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Differentiated Thyroid Cancers in the Wake of the Chernobyl Nuclear Accident May Be Efficiently Treated with I-131 Even in Patients with Disseminated Pulmonary Metastases

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Reiners C, Biko J, Haenscheid H, Hebestreit H, Kirinjuk S, Baranowski O, Marlowe RJ, Demidchik E, Drozd V, Demidchik Y. Twenty-five years after Chernobyl: outcome of radioiodine treatment in children and adolescents with very high-risk radiation-induced differentiated thyroid carcinoma. J Clin Endocrinol Metab 2013;98:3039-48. Epub April 24, 2013.

SUMMARY

Background

Following the Chernobyl nuclear accident, the people living in the surrounding areas were exposed to high ^{131}I radiation and had no access to appropriate countermeasures. Children were at particularly high risk, since the milk they drank was contaminated (1). Among the population who was below 14 years of age in 1986, a total of 5127 cases of differentiated thyroid carcinomas (DTCs) were medically followed. DTC is a very rare pediatric tumor. In the United States, the incidence is 1 to 5 cases per million population per year. In the areas severely hit by the Chernobyl accident, this incidence increased to 40 per million per year. Because of the relatively short half-life of ^{131}I, the contamination did not persist for years. At present, the incidence of DTC in children below 10 years of age is not higher than in children from uncontaminated areas. In 2006 (2), the authors had published a report about the clinical course of 740 surgically treated children. In the present article, they report on the outcome after postsurgical radioiodine therapy (RIT).

Methods

The patients were chosen for ^{131}I treatment in Germany if there was local tumor invasion, and/or lymph-node or distant metastasis. In a typical case, the first cancer surgery took place in early adolescence, approximately 10 years after exposure. The tumors were exclusively papillary cancers. At that stage, three quarters of the study cohort had local invasion. Practically all patients had lymph-node involvement. Following the initial scintigraphy, distant metastases could be visualized in approximately 50% of cases. If affected, the lungs showed a miliary spread or mixed tissue with focal uptake. Clearly defined lung nodules were rarely found. All patients had undergone radical surgery with total thyroidectomy and lymph-node dissection.

Before RIT, a classical workup was performed in Germany, including chest x-ray examination. Thyroxine treatment was stopped for 4 weeks. If a thyroid remnant was found, ablation with 100 MBq per kilogram of body weight (2.7 mCi/kg) was attempted. Follow-ups in Germany were performed 3 to 12 months after each RIT and, if necessary, repeat radioactive iodine treatment was applied. Since 1999 and 2004, intensive pulmonary surveillance by using CT and functional respiratory tests was introduced in order to identify patients with pulmonary fibrosis.

While patients were hypothyroid (TSH >80 mU/L), complete remission was defined by undetectable serum thyroglobulin and a nearly complete remission was characterized by a detectable thyroglobulin of <10 µg/L with negative scintigraphy. Partial remission

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was considered in patients with thyroglobulin measurements >10 µg/L with a response of the tumor to treatment and a progressive decline of serum thyroglobulin values. The remaining patients were considered to be suffering from progressive disease.

Results

In 134 children without distant metastases the cumulative high ^{131}I doses varied between 1 and 25 GBq (27 and 675 mCi). Obviously, 100 patients with distance metastases received higher cumulative doses (4 to 63.6 GBq [100 to 1700 mCi]; median, 16.9 GBq [450 mCi]). Note that because of local circumstances, in some instances the interval between surgery and the first RIT treatment was as long as several years.

