The youngest patient involved in the study was seven years old, the oldest patient 18 years old (mean 13.7 years). Most frequent histological cancer type was PTC (42 cases, 75%). Follicular cancer was diagnosed in five cases (8.9%) and medullar cancer in nine cases (16.1%). A prophylactic thyroidectomy was performed in three cases (5.4%) without clinical signs of thyroid tumor with diagnosed RET gene mutation.
Conclusions: We consider total thyroidectomy with subsequent radioiodine ablation and TSH suppression as the basic approach in the treatment protocol of pediatric WDTC. The observed 100% recurrence-free and overall survival together with a low incidence of postoperative complications strongly supports the idea of a total thyroidectomy with selective neck dissection in the treatment of metastases of WDTC and MTC.

1. Introduction

Thyroid diseases affect all age groups, not excluding children and adolescents, including the possibility of malignant tumors. Iodine deficiency, genetic predisposition (RET mutations) and some developmental disorders which represent important factors in their development [1–3]. Ionizing radiation represents a proven risk factor for thyroid malignancies as confirmed by the sharp increase in thyroid cancer after the Chernobyl disaster [4,5]. Many authors have described the role of cytokines and genes (e.g. VEGF, TGF and EGF) during tumor development [6,7].

Thyroid cancer is rare at a pediatric age, accounting for less than 5% of all thyroid cancer [8]. However thyroid cancer accounts for approximately 10% of pediatric malignancies and 35% of pediatric carcinomas [9]. The estimated rate for childhood thyroid cancer ranges between 0.3 and 2.0 per million depending on the region and the patient's gender [3]. Papillary thyroid carcinoma is the most common histological type (60–97%), observed in childhood patients with both sporadic and radiation-induced thyroid cancer. Follicular thyroid carcinoma is diagnosed in 3–33% of childhood thyroid cancers. Medullary thyroid carcinoma occurs in about 2% with a higher proportion of inherited forms of the disease among children [5]. All children with MEN 2B should be studied shortly after birth, and those with MEN 2A should be studied by one year of age with early therapeutic intervention [10].

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Some features of childhood well-differentiated thyroid cancer (WDTC) represent a rationale for the treatment strategies which differs from adults. The majority of diagnosed tumors show a larger volume which can lead to an earlier involvement of the capsule [11]. Furthermore, it should be considered that thyroid glands are much smaller in children thus staging the tumor as microcarcinoma should be limited to very small cancers. Multicentricity of WDTC seems to be more frequent among pediatric patients [12]. Pediatric WDTC also differs from adult forms in the higher incidence of cervical lymph node metastases, extrathyroid extent, and distant metastases. Lymph node metastases are found in up to 90% of the cases. According to the published data, distant metastases can be detected in up to 15%, almost always in the lungs [13]. Non-pulmonary distant metastases are rare. Pulmonary metastases are overwhelmingly milliary, difficult to diagnose radiographically, and almost always functional. WDTC among children shows a generally higher recurrence rate of 7–40% in the largest published series [9]. Despite the more advanced stage and trend for recurrences, overall survival is assumed to be greater in children than in adults. According to the review by Jarzab, not more than 35 cause-specific deaths occurred among some 2000 reported children and young adults [9].

Because of this strange combination of a relatively good prognosis with an aggressive presentation, there is not just one choice of treatment. Surgery is the principal method for the treatment of thyroid malignancies. Surgery may range from lobectomy to total thyroidectomy. According to the recent guidelines of the national and international societies, total thyroidectomy is the preferred option in cancers > pT1a of WDTC and medullary thyroid cancer (MTC) [14,15]. Modified neck dissection is advocated in the case of confirmed metastases to the lateral lymph node compartment. The main disadvantage of an extensive surgical approach (total or near total thyroidectomy) is the higher incidence of persistent postoperative hypoparathyreosis and the recurrent laryngeal nerve injury [16,17]. In most European centers thyroid remnant radioiodine ablation is routinely performed in the vast majority of WDTC pediatric patients [9]. However, radioiodine is given to complete, not to replace, total thyroidectomy as success rates are significantly lower in patients who have less extensive thyroid surgery. Proponents of the non-extensive approach highlight the progression-free survival not significantly different from the extensive approach with a lower prevalence of surgical complications [18]. A conservative primary treatment strategy is based on stage-oriented, risk-based algorithms which are widely accepted in adult WDTC [18]. Implementing these algorithms lacks definition as high risk pediatric WDTC patients. However, the above mentioned characteristics of pediatric WDTC, would put most of these children into the high-risk group.

