ORIGINAL ARTICLE

Completion Total Thyroidectomy in Children With Thyroid Cancer Secondary to the Chernobyl Accident

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Objective: To evaluate the usefulness of submitting children with thyroid cancer secondary to nuclear accidents to a completion total thyroidectomy.

Design: A case series consisting of patients living and operated on in Belarus whose parents had asked for a clinical evaluation in a western European center.

Setting: A tertiary care referral center.

Patients: The conditions of 47 children from Gomel, Belarus, with differentiated thyroid carcinoma following the nuclear accident at Chernobyl, Ukraine, were evaluated at the University of Pisa, Pisa, Italy. In approximately half of the cases, the treatment in Belarus consisted of a hemithyroidectomy. After a complete evaluation, the decision was made to reoperate on 19 of them by performing a completion total thyroidectomy. The preoperative evaluation revealed that 5 (26%) of the 19 patients who had undergone a hemithyroidectomy had unilateral recurrent nerve palsy and that 2 (10.5%) had hypoparathyroidism.

Interventions: Neck ultrasonography was used for the preoperative localization of thyroid residuals, thyroid nodules, suspicious lymph nodes, and a guided fine-needle aspiration biopsy specimen. The circulating thyroglobulin measurement was obtained before reoperation. An iodine 131 whole-body scan (WBS) was performed and circulating thyroglobulin levels were obtained after completion of the thyroidectomy during withdrawal of levothyroxine sodium therapy.

Main Outcome Measure: The number of patients with a recurrence of thyroid cancer and lung or lymph node metastases after the completion total thyroidectomy.

Results: The results of the histologic examination were positive for papillary thyroid cancer in 6 (28.6%) of 21 patients, 3 with residual cancer in the remaing thyroid lobe and 3 with metastatic lymph node disease. A posttherapy WBS demonstrated lung metastases in 5 (28%) of 18 patients and lymph node metastases in 6 (33%) of 18 patients; the results of a posttherapy WBS were negative for metastases in 7 (39%) of 18 patients. Hypoparathyroidism developed in 4 (21%) of 19 patients who underwent a completion total thyroidectomy; unilateral laringeal nerve palsy developed in 1 (5.2%) of these 19 patients. Among 22 children who previously underwent total thyroidectomy in Belarus, a diagnostic WBS showed lung metastases in 10 (45%) of the children and lymph node metastases alone in 3 (14%) of the children; the results of a diagnostic WBS were negative for metastases in 9 (41%) of the children. Statistical analysis showed a nonsignificant ($P>.05$) difference in the prevalence of lung and lymph node metastases in patients who previously underwent total thyroidectomy compared with patients who underwent completion total thyroidectomy.

Conclusion: Completion total thyroidectomy allowed for the diagnosis and treatment of recurrent thyroid cancer and lung or lymph node metastases in 61% (11/18) of the patients in whom residual differentiated thyroid carcinoma was not previously recognized.

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THE EXTENT of the initial surgical operation in children with differentiated thyroid carcinoma (DTC) has been a matter of controversy in the past because some authors described an increased incidence of major complications when performing total thyroidectomies compared with hemithyroidectomies.[1-4] Furthermore, because of a generally favorable outcome, a notable decrease in thyroid cancer mortality has been difficult to conclusively prove with procedures more extensive than lobectomy. However, more recent reports have advocated that "the most conservative treatment for childhood thyroid carcinoma is total thyroidectomy,"[5] which can be performed without notable morbidity by experienced thyroid surgeons. Although surgeons may disagree about the ideal primary procedure for clinically ap-

