**Thyroid carcinoma in children and adolescents - review of six cases**

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**Abstract**

**Objective:** childhood thyroid carcinoma is a rare entity whose management is controversial. The objective of the present study was to evaluate the characteristics of these patients in terms of diagnosis and evolution.

**Patient and methods:** the evolution of six patients with thyroid cancer, followed at a Pediatric Endocrinology Unit during the past 17 years, was retrospectively reviewed.

**Results:** six female patients with age ranging from 4.5 to 12 years were studied. In all 6 cases, thyroid nodules were present on the initial evaluation. Ultrasonography and 131I scintigraphy showed solid and cold nodules in four patients. Histologic findings indicated four papillary and two follicular carcinomas. All patients were submitted to total thyroidectomy; four were subsequently submitted to radiodine therapy due to the presence metastases and/or residual thyroid tissue.

**Conclusion:** our findings support the notion that children and adolescents with thyroid carcinoma have a positive prognosis; no cases of death occurred after 17 years of follow-up. Our data are in agreement with the literature, which describes low mortality rates for these cases.


**Introduction**

Thyroid carcinoma is a rare entity in the first two decades of life. It is estimated that 10% of total cases of thyroid carcinoma occur within this age range.1 In the general population, the incidence rate of thyroid carcinoma is of 1 new case per million per year.2 Its peak incidence is over people aged 10 to 20 years,3 constituting 0.5 to 3% of all childhood and adolescence malignancies. Childhood thyroid carcinoma has a female predominance, for a ratio of 2.2.5:1.1,4 In areas with increased risk factors, such as in the republic of Belarus, which was affected by the Chernobyl nuclear-plant accident, the incidence of thyroid cancer can increase up to 80-100 cases per million per year.2

The most common histologic form of this cancer is the papillary thyroid cancer; the follicular variant of the carcinoma, in turn, is less common, whereas the medullary and anaplastic variants are very rare. The etiology of thyroid cancer is unknown, but there are specific risk factors that increase incidence of this cancer, including exposure to radiation, iodine deficiency, Hashimoto’s thyroiditis, situations associated with long-term increase in serum levels of thyroid-stimulating-hormone (TSH),3 and genetic factors that can occur due to spontaneous mutation or direct inheritance, such as in medullary thyroid carcinoma. Different studies have demonstrated concomitant thyroiditis in 50% of cases of thyroid carcinomas.3

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The influence of, and exposure to radiation has been widely studied for the last five decades, and it was initially suggested by Duffy and Fitzgerald in 1950. External irradiation due to exposure to atomic bomb explosion and irradiation therapy of the head and neck in children are associated with development of thyroid neoplasia in 10 or more years after the exposure. It is understood that iodine 131 (131I) irradiation used in the treatment of serious diseases is not carcinogenic for the thyroid of adults; this understanding, however, cannot be extended to children and adolescents due to the limited amount of experiences with these two groups.

Between 1951 and 1970 there was a great increase in the prevalence of papillary and follicular carcinoma in children and adolescents, which probably occurred due to the introduction, in 1940, of irradiation of head and neck for the treatment of benign disorders such as increase in thymus size, adenotonsillar hyperplasia, and cervical lymphadenopathy. The objective of our study is to evaluate cases of thyroid carcinoma that are being followed-up at our services while discussing diagnostic and therapeutic characteristics and the degree of malignancy and its resulting life risk.

Patients and methods
A retrospective study of the last 17 years was carried out including 354 patients with thyroid disease and being followed-up at the Pediatric Endocrinology Unit of the Instituto da Criança (IC) at the Hospital de Clínicas Teaching Hospital at Faculdade de Medicina da Universidade de São Paulo (HC-FMUSP). Out of the 354 patients, there were 6 cases of thyroid cancer, all of which were female patients and aged 4.5 to 12 years. The assessment of these cases was carried out using clinical and laboratory data of thyroid hormone (T3, T4, and free-T4), of TSH, of thyroglobulin, of anti-thyroid peroxidase (anti-TPO) antibodies, and anti-thyroglobulin (anti-TG) antibodies; the literature, however, indicates that the prevalence of circulating thyroid autoantibodies was increased nearly 3-fold in patients with thyroid cancer compared with the general population (40% vs. 14%, respectively). The examination for serum thyroglobulin is useful in the follow-up of these patients and it can alert doctors to a possible recurrence of the disease. In our study, thyroglobulin was increased in 2 of the 4 patients who presented metastasis to the lungs, all diagnosed by whole-body scintigraphy and/or dosage of thyroglobulin. All patients were submitted to a therapeutic dosage of radioactive iodine.

Results
Out of the 354 patients being followed-up for thyroidopathy at the Pediatric Endocrinology Unit at the HC-FMUSP during the last 17 years, 6 patients presented thyroid carcinoma, corresponding to 1.7% of the total and 2.7% of the cases of goiter (n=217).

