Pediatrik Cerrahi Dergisi 3: 151-154, 1989

An experience with peripubertal thyroid carcinomas

Hüseyin DİNDAR, N. GÖKÇORA, İ. Haluk GÖKÇORA, M. ÇAKMAK, Meral BARLAS, Selçuk YÜCESAN

Departments of Paediatric Surgery, Ankara University Hospital & Nuclear Medicine, Gazi University Hospital, Ankara, Turkey

Summary

A retrospective analysis of 3158 patients with a thyroid mass revealed five children with thyriod carcinomas (TC). Their ages at the time of diagnosis, ranged between 10-15 yrs. Cytological evidence of lymph node metastases was found in four patients employing the fine needle aspiration technique. Two patients underwent total thyroidectomies, combined with modified radical neck dissection. Another had a subtotal thyroidectomy with modified radical neck dissection, and another boy with right cervical lymph node metastasis received bilateral subtotal thyroidectomy and right cervical lymph node excision. A patient who had no cervical lymph node involvement was treated with left total and right subtotal thyroidectomy without cervical lymph node excision. Postoperative treatment consisted of only TSH supression. Two patients had recurrences of cervical lymph nodes and were further treated by a secondary lymph node dissection. Neither vocal cord palsy nor hypoparathyroidism were encountered. A cervical haematoma was the only operative morbidity. At present all of the five children are alive with a mean period of 5.6 years follow-up.

Key words: Peripubertal thyroid carcinomas

Introduction

The unfamiliarity and lack of awareness of doctors of thyroid cancers (TC) in childhood and their early and extensive spread contribute to the advanced stage at which most of these neoplams are diagnosed and treated [8,20]. TC vary in their biological behavior depending on the histology of the lesion, the stage of the disease, the age and sex of the patient [3]. The most important prognostic factor in a patient with a thyroid neoplasm is its histology. Well-differentiated TC in children, which constitute about 80 % of all thyroid neoplasms, usually have the best prognosis. Age also seems to be an important factor in the prognosis, playing a more important role than either the extent or stage of disease. TC on the whole, have a higher survival rate and a better prognosis in children than adults [3].

Patients and Methods

Out of a total of 3158 patients with thyroid masses admitted to Ankara University Hospital, a computerized analysis was carried out of the 118 children, admitted to the Dept. of Paed. Surg., between 1980-89. The following parameters were recorded: Age, sex, presenting symptoms, clinical findings, results of radiological, ultrasound and radionuclide imaging, cyto and histopathological diagnoses, routine and endocrine laboratory investiagations, treatment modalities and the course of the disease.

Address: I. Haluk Gökçora MD. Şairler Sok. 6, Çankaya -ANKARA

Results

This retrospective analysis revealed that only 118 children were operated on for masses in their thyroid gland or cervical lymph nodes. Histopathological diagnoses revealed 80 nodular goiters, 12 diffuse goiters, 9 cystic nodular goiters, 1 hydatid disease, 11 follicular adenomas, and 5 TC (Table 1).

Three boys and two girls had TC. Their ages, at the time of diagnosis, ranged from 10 to 15 years (mean: 11.8 yrs). The presenting symptom in three was a slow but steadily growing cervical nodule. Palpable cervical lymphadenopathies were detected at the initial examination in all except one. Cytological evidence of lymph node metastases was found in technique. Scintigraphic evaluation revealed cold solitary nodule in two children and normoactive nodules in three (Fig 1).

One patient had postoperative wound haemorrhage and a large cervical hematoma causing respiratory embarrassment. This required neck exploration, haemostasis and temporary tracheotomy. Histopathological examination of the surgical speciment revealed papillary and follicular types of TC (Table 2).