The purpose of this study is to evaluate the characteristics of thyroid gland malignancies at a pediatric age with the main concern on treatment results and complications in the extensive primary treatment (e.g. total thyroidectomy with or without neck dissection and radioiodine ablation for WDTC, and external radiotherapy for MTC).

2. Patients and methods

The records of all patients, 18 years and younger, with surgically treated thyroid diseases in the Prague Hospital Motol between 1991 and 2006 were retrospectively reviewed. Data were collected on presenting symptoms, patient characteristics, ultrasound, fine needle aspiration cytology, tumor histology, clinical and pathological staging and type of surgery, complications of surgery, adjuvant treatment, recurrences, and outcome.

Thyroglobulin blood serum level was observed in children after surgery treatment. The thyroglobulin level was used as well by WDTC children, to help in the decision before radioiodine application and diagnostic scintigraphy. The pulmonary function test by lung metastases by children was done depending on the X-ray results. The function test had physiological results for each of them.

Statistical analysis was carried out with the Student's t test. The Cox regression analyses were used to analyze the differences between the studied groups and literature data. p-Value of ≤ 0.05 was considered as statistically significant.

3. Results

Thyroid surgery was performed on 148 pediatric patients. The youngest patient involved in the study was seven years old, the oldest patient 18 years old (mean 13.7 years). In 92 (62.2%) cases (12 males and 79 females) surgery was performed for benign thyroid diseases: Graves–Basedow's disease and toxic goiter in 40 patients, toxic adenoma in five children, nodular goiter in 16 patients, for solitary thyroid node in 27 children, in Hashimoto's thyroiditis in three girls, and for mechanic syndrome with diffuse goiter in one girl. 52 primary and four revision surgeries for malignant thyroid tumors were performed in 56 patients (37.8%; 14 males and 42 females). The most frequent histological type was papillary cancer in 42 cases (75%). Follicular cancer was diagnosed in five cases (8.9%) and medullar cancer in nine cases (16.1%). The prophylactic thyroidectomy was performed in three cases (5.4%) without clinical signs of thyroid tumor with diagnosed RET gene mutation (MEN 2A or MEN 2B syndrome respectively).

During thyroid surgery, identification and preparation of the recurrent laryngeal nerve was performed with the help of either surgical microscope or enlarging surgical glasses. Neuromonitoring of recurrent nerves was used intraoperatively during the few last years. We used neuromonitoring for reoperation procedures and by difficult anatomical situation (27 tumor cases and four Graves–Basedow goiters). Parathyroid glands were identified and left in the wound and checked for vitality. In the case of deprivation of its vascular supply, parathyroid auto-transplantation was performed in a few fragments into the sternocleidomastoid muscle. The neck dissections were performed at the standard extent (II–V and VI) in case of proven lymph node metastases. The T-, N- and M-stage data are presented only for the persons who underwent primary surgery in accordance with the TNM-classification of UICC 2002.

The first sign of malignant disease among previously untreated patients was the thyroid mass in 28 cases (53.9%) or lymph node enlargement in 24 cases (46.1%). However, with the ultrasonography thyroid, mass was observed in 42 cases (80.8%). FNB was performed in 32 cases which a cytologically confirmed diagnosis of thyroid malignancy in 29 cases (PTC in 25 cases, FTC in three cases and MTC in one case). The cytology was reclassified by the Bethseda system (3 patients were Bethseda III, 23 PTC and 2 FTC patient were Bethseda IV, 2 PTC and 1 FTC were Bethseda V, 1 MTC was Bethseda VI). Basal immunoreactive calcitonin level was increased in all nine patients with MTC.

Among the four patients who underwent revision surgery after the primary surgery was performed elsewhere, the tumor relapse was determined by tumor markers (an increase of thyroglobulin, calcitonin), by radioisotope diagnostics and verified by ultrasound. There were three lymph node recurrences of PTC. Two of these patients have undergone previously total thyroidectomy and one patient hemithyroidectomy. There was one recurrence of MTC in the bed of the thyroid after a declared total thyroidectomy and adjuvant radiotherapy.