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Case of the Month

Case of the Month from Herlev and Gentofte University Hospital, Herlev, Denmark: Ablation of spermatogenesis due to acute spinal cord injury: a case report

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Introduction

Males account for 80% of new spinal cord injuries (SCIs) each year and the majority are of reproductive age. This is important as men with a spinal injury often experience reproductive difficulty including erectile dysfunction, poor sperm quality and ejaculatory dysfunction. Because of these problems, it has been estimated that only 5% of men with SCI will be capable of fathering a child without medical intervention.

Medical advances, such as obtaining a semen sample by electroejaculation (EEJ) or penile vibratory stimulation (PVS), have helped produce an ejaculate in nearly all patients. This development has allowed for many men with SCI to biologically father their own child. However, despite success with obtaining an ejaculate, semen quality often remains poor in many men.

To date, most of the information that is available for patients with SCI covers chronic injuries, several months to years after injury, rather than short-term effects. Semen quality in chronic SCI is typically normal in numbers of sperm present, but with very low motility and viability. An animal study in the acute phase of SCI suggested that the neurological injury had a profound short-term effect on sperm production [1]. As the study was a short-term project, analysis of recovery of spermatogenesis was not possible.

It has been suggested from a small patient cohort that there may be a window to collect normal sperm after acute SCI prior to degradation of production [2]. Therefore, it is essential to know if the acute sperm production decline seen in the animal study occurs in humans and what the time course is. Only then will we be able to make comments on the utility of immediate collection of sperm with cryopreservation following injury.

Here we report a case of a patient with cancer with acute SCI that provides us with a comparative model to the prior animal study. The case gives us insight into the impact of acute SCI on male fertility.

Case Report

A 27-year-old male sought medical attention for mid-back pain and weakness. An MRI of the thoracic and lumbar spine showed a 4.4 cm extradural posterior spinal canal mass located at the level of T10–11. He quickly developed complete lack of sensory and motor activity below the level of the tumour.

He underwent T9–T11 laminectomy and resection of epidural mass. All visible tumour was removed. Pathology review showed high-grade, undifferentiated round cell sarcoma. Chemotherapy and radiation were recommended due to the aggressive nature of the tumour. The patient was referred to reproductive urology prior to the start of treatment to discuss viable options of fertility preservation.

The patient was assessed 6 weeks after laminectomy and resection of the epidural mass at the level of T9–T11. At this time, the patient had anejaculation and continued loss of sensorimotor function below T10. PVS was attempted with no somatic reflex responses and no ejaculation. EEJ was then performed. An ejaculate was obtained with delivery of 25 V at 800 mA. The antegrade sample contained a total sperm count of 35 million sperm/mL. The retrograde sample contained a total sperm count of 1 million sperm/mL. No motility was seen in the antegrade or retrograde sample. A viability stain was performed on the antegrade sample, and no viable sperm were found.

The patient returned 5 days later for a repeat EEJ. To maximise the ejaculate volume, an elevated level of electricity was used (35 V at 1000 mA). The antegrade sample contained a total sperm count of 27 million sperm/mL. The retrograde sample contained a total sperm count of <1 million sperm/mL. No motility was seen in the antegrade or retrograde sample. A viability stain was performed on the antegrade sample and again, no viable sperm were found.

At 30 min after the result of the second EEJ sample, a testicular sperm aspiration (TESA) was performed. The tissue was cut into roughly 2.5 × 2.5 cm pieces and individually

placed into a tissue grinder. The amounting ground tissue was then put through a 20-μm filter. The sample was then centrifuged for 10 min at 450***g***. The sample was brought down to a pellet and evaluated in a 0.5 mL resuspension. After a thorough search, no sperm were found.

Endocrine analyses were acquired during the patient's second visit and showed normal LH (5.3 mIU/mL) and FSH (2.2 mIU/mL). However, the testosterone level result was lower than the normal reference range at 1.90 ng/mL (normal range 2.5–9.5 ng/mL).

Bilateral testicular tissue samples were assessed. As shown in Fig. 1, the pathology result showed peritubular hyalinisation with abundant Sertoli cells and absence of germ cells. No mature spermatids were identified. Due to the absence of viable sperm from both the EEJ and testicular tissue samples, the intended fertility preservation was not performed.

The patient subsequently underwent treatment with radiation therapy and chemotherapy and was last seen 3.5 years after his treatment. At that time his FSH had increased to 10.1 mIU/mL and he still suffers from anejaculation and has not had new attempts of EEJ.