TSH supression with T3 and T4 was routinely employed postoperatively. Two patients had recurrences of cercival lymph nodes; appearing at one and twenty months after the initial excision. Vocal cord palsy and hypoparathyrodism were not

Table I. Total number of thyroid masses encountered in children over an eight year period

Diagnoses	Number		Total
	M	F	
Nodular goiter	10	70	70
Diffuse goiter	2	10	10
Cystic nodular goiter	2	7	7
Hydatid disease	1	-	-
Follicular adenoma	3	8	8
Thyroid Carcinoma	3	2	2
Total	21	99	118

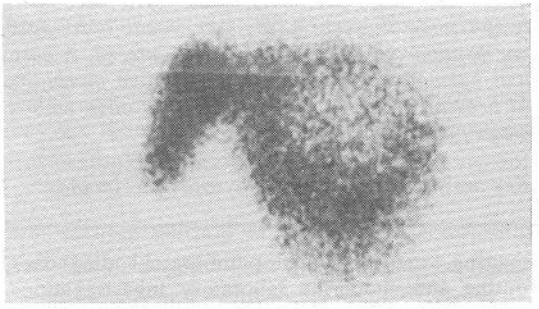

Fig 1. Radionuclide imaging showing a cold nodule in the left thyroid lobe.

encountered. The follow-up period ranged from 2 to 8 years (mean: 5.2 yrs). At present all five patients are alive and well with no evidence of local recurrence or distant metastases (Table 3).

Discussion

TC develop in a fair percentage of patients who have had radiotherapy to the head, neck or mediastinum, and/or have been exposed to carcinogens [11]. Several common drugs such as reserpine, methyldopa, phenothiazines, amphetamine, tricyclic antidepressants, alcohol and antihistamines cause the anterior pituitary to secrete prolactin, TSH and MSH, which in turn cause increased mitotic activity at the target site, hence an increased susceptibility to the development of a malignancy of the thyroid [11]. Iodine depletion in endemic goiter regions results in an increased TSH which may predispose to TC.

In the presented series, none of the patients had previously received irradiation but all came from the endemic goiter areas [9,14]. The reported incidence of carcinoma in nodular goiters found in children and adolescents in higher than that of adults and ranges from 20 % to 83 %. All solitary nodules of the thyroid gland in children and adolescents should be considered as malignant until proven otherwise [20]. The reported sex incidence ration in children is varied, but it is about 2 females to 1 male [3,19,20]. In the presented series however, the set ratio was 3 males to 2 females. This can be explained by the insufficient number of patients. Well-differentiated TC occur more often and poorly-differentiated ones are extemely rare in childhood [3]. Papillary TC are predominant in non-endemic areas. Girls tend to suffer more from follicular TC; this being more so in the younger patients [3]. Conversely, the incidence of papillary TC are higher in boys [20]. The mean incidences are 72, 21 and 3 % for papillary, follicular and medullary TC respectively. The incidence of anaplastic TC in children is fortunately very low, being about 4 % [2,6,7]. In the present series, papillary TC was 60 % and follicular TC was 40 %. This difference can be explained by the low number of patients involved, yet may be due to different aetiological factors.

TC tends to be more extensive in children; these tumours frequently involve the entire gland more extensively and metastasize early to lymph nodes

Table II. Five children with thyroid carcinomas seen over an 8 year period

Mean AGE: 11.8 yrs, M/F: 3/2, LEFT/RIGHT: 3/2, follicular/papillary: 2/3, LMND:left modified radical neck dissection, BMND: bilateral modified radical neck dissection, LTT: Left total thyroidectomy, RSTT: Right subtotal thyroidectomy, BSTT: Bilateral subtotal thyroidectomy, TT: Total thyroidectomy

Age	Sex	Primary Location	Metastasis	Histopathology of the carcinoma	Surgical intervention
10	M	Left	Lymph node (p)	Papillary	LTT+RSTT
15	M	Left	----------	Follicular	LTT+RSTT
12	M	Left	Lymph node (F)	Follicular	TT+LMNDTT+BMND
10	F	Right	Lymph node (P)	Papillary	BSTT+LMND
12	F	Right	Lymph node (F)	Papillary	

Table III. Follow-up & results of thyroid carcinomas
CLAP: cervical lymphadenopathy, L: left, R: right, B: bilateral NG: noduler goiter, MNG: multinoduler goiter

Case	Sex	Age	Presenting Sympton	Cervical Recurrences	Follow-Up Periods (MEAN: 5.6 Years)
SA	M	10	Lclap NG	-	9
SC	M	15	NG	-	8
AB	M	12	Lclap NG	-	5
EBA	F	10	BCLAD MNG	+	3
BY	F	12	lclap MNG	BCLAP + RCLAP	3

and to the lungs. Distant metastases to bone and brain are rare [20]. Metastatic involvement of the cervical lymph nodes remain as the most common presenting symptom of TC in children. The incidence of cervical lymphadenopathy found at the initial physical examination varies from 58 % to 78 % [2,7,8,10,20]. In the presented series, the incidence of cervical lymphadenopathy at the initial physical examination was 60 %, requiring the alertness of the physicians concerned.

