

Hypertestosteronemia and primary infertility from a mediastinal extragonadal germ cell tumor

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Introduction

Extragonadal germ cell tumors (EGCTs) are tumors of gonadal origin representing <5% of germ cell malignancies that form outside gonads. These are typically found in the mediastinum, retroperitoneum or pineal gland.

Clinical Presentation

A 26-year-old male presented to the Reproductive Endocrinology outpatient clinic, in January 2016 with a two year history of infertility. He had known hypertrophic cardiomyopathy due to MYH7 sarcomere mutation, treated with implantable cardioverter-defibrillator while his partner was healthy. Initial investigations performed by their GP, showed hypertestosteronemia (52.9 nmol/L, normal range 9.0-26.0 nmol/L) and azoospermia (0 sperm per 20ml of ejaculate).

During consultation, he reported hoarseness of voice, hypersexuality, and increased hair distribution on torso and extremities over the past 3 years. He denied having used anabolic steroids or any supplements and was only on amiodarone to ameliorate arrhythmias from his hypertrophic cardiomyopathy. On examination he had normal stature, was hirsute with bilaterally small testes (<10cc each) but no evidence of any masses during palpation. A testicular/scrotal U/S was unremarkable. Subsequent investigations revealed consistently elevated testosterone (52.9 nmol/L), β -hCG (900IU/L, normal range: <1IU/L), oestradiol (738pmol/L, normal range: 36.7-147pmol/L) and suppressed FSH and LH (< 1IU/L, normal FSH: 2-9IU/L, LH: 2-12IU/L) while remaining tests were normal. The provisional diagnosis of an EGCT was suspected and whole body CT revealed a 7x6x5cm mass of the anterior mediastinum (Figure 1) without further disease dissemination. Due to his hypertrophic cardiomyopathy and reduced ejection fraction (EF: ~35%) he was not eligible for neo-adjuvant treatment with bleomycin-etoposide-cisplatin (BEP)¹, in view of the increased risk for cardiotoxicity² and was instead referred for surgery. Immediately following excision of the mass, his testosterone dropped to undetectable levels (1.0 nmol/L) (Figure 2) confirming that β -hCG hypersecretion by the tumor was driving hypertestosteronemia. Post-surgically, considering his hypertrophic cardiomyopathy, he was offered one high dose adjuvant carboplatin cycle (6AUC). He was not referred for surgical sperm extraction before chemotherapy due to the low risk of gonadal toxicity from one carboplatin cycle³. At last follow-up, his testosterone was normal (18.7nmol/L) without evidence of disease recurrence and the couple was referred for microsurgical sperm retrieval followed by IVF with ICSI⁴.