All 6 patients with thyroid carcinoma were female patients, aged 4.5 to 12 years. These patients had sought our services due to presence of thyroid nodule. The family history of irradiation of head and neck was negative in all cases. Our services did not report presence of regional lymphadenomegaly, adherence to adjacent tissue, or hoarse voice that could suggest thyroid neoplasia. As to the thyroid function, 5 patients were euthyroid and 1 hypothyroid and negative for anti-TPO and anti-TG antibodies. Thyroglobulin was measured in 2 patients during preoperative procedures; results indicated thyroglobulin levels above the reference values in one of the patients. During postoperative procedures, thyroglobulin levels were high in 2 patients. One patient presented positive for the perchlorate test. Preoperative ultrasonography and scintigraphy procedures were carried out in 4 patients and all showed solid and cold nodules. Two patients were submitted to FNAB for cytological diagnosis and the other 4 patients were submitted to excision biopsy. Cytological and/or histologic findings were diagnostic in 4 patients who had papillary carcinoma and 2 who had follicular carcinoma, without concomitant thyroiditis. All patients were submitted to total thyroidectomy. Whole-body scintigraphy was carried out in all patients during postoperative procedures and indicated uptake in 4 patients. Four patients presented residual thyroid tissue, out of which 1 patient also presented metastasis to the lungs, all diagnosed by whole-body scintigraphy and/or dosage of thyroglobulin. All patients were submitted to a therapeutic dosage of radioactive iodine.

Discussion
All patients sought medical due to presence of asymptomatic thyroid mass. In this sense, the literature indicates that carcinoma of the thyroid most commonly presents as an asymptomatic thyroid mass (60 to 80% of cases). Despite the importance of previous history of exposure to environmental or therapeutic radiation, none of the patients had reported exposure to radiation.

Five patients were clinically euthyroid at presentation and one presented with hypothyroidism due to disorder of hormone synthesis and, consequently with high TSH levels, a risk factor for thyroid carcinoma, as mentioned above. All patients presented negative for anti-TPO and anti-TG antibodies; the literature, however, indicates that the prevalence of circulating thyroid autoantibodies was increased nearly 3-fold in patients with thyroid cancer compared with the general population (40% vs. 14%, respectively). The examination for serum thyroglobulin is useful in the follow-up of these patients and it can alert doctors to a possible recurrence of the disease. In our study, thyroglobulin was increased in 2 of the 4 patients who presented metastasis and/or residual thyroid tissue.

Four patients were submitted to preoperative ultrasonography and scintigraphy, which indicated solid and cold nodule in all cases. The literature describes presence of malignancy in 17 to 36% of these cases. Less so than found in the adult population, there is an increased frequency of carcinoma in children and adolescents who present with...
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References


thyroid nodules; thus excision biopsy should be the choice method over FNAB. Recent studies have demonstrated, however, that experienced doctors should find FNAB useful in the management of pediatric thyroid nodules.\(^7\) Out of the 6 patients, 2 were submitted to FNAB of the nodule with cytological report indicating anatomopathological, postoperative finding of papillary carcinoma. The other 4 patients were submitted to excision biopsy. Histologic findings indicated a total of 4 papillary carcinomas and 2 follicular carcinomas; a prevalence of papillary carcinoma is also described in other studies.\(^1\)-\(^4\),\(^7\),\(^9\)

Total thyroidectomy is the choice procedure for malignant tumors of the thyroid despite its high rate of recurrent lesion to the laryngeal nerve and of hypoparathyroidism, the latter being described in 7 to 27% of cases.\(^8\) It is described that some doctors advocate the excision of the affected lobe, and of adjacent isthmus and lymphonodus for patients with papillary carcinoma and without tumoral invasion, metastases, or history of exposure to radiation during the first 3 decades of life. The advantages indicated for this procedure are low mortality for papillary carcinoma described at 40 years of diagnosis and the suppression of tumors exhibited by the suppressant effect on TSH of thyroxin therapy.\(^2\) Those who advocate the use of total thyroidectomy point out the high incidence of multifocal disease in 40% of cases.\(^5\) In this sense, others have described a better progression-free survival rate in older patients;\(^9\) and relapses occurring in 60% of cases of patients younger than 7 years versus in 27% of cases of patients older than 7 years.\(^8\) All 6 patients included in our population were submitted to total thyroidectomy without any postoperative complication. Following the surgical procedure, patients were submitted to reposision of hormones with thyroxin in order to maintain TSH levels between 0.05 and 0.1 mcU/ml. Higher incidences of relapse have been observed in patients who were not submitted to therapy for suppression of TSH.\(^8\)

During the postoperative period (up to 3 months), the serum levels of thyroglobulin were measured as a marker for tumors, and whole-body scintigraphy exams were carried out with findings of residual thyroid tissue in 4 patients. Out of these 4 patients, 1 patient also presented metastasis to the lungs, which is described in 10 to 20% of cases of childhood thyroid cancer.\(^1\) No patients presented regional lymphatic metastasis despite findings in the literature of an incidence of 80 to 90% of the cases.\(^1,3\) Though follicular carcinoma is biologically more aggressive than papillary carcinoma, the 2 cases of patients with follicular carcinoma did not present metastasis with one of these patients having 16.2 years of follow-up procedures.

All 4 cases of patients with residual thyroid tissue and metastasis were treated with therapeutic dosage of 131I with ablation of the residual tissue. One patient presented persistent lung uptake, but has remained stable with an appropriate dosage of thyroxin for suppression of TSH. The 2 patients who did not present residual thyroid tissue or metastasis were not submitted to treatment with 131I; this procedure, though controversial, has been described elsewhere.\(^12\)

Other authors have found evidence of pulmonary fibrosis and moderate to serious pulmonary restriction in 4 out of 10 patients following pulmonary function test after therapeutic dosage of radioiodine.\(^3\) Our patient with metastasis to the lung did not present symptoms that suggested pulmonary fibrosis.

Our patients were followed-up for 17 years and we verified a positive prognosis for thyroid carcinoma and no deaths; these results are in agreement with findings of low mortality rate for thyroid carcinoma in the literature.\(^1\)-\(^4\),\(^8\)-\(^11\) All patients have remained with a controlled clinical status; 5 patients have not presented active signs of the disease and one has presented stable lung metastasis.


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