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The Clinical Characteristics and Outcomes of Children and Adolescents with Thyroid Carcinoma: A Single Center Experience

Tiroid Karsinomlu Çocuk ve Adölesan Hastalarda Klinik Özelikler ve Prognoz: Tek Merkez Deneyimi

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ABSTRACT

Objective: Thyroid carcinomas are rare in childhood and adolescence. This study was conducted to evaluate the clinical features and outcomes in children and adolescents with thyroid carcinoma at our center.

Material and Methods: Twelve children and adolescents treated for thyroid carcinoma in our departments from 2004 to 2014 were included in the study.

Results: Papillary carcinoma was found in 9 patients and follicular carcinoma in 3 patients. Neck swelling was the most common chief complaint. At the time of surgery, one patient (8%) had cervical lymph node metastasis, and one (8%) had angioinvasion. No patients had lung metastasis. Total thyroidectomy was performed in 4 patients, ipsilateral total and contralateral subtotal thyroidectomy in 5 patients, partial thyroidectomy in 2 patients and thyroglossal duct cyst excision in one patient. Eight patients (66%) required ^{131}I ablation for residual or metastatic disease after thyroidectomy. At the time of this report, all patients were alive without recurrence.

Conclusion: According to our data, children and adolescents with thyroid carcinoma have a good prognosis and benefit from total or near-total thyroidectomy followed by radioiodine therapy. Future prospective studies are required to clarify the short- and long-term side effects of treatment approaches.

Key Words: Adolescents, Children, Follicular carcinoma, Papillary carcinoma, Pediatric thyroid carcinoma

ÖZET

Amaç: Tiroid kanserleri çocuk ve adölesanlarda nadirdir. Çalışmada kliniğimizde takip ettiğmiz çocuk ve adölesan tiriod kanserlerinin klinik özelliklerini ve prognozunu değerlendirmeyi amaçladık.

Gereç ve Yöntemler: 2004-2014 arası kliniğimizde izlenmekte olan 12 tiroid kanserli hasta çalışmaya dahil edildi.

Bulgular: Papillar karsinom 9, folliküler karsinom 3 hastada saptandı. Boyun şişliği en sık başvuru nedeniydi. Bir hastada (%8) servikal lenf nodu metastazı, 1 hastada (%8) anjioinvazyon belirlendi. Akciğer metastazı saptanmadı. Total tiroidektomi 4 hastada, ipsilateral total ve kontralateral subtotal tiroidektomi 5 hastada, parsiyel tiroidektomi 2 hastada, tiroglossal kanal eksizyonu 1 hastada uygulanmıştı. I^{131} ablasyonu 8 hastada (%66) rezidüel veya metastatik hastalık nedeniyle uygulanmıştı. Hastalar hâlâ remisyonda izlenmekte ve rekürrens görülmemiştir.

Sonuç: Tiroid kanserlerinin çocuk ve adölesanlarda prognozu iyi olup total ve near total tiroidektomi ve takiben radyoaktif tedaviden fayda görmektedirler. Bu tedavi yaklaşımlarının kısa ve uzun dönem yan etkilerinin belirlenmesi için prospektif çalışmalara ihtiyaç vardır.

Anahtar Sözcükler: Adölesan, Çocuk, Folliküler karsinom, Papiller karsinom, Pediatrik tiroid karsinom

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INTRODUCTION

Thyroid cancer is a rare pathology in children and adolescents and is responsible for 1.5–3.0% of all carcinomas in this age group in the USA and Europe. The incidence increases rapidly between 15 and 29 years of age and reaches a plateau by the fifth to sixth decades (1,2). Thyroid carcinomas can be classified according to the cell of origin. Tumors derived from the thyroid follicle are well-differentiated thyroid carcinomas and include papillary thyroid carcinomas and follicular thyroid carcinomas. The subtypes of papillary thyroid carcinomas include a follicular variant, tall cell variant, diffuse sclerosing type, and columnar type; follicular thyroid carcinomas include Hurthle cell, clear cell, and insular carcinoma. Medullar and anaplastic thyroid carcinomas are seen very rarely in children. The current treatment recommendation is total thyroidectomy followed by radioiodine therapy, based on a good response and high disease-free survival rate for this age group. However, many authors question the aggressiveness of this treatment given the long lifespan of these patients and long-term complications of high doses of radioiodine (1,2). It has been reported in several studies that children with differentiated thyroid carcinoma present with more advanced disease at diagnosis but they have a more favorable outcome compared with adults. Also, male gender, advanced tumor stage (T3, T4a), and clinical lymphadenopathy were found to be a risk factors for disease-free survival in Stage I pediatric patients with thyroid carcinoma (3,4). In the present study, we aimed to evaluate the clinicopathologic features at presentation and the outcomes of pediatric and adolescent patients with thyroid carcinoma.

