CASE REPORT

Traumatic andropause after combat injury

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SUMMARY

In association with lower extremity amputation, complex genitourinary injuries have emerged as a specific challenge in modern military trauma surgery. Testicular injury or loss has profound implications for the recovering serviceman, in terms of hormone production and future fertility. The initial focus of treatment for patients with traumatic testicular loss is haemostasis, resuscitation and management of concurrent life-threatening injuries. Multiple reoperations are commonly required to control infection in combat wounds; in a review of 300 major lower extremity amputations, 53% of limbs required revisional surgery, with infection the commonest indication. Atypical infections, such as invasive fungal organisms, can also complicate military wounding. We report the case of a severely wounded serviceman with complete traumatic andropause, whose symptomatic temperature swings were initially mistaken for signs of occult sepsis.

BACKGROUND

Major testicular injury or loss is rare in civilian practice, but may occur after animal bites, gunshot wounds and self-mutilation.^{1–5} Initially, the main focus of treatment for patients with traumatic testicular loss is haemostasis, resuscitation and management of the likely concurrent life-threatening injuries.¹ In addition, early sperm retrieval is advocated to mitigate the possible consequences of later testosterone therapy on spermatogenesis.⁶ This case demonstrates the challenges faced in the setting of major trauma with concurrent testicular injury, and should highlight the need to consider hypogonadism as a cause of hot flushing, night sweats, reduced cognition and other symptoms that may be mistaken for an infective aetiology.

In the civilian population, testosterone deficiency is common with an incidence of 5.6% among men up to the age of 70 years.⁷ Incidence increases with age, with rates as high as 50% among those over 80 years.⁸ The health risks associated with low testosterone are unclear due to variation in diagnostic criteria and study designs within the literature.⁹ Suggested risks of androgen deficiency include increased all-cause mortality, coronary artery disease and stroke.¹⁰ Provision of testosterone replacement therapy (TRT) has increased owing to better awareness of androgen deficiency and its associated health risks.

CASE PRESENTATION

A 32-year-old male soldier was airlifted by the Medical Emergency Response Team (MERT) to the Joint Force Hospital Bastion Hospital, Helmand

province, Afghanistan, following an improvised explosive device blast. He had sustained bilateral above knee amputations, an open pelvic fracture with rectal injury, urethral disruption, significant perineal and external genitalia injury. Clinical examination revealed complete absence of testicular tissue, which was confirmed later by MRI.

DIFFERENTIAL DIAGNOSIS

- Occult sepsis
- Atypical fungal infection.

TREATMENT

The wounds were debrided and a pelvic external fixator was applied. Exploratory laparotomy with defunctioning colostomy and placement of a suprapubic catheter were undertaken. He was repatriated to the UK the day after the incident.

On arrival in the Role 4 Hospital, Birmingham, UK, he was taken to theatre for a relook of his wounds and further debridement. With the absence of viable testicular tissue, sperm retrieval was attempted from the remaining vas deferens, as per protocol.¹ The perineal and lower extremity wounds were managed by repeated debridement and topical negative pressure dressings. Tissue cultures grew several bacteria and fungi isolates. Broad-spectrum antibiotics were initiated within 4 h of injury and antifungals within 24 h of injury, and were continued for 6 weeks. After a 4-week stay in intensive care, the patient was stabilised and transferred to the ward.

OUTCOME AND FOLLOW-UP

Following transfer to the ward, the patient's main symptom was intermittent fever, sweating and hot flushes. Roughly three times a week, the patient recorded a temperature above 38°C. All wounds looked healthy, blood and tissue cultures were persistently negative at this stage, and inflammatory markers had fallen to within normal limits. Repeated investigations for the source of presumed sepsis were negative. Baseline androgen testing was not performed. Approximately 6-weeks postinjury, all wounds had been closed, and antibiotics and antifungals were stopped. Intramuscular TRT (Nebido Bayer HealthCare Pharmaceuticals, Montville, New Jersey, USA) was initiated with a significant reduction in hot flushes and documented temperatures (figure 1).

Five years on, the patient remains asymptomatic from androgen deficiency. He currently receives one 4 mL intramuscular injection of Nebido every 12 weeks. This corresponds to 1000 mg of testosterone undecanoate.

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Figure 1 Temperatures recorded from injury to discharge along with key interventions

DISCUSSION

Infection of combat wounds, often with atypical organisms, is a major challenge in the care of patients after major military trauma, and swinging fever often heralds occult soft tissue or cavity sepsis.² However, clinicians must retain a high index of suspicion for testosterone deficiency in patients with testicular trauma.

Quoted values for normal total serum testosterone are 400–700 ng/dL.⁹ Variations in the numerical definition of

androgen deficiency exist with papers stating low total serum testosterone levels below 200–325 ng/dL.^{8 11} Patients usually present with infertility or reduced libido, but any of the symptoms listed below in table 1 may require further investigation.