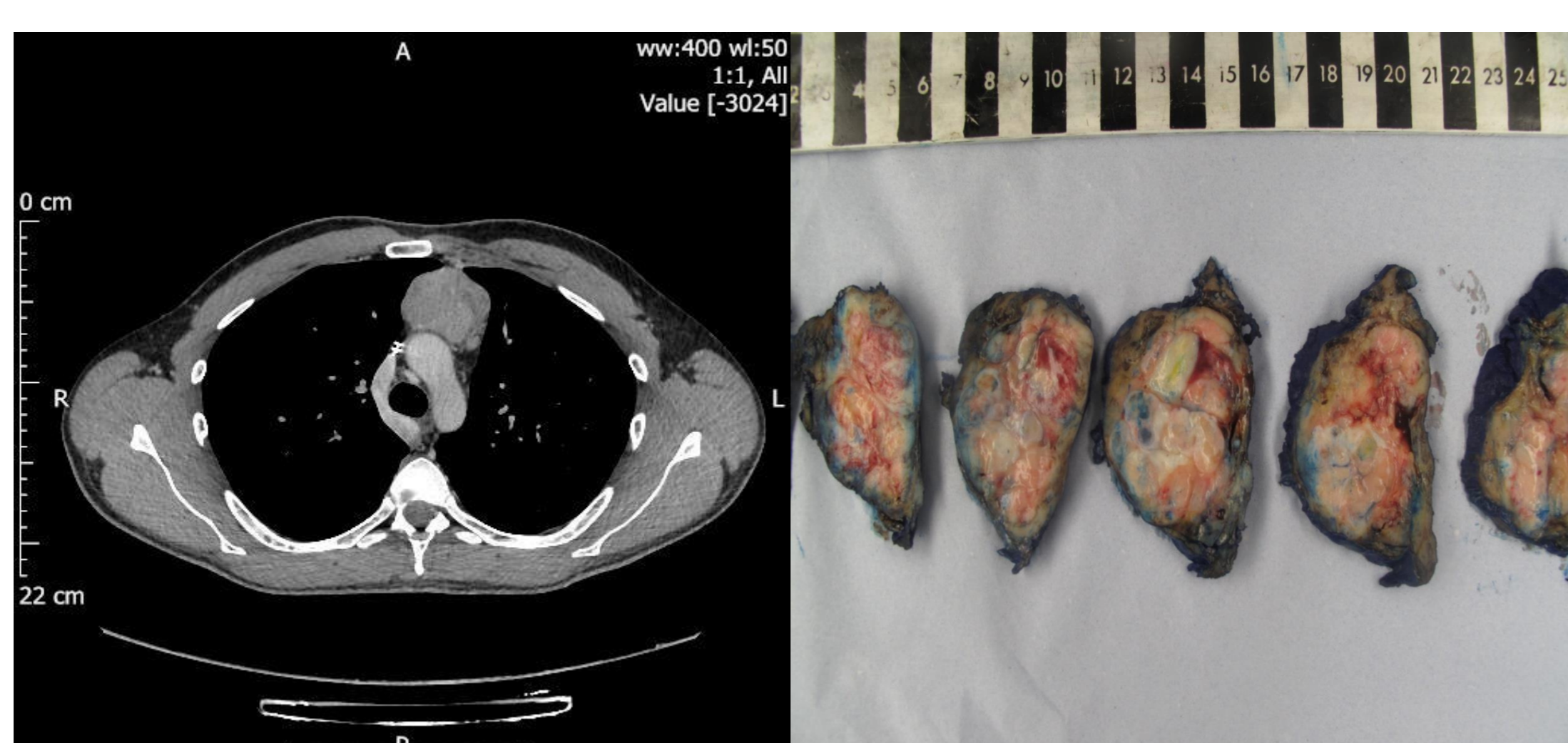
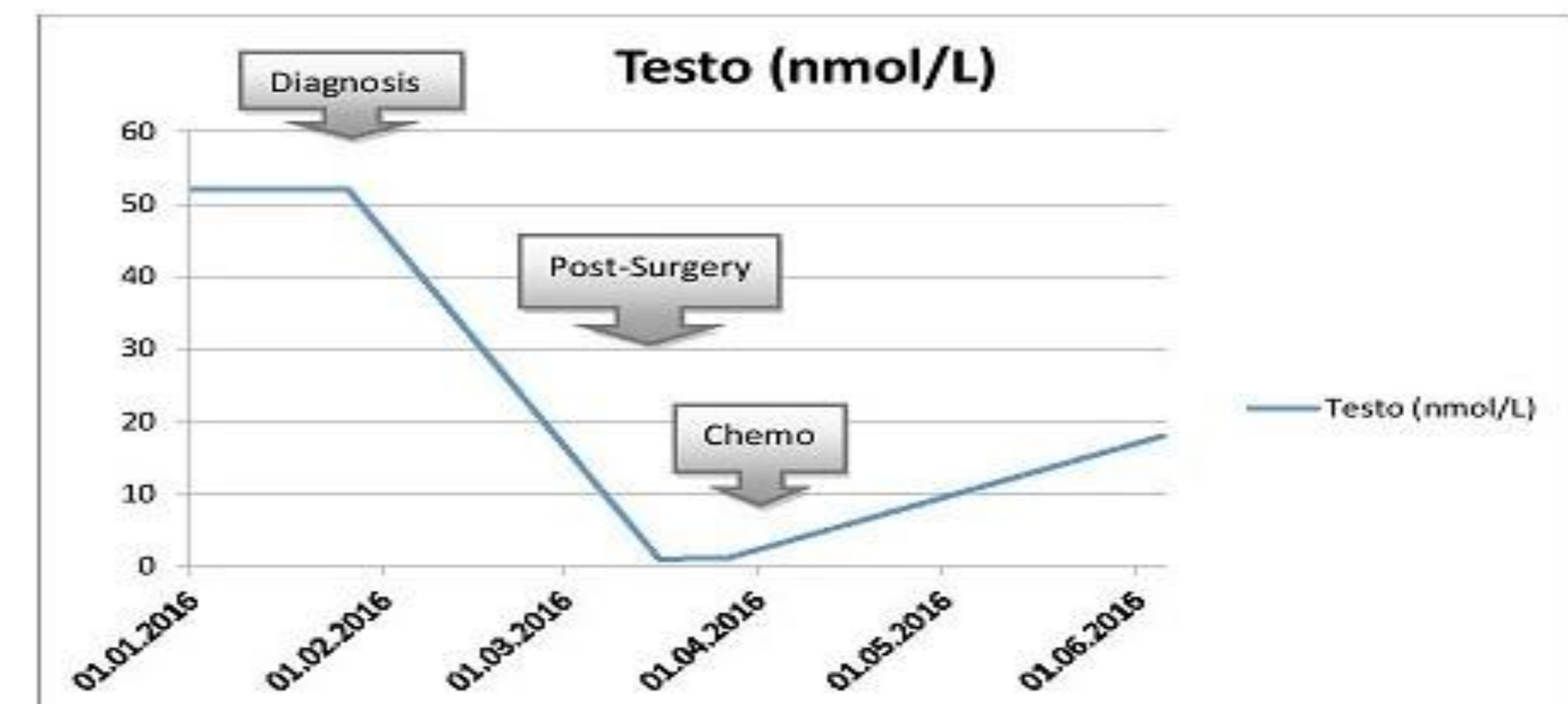