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PATIENTS AND METHODS

CLINICAL EVALUATION

The conditions of 20 boys and 27 girls (ranging in age from 6-17 years) suffering from DTC were evaluated in our hospital at the University of Pisa, Pisa, Italy. These children were not selected by Belarussian physicians based on the stage of their disease; they were selected by humanitarian associations based on their parents' request for a new clinical evaluation to be performed in a western European center. All relevant clinical information, including histologic materials, dates of diagnosis, type of operation first performed, TNM stage, size of the nodule at diagnosis, the thyroid hormonal status, the results of neck ultrasonography, the results of a chest roentgenogram, and, in a few cases, the results of WBSs with ^{131}I, was reviewed. These children underwent further tests, including a clinical examination, a complete thyroid laboratory profile, the determination of thyroid autoantibodies, ultrasonography of the neck, a fine-needle aspiration biopsy of any suspicious mass or area, an ^{131}I WBS, chest roentgenograms, and direct laryngoscopy. Thyroglobulin levels were obtained in all patients, but they were considered not useful in determining therapy mainly for 2 reasons: (1) 4 patients had high levels of antithyroglobulin antibodies; and (2) in the other patients, there was not a notable relationship between the presence or absence of metastases or recurrent disease and the thyroglobulin levels.

SURGICAL FINDINGS

Twenty-one children underwent reoperation in our hospital after informed consent was obtained from their parents in Gomel. Nineteen children in this group had previously undergone a hemithyroidectomy as determined from the medical records from Belarus. An initial hemithyroidectomy was performed, although 8 patients had a T4, 6 patients had a T2, and 2 patients had a T1 N1 tumor (TNM stage); the 3 other children, whose TNM stage was not precisely known, were all operated on at least twice for lymph node metastases. Neck ultrasonography confirmed the presence of a residual lobe in these children and revealed enlarged lymph node metastases without detectable residual thyroid tissue in 2 other patients. The patient sample included 14 girls and 7 boys, who ranged in age from 8 to 16 years. All had a confirmed diagnosis of papillary thyroid carcinoma. Five of the 19 children who had undergone a hemithyroidectomy had previously undergone a second operation because of the presence of metastases to the lymph nodes. Thus, the decision was made to perform a completion total thyroidectomy because, as previously mentioned, 16 children had advanced disease according to TNM stage and the 3 remaining children had previously undergone reoperation for metastases to the lymph nodes. All children who had undergone only hemithyroidectomy underwent reoperation. Thus, the completion total thyroidectomy was performed as described in the literature in 19 patients, and regional lymph node dissection was performed only in 2 other patients.[10,11] The mean interval between the first operation and the completion total thyroidectomy was 38 months (SD, 17 months; range, 12-79 months).

OTHER MEDICAL TREATMENTS AND PROCEDURES

All patients remained free of thyroid hormone supplements following completion total thyroidectomy to obtain high levels of circulating thyrotropin (>50 μU/mL); they underwent radioiodine treatment and a diagnostic WBS using an ^{131}I dose based on body weight. This dose ranged from 1.11×10^9 Bq to 2.96×10^9 Bq and was administered from 4 to 6 weeks after the operation. A WBS was performed 4 days after the administration of ^{131}I; subsequently, it was repeated every 3 to 5 days until a maximum of 15 days after ^{131}I administration.[12]

Following ^{131}I therapy, all patients received thyroid hormone with the replacement dose adjusted with the aim of obtaining suppressed thyrotropin levels (<0.07 μU/mL). When there was evidence of hypocalcemia, patients were given oral calcium and 1,25-$(OH)_2$-cholecalciferol to restore the level of serum calcium to normal.

STATISTICAL ANALYSES

The results are expressed as the mean (±SD) in the range given. The χ^2 and contingency table analyses were used as indicated in the "Results" section.

parent unilateral DTC, most would agree about the necessity for total thyroidectomy in childhood when the disease is apparently secondary to radiation exposure. A problem arises when dealing with radiation-exposed children who have undergone a lobectomy only for DTC. Under these circumstances, reoperations are required for the removal of all remaining thyroid tissue. Some would argue that the increased morbidity of thyroid reoperations is too high to justify such a procedure.[6] For the most part, the existing data cited on childhood thyroid carcinoma in the literature are questionable because most series have been collected over a long period (usually >20 years), often with inconsistency in the surgical approach, the histopathological examination, radiodiagnostic procedures, and the adequacy of follow-up.[7]

After the nuclear accident at Chernobyl, Ukraine, in April 1986, the incidence of thyroid carcinoma in childhood increased sharply in Belarus, reaching 172 new cases between the years of 1986 and 1992.[8] Following the accident at Chernobyl, the highest incidence of DTCs in children there was reported in the province of Gomel, Belarus, where high doses of radiation fallout were registered. In this region, one case of thyroid cancer in children (aged >15 years at diagnosis) was observed during the period from 1981 to 1985 (rate=0.5, expressed as the annual average per million children in the Gomel region in the identified period) before the Chernobyl accident; 143 cases of thyroid cancer in children (rate=97.0) were observed during the period from 1991 to 1994 after the accident.[9]

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We had the opportunity to evaluate the conditions of 47 children suffering from DTC, all coming from Gomel, where the diagnosis of DTC was made following the nuclear accident.