In as many as 89 % of the cases multifoci and metastases are present by the time the carcinoma is clinically detectable [4,7,8,11,14,18]. The true incidence however, can never be quoted, since not all surgeons perform total thyroidectomies for a seemingly unilateral carcinoma, and since whole organ subserial studies are not done on a raotine bases. Local spread is reported to be found in 22 % to 31 % of children with TC, and pulmonary metastases are reported to be present at initial examination in 19 to 22 % of patients [8,14]. Radioiodine uptake and scintigraphic studies have shown that a nodule showing decreased function is four times more likely to contain a maligannt tumour. TC are present in 58 % of "cold" nodules, and only 4.7 % to 6.6 % of "hot", "warm", and "cool" nodules [11,15].

The present philosophy of treating TC during childhood is based on the special characteristics of these neoplasms, i.e., a tendency for multicentric foci, well-differentiated patterns, and excellent response to TSH suppresion and radioactive sodium iodide [14]. If carcinoma is suspected in a solitary nodule or a nodular gland, total lobectomy and isthmectomy followed immediately by frozen-section should be done avoiding incisional biopsy and possible seeding or spread of a carcinoma at the time of operation. If carcinoma is not suspected, local excision of a nodule may be done. Should sections in either of these two situations show TC, the following treatment modalites are referred: The ultra-conservative approach employs no further surgical intervention. If surgery is required, it may take the following forms. Unilateral lobectomy and isthmectomy [3,14], lobectomy and subtotal lobectomy on the contralateral side [3,8,10,14,20], total thyroidectomy without cervical lymphatic dissection (when there are no palpable nodes) [3,8,10,14] or with modified radical or conventional radical neck dissection (when there is lymphadenopathy) [3,8,10,14,20]. When malignancy of the contralateral lobe was ruled out, we referred total lobectomy and isthmectomy with subtotal thyroidectomy of the contralateral lobe. Otherwise, total thyroidectomy was performed. When cervical lymph node involvement was present, a modified neck dissection was added, sparing the sternocleidomastoid muscle. The principal criticism of total thyroidectomy is the high incidence of permanent hypoparathyroidism, a complication seen in 1.1-50 % of the patients [2,4,7,11,13]. The incidence of recurrent laryngeal nerve has been reported to the from 0-16 % [3,8,10,11,14]. Other immediate postoperative problems include paroxismal atrial tachycardia and fibrillation, subcutaneous emphysema of the neck, pneumothorax, parotitis, temporary brachial plexus injury, haemorrhage and wound infection. Later problems include metastases to the brain, lungs, mediastinum and neck. In the presented series, there were only a wound haemotama leading to respiratory embarrassment, and to recurrences in cervical lymph nodes (40 %). The incidence of reurrence is recorded as 6-10 % [3,8]. Hypoparathyroidism and vocal cord pahys were not seen in the presented patients. TSH suppresion: TC during infancy and childhood is relatively more TSH dependent that than that in the adult. Therefore TSH can contribute to a better chance of survival. This form of treatment is most effective in well differentiated (papillary) lesions, and least effective in the undifferentiated

lesions [3,5,20]. In the presented series, suppresion of TSH was preferred as an adjuvant to surgical treatment.

Radioiodine Therapy: Radioiodine ablation not used in the presented series. It has side effects such as, depression of bone-marrow function, gonadal damage, radiation sickness, pulmonary fibrosis, myelogenous leukemia, and a possibility of inducing tumour cell metaplasia [2,5,8,10,13,14].

The effectiveness of radioiodine therapy is also limited by the rapid turnover and excretion of iodine, the lack of uniform uptake in all parts of the thyroid and the difficulty in determining the optimum lethal dose for cancer cells [11]. 75 % of follicular and 25 % of papillary TC will trap iodine. This uptake can be increased by propylthiouracil or TSH [2,7,8,11,13,14].