Figure 1: Whole body contrast enhanced computerized tomography reveals a 7x6x5 cm mass of the anterior mediastinum. Macroscopic image of the excised tumour.



Normotestosteronaemia : 9-26 nmol/L
Hypotestosteronaemia: < 9 nmol/L
Hypertestosteronaemia: > 26 nmol/L

Figure 2: Testosterone levels in relation to interventions throughout disease clinical course

Conclusions

EGCT treatment and prognosis depends on factors like cancer type, tumor location, and tumor size. Treatment of choice remains combined neo-adjuvant chemotherapy followed by surgery. Hypertestosteronemia is defined by abnormally high levels of testosterone, characterized by precocious puberty, increased muscle mass, acne vulgaris and polycythemia. In adult males, hypertestosteronemia and azoospermia can be secondary to congenital adrenal hyperplasia, androgen abuse or testicular or adrenal tumors particularly when testosterone levels exceed normal limit by > 50%. Rarely, hypertestosteronemia and azoospermia are associated with an EGCT. Increased β -hCG is associated with suppression of gonadotropin response to gonadotropin-releasing hormone in the pituitary, resulting in inhibition of LH and FSH. Also, β -hCG secreted by EGCTs may stimulate androgen production by the testes. Hypertestosteronemia can therefore appear as a biochemical finding not to be ignored. Managing physicians should be careful not to erroneously interpret hypertestosteronemia which can easily be attributed to lifestyle factors, as in rare cases such as this, may lead to infertility but more importantly to increased morbidity and mortality.

References

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