These patients had all been operated on by several surgeons in the same center. In approximately half of the patients examined, the surgical treatment had consisted of a hemithyroidectomy. After a careful evaluation of the conditions of these patients, a decision was made to reoperate and perform a completion total thyroidectomy in 19 of these children. The operations were performed between September and October of 1994.

While the primary purpose of this assistance program was humanitarian, during a review of these cases, some of the information collected was deemed to be of scientific interest. In fact, because all of the patients came from a relatively small and compact area (Gomel), where the exposure to fallout was high and relatively uniform, the opportunity existed to study a homogeneous cohort of patients. Furthermore, clinical evaluations and the surgical and nuclear medical procedures were all performed in a short time and with standardized techniques, unlike all other studies in which data were collected for decades and various techniques were used.

The need for a completion total thyroidectomy is discussed, and the results of the surgical operations are presented. The follow-up results with whole-body scans (WBSs) (using iodine 131) of the patients operated on are compared with those of the other patients who previously underwent total thyroidectomy.

RESULTS

SURGICAL FINDINGS

Cervical exploration confirmed the presence of an entire lobe in 18 patients and of almost the entire thyroid gland in 1 patient. These findings were consistent with the preoperative echographic findings. The results of histopathological studies revealed DTC in 3 (15.8%) of the 19 excised lobes. In 2 of these patients, the diagnosis had been suspected based on ultrasonography, whereas in the third patient the lobe appeared normal at echography. In the only child who had positive fine-needle aspiration biopsy cytologic results for metastasis in a lymph node, a modified neck dissection was performed in addition to the completion total thyroidectomy. The results of histopathological studies confirmed the presence of metastases from DTC in 5 of 18 removed nodes. In all the children in whom the results of the fine-needle aspiration biopsy of enlarged lymph nodes were negative, node sampling was all the same done at the time of reoperation. None of the results proved positive on frozen section examination. Lymph nodes were removed from the cervical region in the 2 additional patients who underwent total thyroidectomies. A histologic examination confirmed the presence of metastases in both of them. Thus, the total number of patients with proven DTC at reoperation was 6 (28.6%) of 21.

In summary, 19 children in this group underwent a completion total thyroidectomy and 2 patients had regional lymph node resection because of enlarged lymph node metastases. The results of a histologic examination were positive for papillary thyroid cancer in 6 (28.6%) of the patients, 3 with residual cancer in the remaining thyroid lobe and 3 with metastatic lymph node disease.

Before the operation, 5 (26%) of 19 patients who had undergone a previous hemithyroidectomy were proved to have unilateral recurrent laryngeal nerve palsy by direct laryngoscopy; all of them had also undergone a lymphadenectomy. Furthermore, 2 (10.5%) of them surprisingly were hypoparathyroid despite a supposed unilateral procedure. After reoperation in our department, biochemical hypoparathyroidism developed in 3 (15.8%) of the patients who had undergone completion total thyroidectomy; unilateral laryngeal nerve palsy developed in 1 (5.3%) of these patients. Both complications were confirmed 6 months after surgery during a new clinical evaluation performed in our center so that hypoparathyroidism was defined as permanent. Two children of 21 had transient hypoparathyroidism.

RESULTS OF THE MEDICAL EVALUATION

Patients Previously Treated With Hemithyroidectomy

Patients operated on in Pisa underwent ^{131}I therapy 1 month after their completion total thyroidectomies. A posttherapy WBS in 18 of 19 patients whose conditions were evaluated showed the following results (**Table**):

1. In the 4 patients in whom histologic examination results were positive, a WBS showed lung metastases in 3 (75%) of the patients. In 2 of these patients, lymph node metastases were also demonstrated.
2. In the 15 patients in whom histologic examination results were negative, a WBS showed lung metastases in 2 (13.3%) and lymph node metastases in 6 (40.0%) of the patients. The condition of 1 of these patients was not evaluated by a WBS.

