Gonadal damage due to radioactive iodine (I^{131}) treatment for thyroid carcinoma

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Summary: Papillary carcinoma of the thyroid is the most common type of thyroid cancer and is associated with a good prognosis. Complications of treatment with surgery and radioiodine are uncommon. We report the case of a 13 year old boy who developed testicular damage following treatment with radioactive iodine 350 mCi for a papillary carcinoma of the thyroid. Four years after radioiodine treatment there has been no suggestion of recovery of spermatogenesis. Detailed follow-up studies of similarly treated young patients are required to define the incidence of this complication and to determine its reversibility.

Introduction

Differentiated thyroid carcinoma is a malignancy with a good prognosis (Maheshwari *et al.*, 1981). With longer survival of patients with this and other cancers, increasing attention is being paid to the quality of survival and hence the long term complications of cancer therapy. One such complication is the adverse effect of such treatment on the fertility of young patients during the most reproductive years of their lives. It is established that gonadal damage may be caused by chemotherapy in children treated for Hodgkin's disease, leukaemia or medulloblastoma (Shalet, 1982; Ahmed *et al.*, 1983), and by radiotherapy in children treated for Wilms' tumour (Shalet, 1982). We report the case of a boy in whom testicular damage was caused by radioactive iodine (I^{131}) used in the treatment of thyroid cancer.

Case report

A 13 year old boy presented with cervical lymph node enlargement which was biopsied. Histological examination showed metastatic papillary thyroid carcinoma. Subsequently he had a total thyroidectomy with clearance of involved cervical lymph nodes. Thyroid histology showed mixed papillary and microfollicular carcinoma. He required replacement therapy with triiodothyronine in a dose sufficient to suppress thyrotrophin secretion and 1α -hydroxycholecalciferol

for hypoparathyroidism. At this time he was in early puberty with both genitalia and pubic hair at stage 2 (Tanner, 1962) and testes which measured 8 ml bilaterally. Ten months after the thyroidectomy he developed recurrent metastatic cervical lymphadenopathy and was treated with 200 mCi of radioactive iodine I^{131} . Three months after this he received a second dose of radioactive iodine I^{131} (150 mCi) and a course of external radiation therapy to the neck (3000 rads in 16 fractions/22 days). Subsequent follow up over four years has shown no further recurrence. His growth and development appeared normal, however at the age of 16, despite the fact that he had completed puberty, his testes were rather small (12 ml). The basal follicle stimulating hormone (FSH) level was elevated at 18 IU/l (normal <7) with normal LH (4 IU/l; normal <7.5) and testosterone (14.8 nmol/l; normal 10–30 nmol/l concentrations). One year later semen analysis revealed azoospermia. The gonadotrophin and testosterone concentrations were unchanged. The persistently elevated basal FSH concentration and azoospermia are evidence of testicular germ cell damage. In the absence of any history of cryptorchidism, orchitis or mumps and the presence of a normal karyotype (46XY), it is very likely that the testicular damage is due to the radioactive iodine the patient received.

Discussion

The treatment of differentiated thyroid carcinoma with thyroidectomy and radioactive iodine is associated with an excellent prognosis (Maheshwari *et*

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al., 1981). Survival rates at 20 years range from 68–78% and these figures are even better for patients who are less than 40 years of age, with 25 year survival rates of 90% (Maheshwari *et al.*, 1981). Some of the long term complications of radioactive iodine treatment are bone marrow depression and leukaemia (Werner & Ingbar, 1978). Recently Handlesman & Turtle (1983) have drawn attention to the complication of testicular damage from radioactive iodine in men treated for thyroid carcinoma. They found azoospermia, oligospermia, elevated FSH and LH levels and subnormal testosterone levels, 1 to 42 months after radioiodine therapy. Our patient received a total dose of 350 mCi of radioactive iodine I^{131} in early puberty. There was evidence of damage to the germinal epithelium at least 4 years after treatment. There was no evidence of Leydig cell damage and pubertal development was quite normal. The irradiation received by the testes is derived from free radioactive iodine in the blood and bladder urine and also from radioiodinated thyroglobulin and thyroxine (Jeevanram *et al.*, 1982). The unbound radioiodine is rapidly excreted in 4 to 6 days and it is the protein bound radioactive iodine with the longer half life which is chiefly responsible for irradiation of the gonads, bone marrow and other tissue (Werner & Ingbar, 1978). Estimates of tissue irradiation suggest that the testicular radiation dose is 0.5–1.0 rad/mCi (Werner &

Ingbar, 1978). Therefore our patient would have received a testicular dose of approximately 175–350 rads. Single doses of 15–400 rads external radiation are known to produce testicular damage resulting in oligospermia and azoospermia (Lushbaugh & Casarett, 1976). We have also observed testicular damage in boys who received scatter irradiation to the testes of 268–983 rads (fractionated) following abdominal radiotherapy for Wilms' tumour (Shalet, 1982). Dose fractionation is known to increase the susceptibility of the testis to radiation damage and continuous testicular irradiation by protein bound radioiodine may be considered an extreme form of fractionation (Handlesman & Turtle, 1983). This is the first report of radioiodine induced testicular damage occurring during childhood. Sarkar *et al.* (1974) who reported on the subsequent fertility of children and adolescents treated with radioiodine, found that, 14 to 26 years later, the incidence of infertility in these patients was no more than that in the normal population. Among the surviving males, two of thirteen interviewed by telephone, 14 to 26 years after treatment, were found to be infertile. This suggests that recovery from testicular damage occurs. However, more detailed follow-up studies of similarly treated young patients are required to define the incidence of this complication and to determine its reversibility.

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