Thyroid Function Following Chemotherapy in Testicular Cancer

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Testicular cancer is the most common type of cancer among young men in Western countries. The mean age at diagnosis is 28 years in Finland (1) and the incidence of testicular cancer has been increasing in the past few years. The standard treatment of metastatic testicular cancer is cisplatin-based combination chemotherapy. At present about 90% of the patients with testicular cancer are cured (2).

Different late sequelae have been observed during follow-up of chemotherapy-treated testicular cancer patients. These include changes in gonadal function, serum lipids and cardiovascular status (3–6). Cisplatin has been suggested to contribute to hormonal perturbation through its effects on the hypothalamic-pituitary-gonadal axis (5). Elevated levels of LH, FSH, DHEA, and 17-OH-progesterone have been observed in more than half of the patients treated with cisplatin-based combination chemotherapy and the frequency increases with the increase in cumulative dose of cisplatin (7). Hyperthyreosis has been observed prior to treatment in testicular cancer patients with high HCG levels, and the thyroid function has normalized with the treatment (8). We describe two patients who, after successful treatment for metastatic testicular cancer, developed hypothyroidism during early follow-up. Altered thryoid function in consequence of chemotherapy in testicular cancer has to our knowledge not been reported earlier.

Case 1. The patient was a 33-year-old previously healthy male who was admitted to the hospital because of abdominal pain. A solid tumour of the size of 9 × 7 cm was detected by ultrasound and the tumour was extirpated by laparotomy. The histological diagnosis was seminoma metastasis. In staging investigations the primary tumour, 4 mm in diameter, was detected by ultrasound in the right testis. Tumour marker levels (AFP, HCG) were normal prior to orchiectomy, which was performed. Postoperatively an enlarged lymph node was detected at the CT investigation beside the aortic bifurcation. The patient received four courses of chemotherapy with a combination of cisplatin, bleomycin and etoposide (BEP). A complete response was detected in staging investigations. During the follow-up the patient complained of chills and fatigue. His thyroid function was found to be abnormal. Nine months after finishing chemotherapy he showed elevated TSH 8.9 mU/l (normal range 0.4–4.5) and low free thyroxin, T4V 9.0 pmol/l (normal range 11–24). Thyroid antibodies were negative. Treatment with thyroxin was commenced which resulted in resolving of symptoms and normalizing of thyroid values. Three years later thyroxin substitution was stopped and the patient remains euthyroid with borderline TSH (4.6 mU/l).

Case 2. The patient was a 24-year-old previously healthy man, who was admitted to the hospital because of enlarged left testis. A tumour with a diameter of 4.5 cm was found and an orchiectomy was performed. Histopathology showed a mixed tumour with embryonal carcinoma and teratoma components. After survery, AFP was 23 kU/l (normal range 0–10) and HCG was 12 U/l (normal range <2). Several enlarged lymph nodes more than 1 cm in diameter were detected in the retroperitoneal region in CT and also a metastasis in the right lung hilar region. The patient received four courses of BEP chemotherapy and was in complete remission at the end of treatment. Two months later at a follow-up CT investigation a right-side lung metastasis was found. Further chemotherapy was given with 4 courses of ifosfamide-etoposide (IE) combination.

During follow-up the patient complained of tiredness and hair loss. Thyroid function at 9 months showed elevated TSH, 5.2 and high T4V, 26.1. At control check TSH was 10 mU/l and T4V was 16.4 pmol/l and in further control TSH was 13 and T4V 18.5. Thyroid antibodies were elevated (1 900 kU/l) indicating hypothyroidism based on autoimmune thyroiditis. CT of sella region was normal. Treatment with thyroxin was commenced and resulted in resolving of symptoms and normalizing of thyroid function. Thyroxin was stopped after two years.

Both patients are currently euthyroid with borderline TSH regularly controlled to avoid subclinical hypothyroidism. They have maintained disease-free status at follow up.

Discussion. Late effects are not rare after cisplatin-based combination chemotherapy. Vascular toxicity, hormonal changes and gonadal dysfunction observed among testicular cancer patients have been reported earlier (5–9). Raynaud-like phenomena, peripheral sensory neuropathy and impaired hearing are the most common late effects among testicular cancer patients treated with chemotherapy (9). The patients usually become well adapted to these late effects and rarely find them invalidizing. The symptoms subside spontaneously with time in some patients, while others get accustomed to them.

Hyperthyreosis has been observed to occur occasionally in testicular cancer patients with elevated HCG levels prior to treatment (8). This can be clinically symptomatic or asymptomatic and the thyroid function normalizes with successful treatment of can-

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Table

The relationship between TSH and T4 values in primary and subclinical hypothyroidism

Diagnosis	S-TSH	S-T4/S-FreeT4	
Primary hypothyroidism	elevated	low	(Case 1)
Subclinical hypothyroidism	elevated	normal	(Case 2)

cer. Effects of chemotherapeutic agents on gonadal and hypothalamic hormones have been observed (5–7). There are a few reports on the effects of chemotherapy on thyroid function (10–12). In a series of adult patients treated for acute lymphoblastic leukemia four of 48 patients studied were found to have subclinical impairment of thyroid function after treatment (10). Both of our patients presented with a picture of hypothyroidism. During recovery of serious illness or immunosuppressive treatment thyroid hormone levels can be altered in a way resembling hypothyroidism with elevated TSH and normal T4 or free thyroxin. This condition is known as NTI (non thyroid illness) and it can confuse the interpretation of thyroid function tests. Laboratory findings are similar to those in subclinical hypothyroidism (Table). In our patients both clinical condition and thyroid hormone levels normalized during substitution with thyroxine. Thyroxine therapy is not beneficial in NTI patients (13). Both patients had repeated CT investigations. The iodine-containing organic compounds used as contrast agents for computed tomography can affect thyroid function (11). Repeated investigations have been suggeted to cause hypothyreoidism in chemotherapy-treated children (14). Another explanation is an autoimmune thyreoiditis which develops as a consequence to intensive chemotherapy regimen.

Hormonal changes caused by chemotherapy usually subside after treatment. Thyroid function of our patients has improved during follow-up, and the patients have discontinued thyroxin substitution. In case of a slow recovery after chemotherapy for testicular cancer, the control of thyroid function is recommended and those with raised thyroid stimulating hormone concentrations should receive thyroid hormone replacement. We have included the thyroid function tests in our routine investigations for testicular cancer undergoing chemotherapy and continue to follow thyroid function tests after recovery to prevent the development of subclinical hypothyroidism.

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