CASE REPORT

Symptomatic hyperthyroidism in metastatic testicular mixed germ cell tumour

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Accepted 23 May 2018

SUMMARY

This is a case of a young 34-year-old man who had symptomatic hyperthyroidism from an extremely high serum beta HCG level in the setting of a metastatic stage IIIC mixed germ cell tumour. The patient's thyroid function normalised with treatment of the cancer as the beta HCG levels declined.

BACKGROUND

There are many forms of testicular cancer and, when diagnosed early, most have a favourable prognosis. Hyperthyroidism is a rare paraneoplastic complication. Its association with germ cell testicular cancer is related to high beta Human chorionic gonadotropin (HCG) levels. In most cases hyperthyroidism remains subclinical; only a few cases of clinically symptomatic hyperthyroidism have been published in the literature.^{1–3} This is one such case.

CASE PRESENTATION

A 34-year-old man presented with painless scrotal swelling which had waxed and waned for 6 months. He reported several months of weight loss, along with intermittent palpitations and diarrhoea. On

the day of presentation, he had an episode of haemoptysis, and reported mild shortness of breath while he was hiking.

On presentation to the emergency room, his physical exam was remarkable for tachycardia (124 beats/min), mild hypoxia (89%) on room air, gynecomastia and a swelling on the left side of the scrotum.

INVESTIGATIONS

Testicular ultrasonography showed a left-sided heterogeneous tumour 7.4×5.8×5.5 cm in size with both solid and cystic parts, along with calcifications and a large left-sided hydrocoele. The right testis was ultrasonographically normal.

A chest X-ray revealed cannonball lesions throughout the chest (figure 1). CT of the chest confirmed these findings pointing towards metastatic disease (figure 2). A CT of the abdomen and pelvis showed a metastatic lesion in the liver, and an MRI of the brain did show multiple areas of metastasis. Pathology showed a 10 cm mixed germ cell tumour, which was approximately 60% composed of yolk sac tumour, 30% teratoma and 10% choriocarcinoma. Thus he was diagnosed with stage IIIC mixed germ cell tumour.

Laboratory data revealed beta Human chorionic gonadotropin level of 833 531 IU/L (normal <1.4 IU/L) and Alpha-fetoprotein (AFP) of 742.4 ng/mL (normal range 0.0–8.0 ng/mL). Additional testing showed a thyroid-stimulating hormone (TSH) of 0.01 (0.55–4.78 uIU/mL), T3 of 200 (60–181 ng/dL) and free T4 of 2.8 (0.9–1.8 ng/dL).

TREATMENT

The patient underwent an immediate left-sided radical orchiectomy and chemotherapy was started on the next day.

OUTCOME AND FOLLOW-UP

He was started on bleomycin, cisplatin and etoposide. He also received whole-brain radiation. After four cycles of treatment, his beta Human chorionic gonadotropin went down to 66. His TSH was 1.19, T3 was 150 and free T4 was 1.0. His symptoms of intermittent palpitations and diarrhoea had resolved.

The patient then received salvage chemotherapy with paclitaxel, ifosfamide and cisplatin as he continued to have some residual pulmonary disease and an elevated tumour marker beta

Figure 1 Chest X-ray showing innumerable pulmonary nodules scattered diffusely throughout the bilateral lungs from metastatic disease.

To cite: Shah D, Khalid N. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2018-224877

Figure 2 CT scan showing typical cannonball lung metastases.

Human chorionic gonadotropin. Despite initial remission that was achieved after this round of chemotherapy, the patient's disease relapsed, and even after trial of immunotherapy with nivolumab the patient had disease progression and passed away in hospice care.

DISCUSSION

The association of non-seminomatous germ cell tumours producing beta Human chorionic gonadotropin was first described in 1964 by Steigbigel *et al.*⁴ In a following study, beta Human chorionic gonadotropin levels $>50\,000$ IU/L were associated with hyperthyroidism in 7 of 17 patients.⁵

This association comes down to the basic structure of two hormones.⁶ Beta Human chorionic gonadotropin has two subunits. The α subunit is homologous to TSH. This configurational homology can result in hyperthyroidism. The high levels of beta Human chorionic gonadotropin stimulate the TSH receptor in the thyroid gland leading to increased thyroid hormone production. The normalisation of thyroid function after treatment combined with the profound reduction of beta

Human chorionic gonadotropin serum levels (as seen in our patient) supports the correlation of beta Human chorionic gonadotropin and hyperthyroidism. Therefore some authors recommend screening for hyperthyroidism in patients with beta Human chorionic gonadotropin levels of $>20\,000$ IU/L.²

Only a handful of patients have been reported to require thyrostatic therapy.^{2–4} Our patient had an orchiectomy on day of presentation, which was promptly followed by chemotherapy the next day. With the initiation of this treatment, his tachycardia and diarrhoea had started to resolve, and therefore endocrinology did not recommend starting thyrostatic therapy with methimazole or propylthiouracil. His symptoms had completely resolved after his thyroid function returned to normal.

Learning points

- ▶ Clinicians need to be aware that there is an association between hyperthyroidism and germ cell tumours in men with high beta Human chorionic gonadotropin levels.
- ▶ There is a normalisation of thyroid function, which is usually achieved with treatment of the cancer and reduction in beta Human chorionic gonadotropin levels.
- ▶ Rarely these patients may need thyrostatic treatment.

Contributors DS: responsible for writing, editing, planning and literature review of the case. NK: responsible for editing, literature review of the case and taking consent from the patient's wife.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Next of kin consent obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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