Patients Previously Treated With Total Thyroidectomy

Among 23 patients who previously underwent total thyroidectomy, 20 underwent diagnostic WBSs. Eight (40%) had lung metastases; these metastases were associated with cervical or mediastinal lymph node metastases in 5 of the patients. Lymph node metastases alone were detected in 3 (15%) of the patients. The 3 patients whose conditions were not evaluated by a WBS showed no evidence of radiologically detectable metastases. Two patients who underwent regional lymph node dissection in our hospital because of palpable nodes demonstrated lung metastases as well as other lymph node metastases on a subsequent WBS. One of these patients also had bone metastases.

STATISTICAL ANALYSES

Contingency table and χ^2 analyses showed a nonsignificant ($P>.05$) difference in the prevalence of lung and lymph node metastases in patients who previously un-

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Prevalence of Lung and Lymph Node Metastases, by a WBS, in Patients Treated With Completion Total Thyroidectomy or in Patients Who Previously Underwent Total Thyroidectomy*

Location of Metastases	Patients Treated With a Completion Total Thyroidectomy	Patients Who Previously Underwent Total Thyroidectomy
Lung	5†	10‡
Lymph node	6	3
No cancer	7	9
Total	**18** (1 not evaluated)	**22**

**All data are given as the number of metastases. WBS indicates whole-body scan.*
†Plus 2 lymph node metastases.
‡Plus 8 lymph node metastases.

derwent total thyroidectomy compared with patients who underwent completion total thyroidectomy.

COMMENT

Although no consensus exists about the idea l surgical treatment for DTC, there are undeniable advantages to the use of total thyroidectomy that are particularly pertinent in the management of children with this disease.[13] Among the arguments favoring total thyroidectomy, the most important is the ability to detect occult metastases with a WBS and to subsequently treat them effectively with therapeutic doses of radioactive iodine.[14-16] Furthermore, a total thyroidectomy eliminates any residual contralateral neoplasm and eliminates the subsequent possibility of remnant recurrence.[17] The ablation of all thyroid neoplasms also prevents the possible transformation of residual DTC to an undifferentiated or anaplastic thyroid carcinoma with the passage of time.[14] Another added advantage is the fact that thyroglobulin levels are more useful indicators of recurrent disease when all thyroid tissue has been entirely removed.[16] Finally, some recent studies suggest that there is an improved survival and decreased recurrence rate in patients who have undergone a total or an almost total thyroidectomy.[17,18] In one study of children, cervical recurrence in a large series of patients treated by a total thyroidectomy was significantly lower than that reported in a similar series in which a less radical procedure was performed.[5] The rationale for routinely performing total thyroidectomy in children previously exposed either to external radiation or to nuclear fallout is supported by the prevalence of multifocal disease and the high incidence of regional and distant metastases. The incidence of pulmonary metastases is from 5 to 10 times higher than in adults with DTC.

