Surgical Treatment of Medullary Thyroid Carcinoma in a Thirteen-Year-Old Girl with MEN 2B

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Patients with palpable medullary thyroid carcinoma (MTC) have lymph node metastases in 90% of cases. In most series such patients continue to have elevated serum calcitonin (CT) levels after surgery indicating residual tumor tissue. We attempted a microdissection technique for the treatment of MTC. “Micro” refers not to a small incision or a limited exploration but to a more safe operation associated with good lighting and magnification and minimal bleeding. This technique was used in a 13-year-old girl with multiple endocrine neoplasia type 2B (MEN 2B). The prognosis for MTC in MEN 2B is worse than for sporadic MTC and the MTC of MEN 2A. Every possible effort should be made to remove all tumor tissue in MEN 2B patients with MTC. In this case the pathologist found bilateral MTC and metastases in eight of 129 lymph nodes removed. The preoperative stimulated CT levels, which were markedly elevated, decreased to near normal postoperatively. (Henry Ford Hosp Med J 1989;37:157-9)

The American Joint Committee on Cancer found the ten-year survival rate in patients with medullary thyroid carcinoma (MTC) to be only 49% (1). This finding suggested that the diagnosis and treatment of patients with MTC was far from optimal. The prognosis for patients with hereditary MTC has been considerably improved by the introduction of screening for hypercalcitoninemia in family members at risk for developing MTC (2-4). The only effective treatment in MTC is surgery. If the surgical technique can be improved, the prognosis of MTC should also be further improved.

Patients with palpable MTC have lymph node metastases in 90% of cases (4). In most series such patients continue to have elevated serum calcitonin (CT) levels after surgery indicating residual tumor. We have worked out a microdissection technique for the treatment of MTC (5). “Micro” does not indicate a small incision or a limited exploration but a safe operation provided by good lighting and magnification and minimal bleeding.† We performed this microdissection technique on a 13-year-old girl with MTC as part of the hereditary syndrome of multiple endocrine neoplasia type 2B (MEN 2B). The prognosis for MTC when it occurs as part of MEN 2B is worse than for both the sporadic and MEN 2A varieties (6).

Case History

The father of the patient had his first operation—a subtotal thyroidectomy and a limited node dissection—for palpable symptomatic bilateral MTC in 1971 when he was 31 years old. Postoperatively he received radiation treatment to the neck region in a dose of 10 Gy. In 1977 recurrent tumor was diagnosed, and he was referred to our surgical unit for further treatment. The thyroidectomy was completed and neck dissection performed. Postoperatively his CT levels remained elevated, and in 1987 liver metastases were diagnosed. He has ganglioneuromatosis of the eyelids and gastrointestinal tract and also a marfanoid habitus as evidence of MEN 2B (7). The liver metastases were treated by embolizations of the hepatic arteries, and at present his disease is stable. He is not married, and we did not discover that he had a daughter until 1987 when she was 13 years old.

The daughter was found to have ganglioneuromatosis of the eyelids, lips, and tongue indicating that she had inherited MEN 2B. She had palpable bilateral thyroid tumors and markedly elevated basal and provoked CT levels (Fig 1). Her urinary excretion of catecholamines was within normal limits on repeated testing, and her adrenal glands were of normal size and appearance on computed tomography.

The Operation

Good lighting was provided by the use of a headlamp, and good hemostasis was obtained by the use of bipolar and unipolar electrical cautery. An anatomical dissection was done without dividing the strap or the sternocleidomastoid muscles. The operative field included the central compartment from the hyoid bone down to the brachiocephalic veins and the lateral regions on both sides from the mastoid process downwards including the jugular chain, the cervical nerve plexus, and the su-
Fig 1—Serum calcitonin (CT) levels of the 13-year-old girl who had MTC as part of the MEN 2B syndrome. The provoked CT level is the highest value of the samples taken 2 and 5 minutes after intravenous injection of calcium gluconate solution (10%), 2 mg Ca\(^{2+}\)/kg body weight/60 sec, followed by an intravenous bolus injection of pentagastrin, 0.5 \(\mu\)g/kg body weight.

Results

The histopathologic examination demonstrated bilateral MTC and C-cell hyperplasia. The tumors in both lobes had diameters of about 1 cm. Of the 129 lymph nodes removed, eight contained metastatic tumor. Bilateral central and lateral neck metastases were noted. The PAP method demonstrated CT immunoreactivity both in the thyroid tumors and in the lymph node metastases.

The results of CT testing are shown in Fig 1. Preoperatively the CT levels were markedly high. Postoperatively the peak and basal CT levels were below the upper normal limit. However, the peak value was 40% higher than the basal value which is noteworthy in a patient who had had a total thyroidectomy.

Two years after the operation the CT levels were definitely elevated with a peak value 100% higher than the basal value. The serum value of carcinoembryonic antigen (CEA) was 34 \(\mu\)g/L preoperatively as compared to an upper reference limit of < 5 \(\mu\)g/L. After surgery the CEA level was normal and has remained normal during the two-year follow-up period. Despite the extensive surgery, a good cosmetic result was achieved.

Discussion

In our MTC series consisting of 101 operated patients, we have encountered only four patients with MEN 2B, two of whom have been reviewed here. The other two MEN 2B patients died from metastasizing MTC at ages 42 and 46 years. Neither of these deceased patients had children.

During the last 18 years, when MTC patients have been more systematically treated and diagnosed at our clinic, only one of our 44 patients having MTC as part of the MEN 2A syndrome has died from MTC. The relatives of that patient had thought that he should not be bothered by any screening examinations because he was mentally retarded. When his disease was diagnosed he could only take liquids and was emaciated. At surgery he was found to have MTC infiltrating and constricting the esophagus and trachea and thus only a palliative procedure could be performed. He died three years later as a result of progressive tumor growth.

During these 18 years, 15% of our sporadic MTC patients died from MTC (4). Our experience with the MEN 2B patients concurs with that of other reports indicating that the MEN 2B variety of MTC has the worst prognosis (6). In about 50% of cases the MEN 2B appears to be sporadic whereas in the remainder it is inherited as an autosomal dominant trait (9,10). Sporadic MEN 2B cases are diagnosed by their typical appearance, with a marfanoid habitus, an egg-shaped head, and thick nodular lips (Fig 2).

Camey et al (7) reported two hereditary MEN 2B cases, aged 2 and 5 years. Both had elevated CT levels. The older patient had MTC, and the younger patient had C-cell hyperplasia. Other reports also indicate a lower age at diagnosis in MEN 2B com-
pared to MEN 2A patients (6,9). The early onset of disease in MEN 2B patients is illustrated by the finding of metastasizing MTC in our 13-year-old patient. After surgery she has only minimally elevated provoked CT levels. She will require close follow-up, and if more substantial elevations of CT levels occur she can be offered repeated surgery with the hope of a biochemical cure (4,5). This case illustrates that good surgical results can be obtained even in cases with metastases and emphasizes that every effort should be made to trace all MEN 2B relatives and offer screening for MTC. In children such screening should start by age 5 years whenever possible.

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References