Irradiation: External irradiation (5000-6000 rads) and radium needles implanted interstitially have been used to treat inoperable TC and its distant metastases [11,13]. Chemotherapy for metastatic TC has been disappointing. Adriamycin is the only proven active agent and results are often temporary [13].

Conclusions

Despite a better prognosis, cytological and histopathological typing characteristics of paediatric TC, excisional surgery still seems to be the treatment of choice. This approach is mainly based on the significantly high incidence of malignancy in peripubertal children with thyroid nodules, on the increased tendency of TC to be much more extensive in the paediatric age group, and in view of the inability to make a definitive diagnosis by clinical and laboratory examinations or medical imaging procedures. Differentiated TC in children can mostly be controlled by surgery, radioactive iodine, and hormonal suppressive treatment. A close follow-up is mandatory, with serial estimations of TSH, T3 and T4 and, if possible, thyroglobulin in the blood serum to monitor the appearance of metastases.

The excellent prognosis and life expectancy associated with well-differentiated TC in children is conditioned by the adoption of an agressive, but not mutilating surgical treatment, excising local and cervical recurrences while complementing by hormonal therapy.

References

1. Alrich EM: Carcinoma of thyroid. Am J Surg 109:736, 1965.
2. Bell RM: Thyroid carcinoma. Surg Clin North Am 66:13, 1986.
3. Buckwalter JA, Thomas CG, Freeman JB: Is childhood thyroid cancer a lethal disease? Ann Surg 181:632, 1975.
4. Clarkk Rl, White EC, Russel WO: Total thyroidectomy for dissemination. Ann Surg 149:858, 1959.
5. Crile G Jr, Antunez AR, Esselstyn CB Jr, et al: The advantages of subtotal thyroidectomy and suppression of TSH in primary treatment of papillary carcinoma of the thyroid. Cancer 55:2691, 1985.
6. Eckstein HB, Tatman N: Carcinoma of the thyroid gland in childhood. Report of a case. Turk J Pediatrics. 2:100, 1960.
7. Exeelby P, Frazell E: Carcinoma of the thyroid in children. Surg Clin North Am 49:249, 1969.
8. Harness JK, Thompson NW, Nishiyama RH: Childhood thyroid carcinoma. Arch Surg 102:278, 1971.
9. Hatemi H, Urgancıoğlu İ, Seyahi V: İç hastalıkları kürsüsü endokrinoloji materyalinin bioistatistik incelenmesi. İstanbul Üniv. Cerrahpaşa Nükleer Tıp Enst. İstanbul 1981.
10. Hayles AB, Jhonson ML, Bearhs OH: Carcinoma of the thyroid in children. Am J Surg 106:735, 1963.
11. Hoffman E: Carcinoma of the thyroid: Review of 304 cases. South Med J 80:741, 1987.
12. Lacher AB, Stucker FY, Hirokawa RH: Management of thyroid nodulhe. Otolaryngol Clin North Am 13:59, 1980.
13. Leeper RD: Thyroid cancer. Med Clin North Am 5:1079, 1985.
14. Liechty RD, Safaie-Shirazi S, Soper RT: Carcinoma of the thyroid in children. Surg Gynecol Obstet 134:595, 1972.
15. Meadows PM: Scintillation scanining in management of the clinically single thyroid nodule. JAMA 177:229, 1961.
16. Öcal B, Berki R, Abal G: Goiter in pediatric age group. J Ankara Medical School 5:199, 1983.
17. Sisson GA, Feldman DE: The management of thyroid carcinoma metastatic to the neck and mediastinum. Otolaryngol Clin North Am 13:119, 1980.
18. Tawes RL, DeLorimier AA: Thyroid carcinoma during youth. J Pediatr Surg 3:210, 1968.
19. Thompson N: Thyroid and parathyroid in Pediatric Surgery Welch KJ, Randolph JG, Ravitch MM, O'Neill JA Jr, and Rowe MI (Ed), Year Book med Pub Inc, 2d ed, Chicago 1986 pp:522.
20. Zohar Y, Straus M, Laurian N: Adolescent versus adult thyroid carcinoma. Laryngoscope 96:555, 1986.