The detection of occult metastases by a WBS is only feasible after a total thyroidectomy has been done. The high incidence of lung metastases in children has previously been documented in several series.[19,20] However, most are first detected by an ^{131}I scintiscan after total thyroidectomy and not by either a chest roentgenogram or a computed tomographic scan.[19,21] In the absence of a WBS follow-up after operation, it is likely that the incidence of pulmonary metastases is grossly underestimated.[22] If pulmonary metastases progress to a stage at which they become apparent by standard x-ray film, it may be too late to treat them effectively, even with high doses of ^{131}I.[21] Our experience confirms the high incidence of lung metastases that were occult until a completion total thyroidectomy was performed. In 5 of 18 patients, chest x-ray films were negative for pulmonary metastases that only became apparent following a WBS after operation. These lung metastases would have been missed at a time when they could have been effectively treated with radioactive iodine. When lung metastases were considered with additional node and bone metastases detected by a WBS, we were able to diagnosis the recurrence or persistence of DTC in 61% (11/18) of the patients who underwent completion total thyroidectomy. The absence of any notable difference in the prevalence of lung and lymph node metastases between the group previously treated with total thyroidectomy and the group that underwent completion total thyroidectomy is noteworthy. It is apparent that the criteria used to estimate the clinical disease stage that led to a "less radical approach" were incapable of judging the extent of the disease. A total thyroidectomy should have been considered a more conservative approach rather than radical in the management of these children.[5] The incidence of residual disease found in the contralateral lobe after completion total thyroidectomy in patients with DTC has been reported to be as high as 40%.[23] In our series, the presence of papillary thyroid cancer within the thyroid was found in 3 cases and the presence of residual metastatic cervical lymph nodes was found in another case, resulting in an incidence of residual cervical disease in 4 (21%) of 19 patients who underwent completion total thyroidectomy. This figure is considerably lower than that reported by Levin et al,[23] who demonstrated that 64% of their patients who underwent completion total thyroidectomy had residual carcinoma. Unlike other studies that included patients who were selected during 3 or more decades, the observations reported in this study have been obtained during a short time in which standardized techniques were used for the operative procedures and the ^{131}I scintiscan. This is a distinctive feature of this report when compared with all others in the literature.[7] Because of the high incidence of unsuspected carcinoma in children with DTC who have undergone a unilateral lobectomy, almost all authors agree that it is important to remove the remaining thyroid lobe even though there is considerable concern about possible complications. Reoperative thyroid surgery has been associated with a high morbidity, according to some of the older series reported in the literature.[6] Some authors have even advocated ^{131}I ablation of an entire remaining thyroid lobe to achieve a similar result.[24] There are disadvantages to this method that make it a poor alternative. Complete thyroid ablation often requires the use of several large doses of radioactive iodine, and even then it may not be successful. This is more likely to be the case when a large thyroid remnant or an entire lobe is left. Another concern is that there may be sublethal injury to thyroid cancer cells from minimal uptake of ^{131}I, sufficient to impair subsequent uptake of ^{131}I and negating its therapeutic effectiveness.[25] One other recently recognized problem is the possibility of radiation injury to adjacent parathyroid glands, causing a long-term risk for the subsequent

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development of parathyroid neoplasm. Some authors have reported an increased risk of parathyroid, salivary gland, brain, and breast tumors after external radiation.[26] These concerns are even further increased in children previously submitted to radiation to the neck or radioactive fallout; restricting the use of ^{131}I specifically for the therapy of nonresectable DTC is recommended. Because of these concerns, surgical resection is preferred for ablating any notable amount of thyroid tissue. In experienced hands, a completion total thyroidectomy can be performed safely with little morbidity to the patient.[27-29] In our series, an injury to the recurrent laryngeal nerve did occur in one patient of 19, but the child was undergoing her fourth operation and reaction around the residual lobe was extensive. Our experience confirms that nerve complications should be infrequent even during repeated surgical procedures. In contrast, hypoparathyroidism occurred in 3 patients who underwent completion total thyroidectomy. This is disappointingly high, even when considering that these patients were all undergoing their second, third, or fourth operation. It must be assumed that at least 2 parathyroid glands were injured or excised at the time of the initial lobectomy. We were surprised to detect 2 patients with hypoparathyroidism prior to reoperation, even though they had only undergone hemithyroidectomies. This suggests that a bilateral surgical dissection had been performed during the first operation, despite the fact that only one lobe had been removed. When hemithyroidectomy has been chosen as treatment, any dissection of the contralateral lobe should be avoided. However, we would strongly recommend that children with thyroid nodules exposed to nuclear fallout undergo a total thyroidectomy when DTC is present. When that policy is widely accepted, there should be no need for a completion total thyroidectomy. In conclusion, in our series of children with DTC secondary to the Chernobyl accident, completion total thyroidectomy allowed for the diagnosis and treatment of residual DTC in 21% (4/19) of the patients and treatment of lung or lymph node metastases in 61% (11/18) of the patients in whom residual DTC was not previously recognized. Completion total thyroidectomy avoids the use of large doses of ^{131}I, which destroys normal thyroid tissue, and allows for the earlier and more effective use of ^{131}I specifically for persistent DTC that is not surgically resectable. Reoperations for completion total thyroidectomy are usually safe, providing that the contralateral lobe has not been extensively mobilized during the first procedure.

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