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 Measures: 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 remaining 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 laryngeal 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," which can be performed without notable morbidity by experienced thyroid surgeons. Although surgeons may disagree about the ideal primary procedure for clinically ap-
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 examination 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 WBs with 131I, 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 131I 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 other 3 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 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. 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 131I dose based on body weight. This dose ranged from 1.11×10⁷ Bq to 2.96×10⁷ Bq and was administered from 4 to 6 weeks after the operation. A WBs was performed 4 days after the administration of 131I; subsequently, it was repeated every 3 to 5 days until a maximum of 15 days after 131I administration. Following 131I 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 hypocalemia, 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 χ² and contingency table analyses were used as indicated in the “Results” section.

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. 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.
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 131I) 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 131I 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 WBS. 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 (13%) 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 $\chi^2$ analyses showed a nonsignificant ($P>.05$) difference in the prevalence of lung and lymph node metastases in patients who previously un-
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*

<table>
<thead>
<tr>
<th>Location of Metastases</th>
<th>Patients Treated With a Completion Total Thyroidectomy</th>
<th>Patients Who Previously Underwent Total Thyroidectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>5†</td>
<td>10‡</td>
</tr>
<tr>
<td>Lymph node</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>No cancer</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>18 (1 not evaluated)</td>
<td>22</td>
</tr>
</tbody>
</table>

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

COMMENT

Although no consensus exists about the idea of 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. 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. Furthermore, a total thyroidectomy eliminates any residual contralateral neoplasm and eliminates the subsequent possibility of remnant recurrence. 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. Another added advantage is the fact that thyroglobulin levels are more useful indicators of residual disease found in the contralateral 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 131I, sufficient to impair subsequent uptake of 131I and negating its therapeutic effectiveness. One other recently recognized problem is the possibility of radiation injury to adjacent parathyroid glands, causing a long-term risk for the subsequent
development of parathyroid neoplasm. Some authors have reported an increased risk of parathyroid, salivary gland, brain, and breast tumors after external radiation. These concerns are even further increased in children previously submitted to radiation to the neck or radioactive fallout; restricting the use of 131I 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. 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 thyroidectomy allowed for the diagnosis and treatment of residual thyroid tissue, and allows for the earlier and more effective 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 131I, which destroys normal thyroid tissue, and allows for the earlier and more effective use of 131I 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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REFERENCES

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