Case series – Azoospermia to oligozoospermia following bilateral orchidopexy in adults with undescended testicles: A Canadian first

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INTRODUCTION

Male infertility globally impacts approximately 56 530 400 individuals, with azoospermia responsible for up to 15% of cases.[1] Azoospermia can be classified as either obstructive (7-51%) or non-obstructive azoospermia (NOA; 49-93%).[2, 3] Undescended testicles (UDT) are a cause of male infertility, and 89% of male adults with untreated bilateral UDT will be diagnosed with NOA.[5, 6] NOA in UDT is secondary to prolonged exposure to elevated temperatures. It follows that the treatment of UDT may improve sperm parameters.[2, 3] Given the increasing accessibility of reproductive technology, cases of reestablishment of spermatogenesis must be reported in this population. We present the first Canadian cases of spermatogenic recovery from NOA following bilateral orchidopexy for UDT.

CASE SERIES

Case 1

A 20-year-old healthy male presented for evaluation of bilateral UDT. The patient was asymptomatic with no family history of UDT or infertility. The patient had a normal phallus with a flattened, empty scrotum. The left testicle was palpated in the inguinal canal close to the external ring, and the right testicle was located higher in the mid-inguinal canal.

Ultrasound (US) revealed the testicles within the inguinal canal, with the right measuring 4.5 x 1.4 x 2.1cm (9.4cc) and the left measuring 4.6 x 1.3 x 2.4 cm (10.2cc) (Table 1). The FSH was 6.4 IU/L, and testosterone was 11.02 nmol/L (drawn at 1600 hours). Semen analysis reported azoospermia with a volume of 0.5mL. Of note, the patient felt that his sample was lower

volume than his typical ejaculatory volume. Karyotype revealed 46 XY and no Y chromosome microdeletion. The patient was informed of the possibility of obstruction and decided to proceed with the surgery, while adding in an intraoperative testicular biopsy to confirm NOA. The patient elected to proceed with bilateral orchidopexy for improved testicular cancer surveillance, cosmesis, and possibly fertility.

After examination under anesbilatthesia, an inguinal approach was completed. The testicles were identified in the superficial inguinal pouch. The cord structures were isolated from the processus vaginalis, and the cremasteric and external spermatic fibers were cleared. Adequate length was obtained to place the testicle in a subdartos pouch without tension. Pathology demonstrated maturation arrest, with most tubules demonstrating Sertoli cells with a few scattered spermatogonia. No normal spermatogenesis was noted and several seminiferous tubules showed a mildly thickened basement membrane.

Scrotal US performed four months postoperatively visualized both the right (5.2x1.6x2.3cm; 13.6cc) and left testicle (4.0x2.0x2.9cm; 16.5cc) in the scrotum (**Table 1**). Semen analysis was done 16 months postoperatively. Rare (n=3) non-motile spermatozoa were reported on wet mount smear post-centrifugation, indicating cryptozoospermia.

Case 2

A 22-year-old male presented with a history of bilateral UDT as an incidental finding from a computed tomography scan. At age 19, a pediatric urologist completed an assessment for UDT. At that time, semen analysis revealed azoospermia and a physical exam identified small testicles palpable high in the inguinal canal. The patient was asymptomatic with no relevant family history.

On US the right testicle measured 3.54 x 1.31 x 1.89cm (6.2cc), and the left 3.19 x 1.29 x 2.03cm (5.9cc) in the inguinal canals (**Table 1**). Physical exam revealed a normal phallus and hypoplastic scrotum. The testes were located above the external ring. Investigations showed a 46 XY karyotype, no Y chromosome microdeletions, with an elevated FSH and LH at 62.9 IU/L and 18.5 IU/L, respectively. Testosterone was 18.24 nmol/L (drawn at 1159 hours).

This patient was assessed by the same pediatric and adult urologists as in *Case 1* and elected to undergo bilateral orchidopexy. Intraoperatively, the testicles were superior to the external oblique fascia at the level of the external ring. The testicles were small, and fatty infiltration appeared in the epididymis. Spermatic cord length was achieved in the same fashion as *Case 1* with tension-free placement of the testicles within a subdartos pouch.

Post-operative scrotal US visualized both the right (3.7x0.9x2.7cm; 6.3cc) and left testicle (3.0x1.1x1.9cm; 4.5cc) in the scrotum (**Table 1**) A semen analysis done 11 months postoperatively showed rare, motile sperm (n=2) on wet mount smear, indicating severe oligospermia.

DISCUSSION

These are the first Canadian cases reporting the transition from NOA to cryptozoospermia and

severe oligospermia following bilateral orchidopexy in adult males with UDT. This adds to the growing but limited body of evidence on this topic.