MATERIAL and METHOD

The twelve children and adolescents (9 girls and 3 boys, aged 6.5 to 18.0 years; median: 14 years) treated for thyroid carcinoma at our departments between 2004 and 2014 were included in the study. The medical data regarding gender, age at the time of surgery, clinico-pathologic characteristics, TNM stage, type of surgery, internal irradiation by ^{131}I, recurrence and survival rate were recorded. The clinico-pathologic characteristics included chief complaint at diagnosis, tumor size, multifocality, bilaterality, family history, thyroiditis and lymph node involvement. Surgery consisted of total thyroidectomy and less than total thyroidectomy (unilateral thyroid lobectomy, ipsilateral total and contralateral partial thyroidectomy or ipsilateral total and contralateral subtotal thyroidectomy). Total thyroidectomy was performed in patients with tumours greater than 4 cm in diameter, or tumours of any size in association with any of the following characteristics: multifocal disease, bilateral disease, extra-thyroidal spread, familial disease, and those with clinically or radiologically involved nodes and/or distant metastases. RAI for ablation was performed in patients with multifocal tumor, tumor focus >1 cm, local (lymphovascular) invasion, or residual thyroid gland >2 g and lymph node metastasis within 6 weeks after surgery. Dose of radioactive iodine for children was calculated based on the patient's body weight (0.5-1.5 mCi/kg). All patients received thyroid-stimulating hormone suppression treatment with levothyroxine except one patient where the tumor was derived from a thyroglossal duct cyst. All patients were evaluated by regular follow-up every 3 or 6 months by neck ultrasonography and serum thyroglobulin levels.

RESULTS

Papillary carcinoma was found in 9 (75%) patients and follicular carcinoma in 3 (25%) patients. Medullary thyroid carcinoma or anaplastic thyroid carcinoma were not found in our series. Neck swelling was the most common chief complaint. Five patients (42%) had neck swelling, 3 (25%) patients had nodular goiter, 2 (17%) patients had congenital hypothyroidism and a solid nodule, 1 (8%) patient had palpitation-chest pain and 1(8%) patient submental lymphadenopathy that was operated for thyroglossal duct cyst and diagnosed as papillary thyroid carcinoma. Four patients (33%) had a family history of thyroid disease. One of the patients with papillary thyroid carcinoma had a previous history of exposure to ionizing radiation to the cranium and spine because of acute leukemia (24/15 Gy). Pathologic characteristics of patients with thyroid carcinoma are presented in Table I. At the time of surgery, one patient (8%) had cervical lymph node metastasis, and one patient (8%) had angioinvasion. No patients had lung metastasis. All patients were defined as TNM stage I. As a preoperative diagnostic modality, fine needle aspiration biopsy (FNAB) cytology was performed for all patients. Ultrasonography and computed tomography were also performed before surgery to evaluate local disease and the presence or absence of lung metastasis. In patients with thyroid cancer, total thyroidectomy was performed in 4 (34%) patients, ipsilateral total and contralateral subtotal thyroidectomy in 5 (42%) patients, partial thyroidectomy in 2 (16%) patients and thyroglossal duct excision in one patient (8%). Internal irradiation with ^{131}I was administered to 8 of 12 patients (66%). After a median follow-up period of 28 months (range 4-117 months), all patients were alive and disease-free. No recurrence was observed.

DISCUSSION

Thyroid carcinoma in children is a rare type of malignancy and displays different tumor characteristics compared with adult thyroid cancers. According to the literature, pediatric thyroid cancer is aggressive, has a higher prevalence of lymph node metastasis and pulmonary metastasis at the time of initial diagnosis, and occurs more frequently after surgery. In general, papillary thyroid carcinomas represent about 80% and follicular thyroid carcinoma accounts for 20% of differentiated thyroid

Table I: Pathologic characteristics of patients with thyroid carcinoma.

Characteristics	No(%)
Max. tumor size (mm)	range: 10-45 mm (median: 18 mm)
Microcarcinoma	3/12(25)
Bilaterality	2/12(16.6)
Multifocality	3/12(25)
Thyroiditis	3/12(25)
TNM stage I	12/12(100)
Metastasis	2/12(16.6)
Distant metastasis	NA

NA: *not available.*

carcinomas (1-5). In the present study, papillary carcinoma and follicular carcinoma made up 75% and 25%, respectively.

In the latest records of the SEER cohort (Surveillance, Epidemiology and End Results), a greater incidence in girls (0.89 cases/100,000 for girls versus 0.2 cases/100,000 for boys) was found in a group of 1753 patients aged less than 20 years (6). The incidence of thyroid carcinoma in girls was also observed to be higher than in boys in the present study.