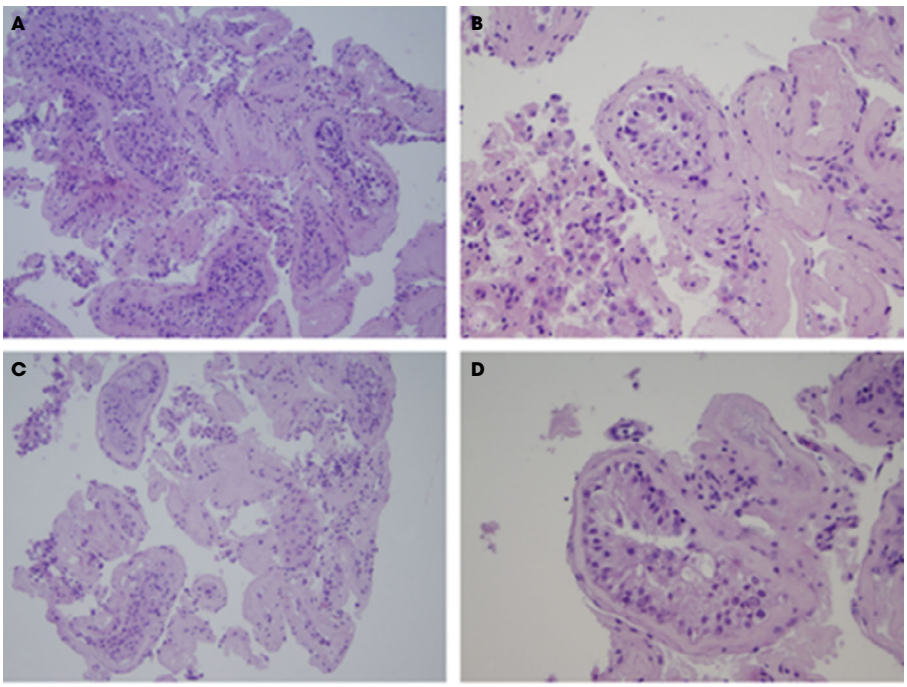
Discussion

We report a case of a 27-year-old patient with cancer presenting with acute SCI, as a result of laminectomy and epidural mass resection, attempting cryopreservation of sperm. The first semen sample was collected 6 weeks after SCI. This sample showed a normal total concentration with no motility. The second sample obtained 5 days later, again, showed a normal total concentration and no motility. A bilateral TESA was then performed on the same day as the second EEJ and surprisingly no sperm were found.

To date, the aetiology of how spermatogenesis is altered due to SCI is unknown. Existing theories, such as hormonal abnormality and changes in seminal plasma composition as a result of SCI, offer possible insight to how semen quality is impacted. However, these aetiologies have not been verified by studies and remain controversial. Several other factors, e.g., elevated scrotal temperature, have been shown to not be a contributing factor to poor semen quality following SCI.

Limited information is available on semen quality within a few weeks of SCI. Mallidis et al. [2] examined semen samples from a small cohort of males between 2 and 15 days after SCI. Semen quality peaked between days 2 and 6 followed by diminishing quality in the subsequent samples on the following days. Semen samples that were collected, via EEJ, between days 2 and 6 were cryopreserved for future use. Of the samples collected during this time, the post-thaw parameters were similar to those of healthy sperm donors. Das et al. [3] examined EEJ samples on days 5 and 14 after SCI in a 28-year-old man with acute SCI after a falling accident. This case demonstrated a drastic decrease in sperm concentration within 2 weeks of SCI. Samples obtained 18 months after SCI showed a remarkable decrease in semen quality including a low concentration and low motility.

Fig. 1 Pathology slides from the testis biopsy. Minimal germ cells present.



Ohl et al. [4] identified significant abnormalities in semen quality and spermatogenesis of male dogs 3 weeks after surgically induced SCI. During the 3 weeks following SCI, a significant reduction in sperm quality was seen on serial EEJs. The percentage of haploid cells on bi-weekly fine-needle aspiration, a quantitative surrogate for a level of spermatogenesis, was rapidly reduced after injury. Finally, at the end of the study, a marked reduction in spermatogenesis was seen on testis biopsy. Control dogs were not impacted by the repeated procedure or biopsy.

The previous dog study is important because it implies there is a potential neurological control mechanism involved in spermatogenesis as opposed to being solely under hormonal control. Billups et al. [5] has demonstrated in a sympathectomised rodent model that epididymal transport is altered but prior to the dog study there has never been a demonstrated neurological impact on spermatogenesis. The dog study suggested that a major neurological incident can induce a marked reduction in spermatogenesis. However, to date, we have no convincing clinical data that the same result may occur in humans following SCI.

The patient discussed in this case study was referred to a reproductive urologist for fertility preservation prior to the start of chemotherapy, which is known to adversely impact spermatogenesis. Because the patient was still in spinal shock on presentation this provided a unique situation to examine the effects of acute SCI on spermatogenesis. Because he had high numbers of sperm on EEJ this clearly shows that spermatogenesis was present in the recent past. The fact that he had zero motility was likely due to distal migration of the sperm into the seminal vesicles, which has been demonstrated after SCI. The seminal vesicles are a toxic environment and do not support sperm survival offering a possible explanation of low motility. As there is evidence of recent spermatogenesis but a biopsy showing an absence of sperm, this is strong evidence that the SCI is the direct cause of cessation of spermatogenesis. After the spinal shock phase then there likely is some recovery but we were not able to follow the natural cause in this patient as he subsequently underwent chemotherapy.

In conclusion, the present report demonstrates the characteristics of sperm quality and spermatogenesis in the spinal shock phase after acute SCI. This opens the possibility of a neurological control mechanism of spermatogenesis. This implies SCI can induce a marked and acute reduction in spermatogenesis and suggests that the dog model and the human follow a similar progression after SCI. More studies are needed to determine the timeline after SCI to retrieve sperm in order to optimise future fertility.

Disclosure of Interests

The authors have no conflicts of interest to declare.

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Abbreviations: EEJ, electroejaculation; PVS, penile vibratory stimulation; SCI, spinal cord injury; TESA, testicular sperm aspiration.