The first case reporting the return of sperm to the ejaculate following bilateral orchidopexy was published in 1993, involving a 23-year-old male with two previous semen samples showing NOA. Post-operative semen analysis at three months reported few spermatozoa. Notably, four successful pregnancies were achieved.[8] A recent meta-analysis describes nine published cases of return of spermatozoa in the ejaculate of previously azoospermic males following bilateral orchidopexy.[10] It was noted that in all orchidopexy cases where testicle location was reported (n=8), one (n=1) or both (n=7) testes were located in the inguinal canal, consistent with previous literature supporting that inguinal UDT are more likely to produce spermatozoa than intra-abdominal testes.[5, 10] In conjunction with the present case, these findings suggest that fertility may be regained in NOA with bilateral orchidopexy even following puberty.

There are numerous reasons to consider performing orchidopexy in patients with bilateral UDT. While fertility improvement is rarely reported, these patients may have no viable options to achieve a biological pregnancy otherwise. In addition, males with UDT have a 2.75–8 relative risk of testicular cancer.[11] Testicular self-exam in the setting of UDT is difficult or impossible, and US surveillance is resource intensive.[12] Psychological benefits may also be derived from achieving a more typical scrotal appearance.

The current Canadian Urology Association (CUA) azoospermia guideline includes no specific recommendations on managing NOA secondary to bilateral UDT in adults. However, it does outline family completion options for patients with testicular failure azoospermia.[3] The CUA guideline on UDT addresses the rationale for orchidopexy in depth, including the importance of self-examination for testicular masses, the psychological benefits of restored anatomy, and minimizing the need for scrotal imaging studies. The guideline also mentions that only 33-65% of male adults with bilateral UDT will successfully conceive. Conversely, it does not discuss the fertility implications of treating bilateral UDT in male adults, likely due to the paucity of cases and evidence available.[11] This underscores the importance of data collection and publication on fertility-related outcomes of bilateral orchidopexy in adults.

Notably, there is the inherent limitation of being a case series of only two patients with a short follow-up time. Although there was improvement in semen analysis findings, pregnancy outcomes are not yet reported. It is important to note that semen analysis for both patients was performed at the same lab. Furthermore, there was only one semen analysis pre-operatively with each subject, which may impact the reliability of the azoospermia diagnosis. The World Health Organization (WHO) recommends two analyses to reduce the risk of confounding variables causing temporary azoospermia.[16] Despite this, the results of this study are valuable. In both cases, there was no evidence from history or a physical exam to suggest causes of temporary azoospermia, such as a toxin or environmental exposure. Though two samples are ideal, our patient in Case 1 was hesitant to pursue semen analysis, and given his biopsy demonstrating

azoospermia and clinical picture of NOA, repeat analysis was forgone per patient preference. In terms of his FSH, a recent study assessing 153 azoospermic men found that only 89% of men with NOA have an FSH greater than 7.6 mIU/ml, suggesting that low/normal FSH may be seen more commonly in NOA than previously described.[17] In Case 2, the patient's significantly elevated FSH (60) and small testicles provided sufficient clinical evidence to diagnose NOA. Overall, this management approach challenges the dogma in urology of recommending orchiectomy in post-pubertal patients with UDT and highlights the importance of shared decision-making. Given the uncommon nature of this condition, collaboration between an adult fertility specialist and pediatric urologist to provide comprehensive care is important to emphasize.

CONCLUSIONS

This is the first Canadian case series of spermatogenic recovery following bilateral orchidopexy in adult male patients with UDT and NOA. This represents a deviation from standard management of this condition and offers an alternative strategy for fertility preservation in this population. Further, this underscores that collaboration between adult fertility and pediatric urology specialists is valuable. Further studies to quantify the impact on fertility and long-term outcomes will be critical to ensure safety and efficacy.

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FIGURES AND TABLES

Table 1. Comparison of pre- and post-operative scrotal ultrasound and semen analysis

Investigation	**Case 1**		**Case 2**	
	Index consultation	**Postoperative**	**Index consultation**	**Postoperative**
Scrotal ultrasound				
Testicle volume (right)	9.4 cc	13.6 cc	6.2 cc	6.3 cc
Testicle volume (left)	10.2 cc	16.5 cc	5.9 cc	4.5 cc
Testicle location (right)	Inguinal canal	Scrotum	Inguinal canal	Scotum
Testicle location (left)	Inguinal canal	Scrotum	Inguinal canal	Scotum
Semen analysis				
Findings	Azoospermia	Cryptozoospermia*	Azoospermia	Severe oligospermia**
Semen volume (ml)	0.5	3*	Unknown	3**
Sperm count/motility	0	3 non-motile sperm post-centrifugation*	0	2 motile sperm seen on wet mount**

*16 months postoperatively. **11 months postoperatively.