The most common presenting complaint in children is a painless or tender thyroid mass with or without painless cervical lymphadenopathy (1). In our series, neck swelling was the most striking finding. Thyroid cancer can arise if TSH is consistently increased as a result of inappropriate L-thyroxine treatment in children with congenital hypothyroidism due to dyshormogenesis or iodide organification defect. Therefore, it is recommended that a more aggressive approach for thyroid nodules is used in children with congenital hypothyroidism. If the thyroid nodule is more than 1 cm in diameter or if its size is observed to increase, fine-needle aspiration biopsy is recommended for thyroid nodules found in children and adolescents. Also, malignancy should be suspected if there is a nodule that accompanies cervical lymph node enlargement clinically or on ultrasonography (7). Two patients in our study group had congenital hypothyroidism with thyroid nodules. One had been diagnosed as a papillary thyroid carcinoma, follicular solid variant, and the other as a follicular thyroid carcinoma.

The most common sites of metastases of thyroid carcinoma are the neck and the lungs. Zimmerman et al. (4) compared 58 children and 981 adults and found that childhood papillary thyroid carcinoma was more often metastatic to lymph nodes and lungs at presentation, and more often recurrent in neck lymph nodes postoperatively. Thompson et al. (8) reviewed 21 worldwide studies of thyroid carcinoma and reported on nearly 1800 patients. They found that regional nodal metastases were found in 27% to 100%, local invasion in 6% to 71% and distant metastases in 6% to 28% (8). In the present study,one patient (8%) had cervical lymph node metastasis, and one patient (8%) had angioinvasion at the time of surgery. This result may be explained with good management and evaluation of patients with thyroid nodules at our center. Also, it emphasizes the importance of the multidisciplinary follow-up for early diagnosis.

Thyroglossal duct cysts are the most common congenital abnormality of thyroid development. Seventy percent of thyroglossal duct cysts are diagnosed during childhood and 7% are diagnosed in adulthood. Less than 1% of these cases are malignant with most being papillary in nature. It is often diagnosed incidentally after surgical excision (9). The patient with thyroid papillary carcinoma arising from the thyroglossal duct in our series was diagnosed incidentally after surgical excision.

The effects of ionizing radiation on the thyroid has remained of great interest to the scientific community. Therefore, the examination of the thyroid gland at regular intervals during the follow-up period of cancer survivors who have received radiation therapy to the head and neck region has been recommended by authors (10). One patient had a secondary papillary thyroid carcinoma with a history of previous radiation exposure to the cranium and spine 4 years ago during leukemia treatment in present study.

In the previous study, the recurrence rate of differentiated thyroid carcinoma was reported as 26%, with a median of 16 months after the diagnosis. This result was similar to the previous studies that have been reported so far (3). In contrast, none of patients presented with recurrence during the follow-up period, with a median of 28 months in the present study.

Regardless of the biology of papillary and follicular tumors, the therapeutic approach is very similar for both subtypes of tumors. As in adults, the treatment of differentiated thyroid carcinoma is based on the combination of three therapeutic modalities: surgery, hormone replacement with levothyroxine, and radioiodine treatment[2]. Although there is some controversy, three surgical approaches have been advocated among experts. These are thyroid lobectomy or hemithyroidectomy (total removal of one lobe and the isthmus), near-total thyroidectomy (total lobectomy and subtotal resection on the contralateral side to leave 1 g of thyroid tissue), and total thyroidectomy. Some investigators consider the best therapeutic approach to be nonextended surgery (thyroid lobectomy or hemithyroidectomy), while others claim that the safest and most effective primary treatment in children is total thyroidectomy. Multivariate analysis in large retrospective studies, both in children and adults, have reported higher recurrence and mortality rates in patients who have undergone procedures less than total thyroidectomy (11). Jarzab et al. (12) performed a retrospective analysis on 109 patients and found that total thyroidectomy resulted in 97% disease-free survival at 10 years, whereas non radical operation was associated with 59 % and 85 % risk of relapse at 5 and 10 years, retrospectively. Welch Dinauer et al. (13) found that patients with stage I papillary thyroid carcinoma treated with

lobectomy were more likely to have recurrence with subtotal or total thyroidectomy. There are some advantage of the total/near total thyroidectomy: First, these types of resections will facilitate radioiodine treatment and imaging; second, serum thyroglobulin can be used as a tumor marker for recurrent or residual disease (1). Total or near total thyroidectomy was the most frequent surgery type in our patients.

In conclusion, our data indicate that children and adolescents with thyroid carcinoma have a good prognosis and benefit from total or near-total thyroidectomy followed by radioiodine therapy. The future prospective studies are required to clarify the short- and long-term side effects of these treatment approaches.

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