Case Report

Germ Cell Neoplasia in Situ of the Testis and Azoospermia: Case Report and Review of the Literature

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Abstract
An increased risk of testicular cancer in men with infertility and poor semen quality has been reported. We aim to present a patient who was being studied for infertility and incidentally found a testicular nodule, discuss management and prevalence of small testicular masses.

Keywords
Germ Cell Neoplasia in Situ, Azoospermia, Infertility, Small Testicular Masses, Case Report

Abbreviations
GCNIS: Germ Cell Neoplasia in Situ; STMs: Small Testicular Masses; US: Ultrasound; NOA: Non-Obstructive Azoospermia

Introduction
Historically testicular masses have presented as palpable lesions but scrotal Ultrasound (US) has rapidly become the preferred modality to detect scrotal pathology with sensitivity approaching 100% for testicular masses [1,2]. Now with increasing use and availability of US technology, we are seeing an increase in incidental masses in other organs such as the testes and we are faced with the question of how to act upon these findings without compromising patient care [3,4]. The current literature on long-term follow-up and safety data on nonpalpable small testicular masses (STMs) is lacking [5].

The prevalence of germ cell neoplasia in situ (GCNIS) is increased in non-obstructive azoospermia (NOA) [6] and increases with the degree of spermatogenic impairment [7]. GCNIS is a precursor lesion that eventually becomes malignant [8].

Histologic evaluation of the testicular biopsy is considered the gold standard for diagnosis of GCNIS [9]. Additional use of the immunohistochemical tumor markers PLAP and OCT 3/4 enhances the accuracy of histologic evaluation [10,11]. However, when only a standard testicular biopsy (3x3 mm) is performed, a false-negative result is possible due to the focal distribution of GCNIS [12,13].

Case Presentation
A 42-year-old male patient presented with secondary infertility. Physical exam was unremarkable.
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Fig-1: Ultrasound

Fig-2: Magnetic Resonance
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US showed right testis with multiple calcifications and hypoechogetic oval images with poor vascular peripheral signal measuring 6 to 8 mm (Fig-1). Spermogram showed NOA. Laboratory workup revealed normal tumor markers. He was submitted to a Magnetic resonance (MR) that showed in lower pole of the right testis pseudonodular images without contrast enhancing (Fig-2).

The patient was scheduled for testicular sperm extraction (TESE) and biopsy of lower pole. Intraoperative biopsy showed azoospermia and seminoma. Therefore, he underwent right orchiectomy (Fig-3). The postoperative period was uneventful and the patient exited the hospital the next day.

Histopathological evaluation of the specimens revealed GCNIS. Tumor cells stained positive for OCT ¾. Chest abdomen pelvis Computed Tomography (CT) scan showed multiple nodules smaller than 5 mm and mediastinal lymph nodes (Fig-4). Biopsy of mediastinal lymph nodes revealed Sarcoidosis.

Fig-3: Right orchiectomy
Discussion
Infertility and testicular cancer have been linked, with germ cell tumors found in up to 0.5% of men with infertility, a nearly 20-fold greater prevalence than in the general population [14,15]. Classic teaching about the treatment of solid testicular lesions is extirpative surgery with radical orchiectomy due to the risk of germ cell tumor [5]. However, this dogma is changing as experience has demonstrated that many incidentally discovered small masses prove to be benign [5]. Bieniek et al., reported 120 infertile men that were diagnosed with incidental sub centimeter hypoechoic testicular masses. Average follow up was 1.3 years and 18 men underwent surgical exploration. Malignant seminoma was found in 6 patients, comprising 5% of the overall cohort [5]. Eifler et al., discovered 49 testicular abnormalities, including 20 that were hypoechoic, in a total of 145 men undergoing scrotal US to evaluate non-obstructive azoospermia [16]. At sperm retrieval 14 men with hypoechoic masses 1 cm or less underwent excision and all showed benign pathology.

Novel biomarkers and imaging techniques may eventually help define the malignant risk in men found to have incidental STMs (Fig-5) [5] Routine staging CT appears unnecessary for these lesions [17]. A high number of non-palpable testicular nodules may be found by the combined use of testicular ultrasound and biopsy in azoospermic men examined for infertility [7]. Mancini et al., evaluated 145 azoospermic patients. Testicular ultrasonographic nodules were found in 11 out of 145 patients (7.5%). Ninety-seven, including the 11 with testicular nodules, where asked to submit to TESE and biopsy to search for spermatozoa. Nine out of the 11 subjects with testicular nodules underwent a more extensive microsurgical exploration and they found one seminoma, one embryonal carcinoma, three Leydig cell tumours and four Leydig hyperplasias. The biopsies which were routinely performed during TESE detect two additional GCNIS [7]. In azoospermic patients TESE must be accompanied by anatomopathological study, not only for define the cause of infertility but to discard also associated serious diseases, such as tumors of germ cells and GCNIS [18].

Conclusion
Small, nonpalpable, hypoechoic lesions with negative tumor markers detected incidentally during evaluation for infertility can be safely follow up with serial ultrasound. Before TESE, in azoospermic
patients it should be mandatory to submit the patient to scrotal US based on the high prevalence of non-palpable testicular nodules detected as small cancer upon surgery.

Conflict of Interest

The authors have read and approved the final version of the manuscript. The authors have no conflicts of interest to declare.

References