Complete remission was achieved in 64% of the 134 children, nearly complete remission in 30%, and partial remission in 4.8%; there was no relapse. The follow-up between the last ^{131}I therapy and the latest examination ranged from 7.4 to 13.9 years. Most importantly, there were no local or distant DTC recurrences in incomplete responders or any sign of disease progression in nearly complete responders. One patient died of advanced pulmonary fibrosis 19 years after diagnosis and 17 years after treatment. Two other patients died of causes unrelated to DTC. No patient died of DTC. As expected, complete remissions were more frequent in patients in whom the disease was discovered long after 1986 and in those with low initial serum thyroglobulin levels. Pulmonary fibrosis was not limited to the one patient who died of it: seven other patients showed persistence or transient evidence of lung fibrosis. All these cases had diffuse pulmonary metastases with high initial TG levels (290 to 9760 µg/L).

Clinical follow-up indicates that reproductive function was impaired in males, since only 24% of the affected men have children while 51% of the women have children.

Conclusions

This cohort of patients with DTC with local invasion and/or distant metastases is a selected group of patients at increased risk. The follow-up, which now extends over 11 years after RIT, is very encouraging; none of the patients died of progressive thyroid cancer, the majority (64%) were in complete remission, and some (4.8%) had partial remission, with clinical follow-up indicating an improvement of their health status because thyroglobulin levels tended to decrease over years with suppressive doses of thyroxine alone. In some cases, the ^{131}I doses that had to be given were very high, but on the average dose of 141 MBq/kg (3.8 mCi/kg) was still acceptable. Lung fibrosis was seen in several cases, but only in patients initially presenting with pulmonary metastases. One of these patients died of pulmonary insufficiency.

ANALYSIS AND COMMENTARY

Among the 5127 young patients with papillary thyroid carcinoma in the Chernobyl area, no aggressive forms (e.g., tall-cell, insular, or columnar-cell carcinoma) were found; therefore, the prognosis of these tumors is essentially good, provided the children have access to adequate treatment (3). In control populations, the more aggressive forms are also extremely rare, so it is premature to conclude that aggressive forms do not occur after incidents like that in Chernobyl. Although, the increased cancer risk was limited to children and adolescents below 14 years of age in 1986, the whole population continues to be surveyed.

The results of this study are highly encouraging. Some patients had very advanced disease with disseminated miliary pulmonary metastases. Following repeat treatments with radioactive iodine, the pulmonary

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seeding disappeared or was markedly reduced. This experience certainly contrasts with the rare success rate in sporadic DTC with pulmonary involvement in adults.

The most difficult question is with regard to the balance between treatment and secondary effects of treatment, particularly pulmonary fibrosis. In this context, it would be interesting to know the cumulative dose of ^{131}I in the patient who died of pulmonary fibrosis. Also, we do not know the incidence of secondary tumors that have been reported in the adult DTC population treated with ^{131}I. For the moment, however, there is no alternative way of treating these cancers.

References

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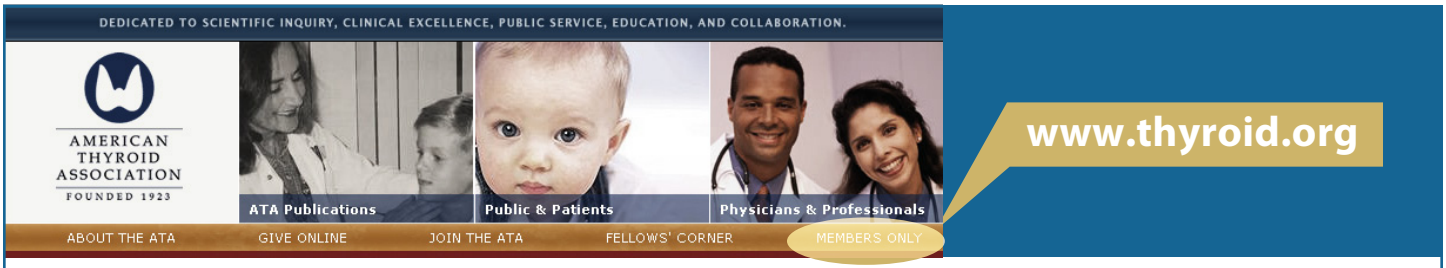

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