Following a diagnosis of androgen deficiency, clinicians must next establish where in the hypothalamic–pituitary–testicular axis the problem may exist. Gonadotropin hormones can be measured to differentiate between primary and secondary testicular failure. Primary testicular failure suggests a problem with the testis underproducing testosterone. Secondary testicular failure suggests a central cause, and may represent pituitary or

Table 1 Table of symptoms associated with androgen deficiency in males ¹⁰	
More specific symptoms	Incomplete or delayed sexual development, eunuchoidism Reduced sexual desire (libido) and activity Decreased spontaneous erections Breast discomfort, gynaecomastia Loss of body (axillary and pubic) hair, reduced shaving Very small (especially 5 ml) or shrinking testes Inability to father children, low or zero sperm count Height loss, low-trauma fracture, low bone mineral density Hot flushes, sweats
Less specific symptoms	Decreased energy, motivation, initiative and self-confidence Feeling sad or blue, depressed mood, dysthymia Poor concentration and memory Sleep disturbance, increased sleepiness Mild anaemia (normochromic, normocytic, in the female range) Reduced muscle bulk and strength Increased body fat, body mass index Diminished physical or work performance

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Figure 2 Investigation pathway for patients with androgen deficiency (FSH, follicle-stimulating hormone; LH, luteinising hormone; SHBG, sex hormone-binding globulin; T, testosterone). Permission to reproduce granted via copyright clearance centre (<http://www.copyright.com>) by The Journal of Clinical Endocrinology and Metabolism (figure 1 from ref 10, p 2542).

hypothalamic pathology. In secondary hypogonadism, fertility can be restored with the use of gonadotropin hormones. Fertility problems related to primary hypogonadism are difficult to treat effectively.

In conjunction with the Endocrine Society, Shalender *et al* developed a practice guideline to assist clinicians with the management of androgen deficiency.¹⁰ The Society developed a recommended investigation pathway for such patients (figure 2). The Endocrine Society guidance suggests an initial follow-up at 3–6 months following testosterone therapy initiation and then annually to check therapeutic levels (400–700 ng/dL) and ensure symptom resolution, patient compliance, and to monitor side effects.¹⁰ Haematocrit should be measured at these follow-up intervals. Therapy should cease if haematocrit rises over 54% and be restarted at a lower dose. Bone density scanning is required after 2 years of therapy in osteoporotic men or those suffering low-energy fractures.¹⁰ Care is required in men over 40 years of age with a baseline prostate-specific antigen (PSA) above 0.6 ng/mL; they require serial digital rectal examinations and a urological opinion if an abnormality is detected or a PSA rise.¹⁰

TRT comes in different preparations and is tailored to the patient's preference and requirements. It is available as an intramuscular injection, a once daily dermal patch, a once daily dermal gel application, a twice daily buccal tablet and a 3–6 monthly subcutaneous implant.¹⁰

The three most reported complications of endogenous TRT are polycythaemia, reduced high-density lipoprotein cholesterol and prostate enlargement.⁹ Studies have suggested an increased risk of cardiovascular (CV) and cerebrovascular events in patients receiving TRT. Two systematic reviews disagree about the risk of CV complications from TRT. Xu *et al*,¹² in their systematic review in 2013, stated a 1.54 times increase in CV events with TRT use. Later in 2014, Corona *et al*¹³ suggested

no associated risk in their systematic review. Along with the aforementioned risks, there are the alleged risks of prostate cancer, spermatogenesis suppression¹⁰ fluid retention, gynaecomastia, liver disorders and sleep apnoea with TRT use.⁹ No long-term follow-up studies exist to quantify the long-term safety of testosterone administration.

In the setting of testicular trauma, testosterone assays may be useful. Early treatment with exogenous testosterone can alleviate symptoms of hot flushes and night sweats, reducing the associated morbidity and alleviating clinicians' concerns of an underlying infective process.⁶

This patient's report is the first, to the best of our knowledge, to describe traumatic andropause after combat injury and the experience gained helped in our management of other similar patients who presented later in the conflict. The delay in recognition of the cause of his fever and flushing highlights why early recognition of androgen deficiency is crucial in case management; this may involve early testing, where appropriate.

Contributors GHJ prepared the manuscript. JK-B assisted the write up and referencing of the manuscript. DMS edited the manuscript and performed a literature search. DB suggested the case study and edited the final manuscript.

Competing interests None declared.

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Learning points

- Injury to male external genitalia and acute androgen deficiency in the setting of trauma may mimic occult sepsis with symptoms of hot flushing, sweating and reduced cognition.
- The initial focus of treatment for patients with traumatic testicular loss is haemostasis, resuscitation and management of the likely concurrent life-threatening injuries.
- Testosterone deficiency is associated with increased all-cause mortality and morbidity; therefore, early diagnosis and treatment is important.
- Exogenous testosterone is available in a variety of preparations and should be prescribed according to the patient's wishes and needs.

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