Successful sperm retrieval in prune belly syndrome

Dear Editor,

Eagle-Barrett or prune belly syndrome (PBS) is a rare congenital condition with an estimated incidence of 3.8 cases per 100,000 live births in the United States [1]. The syndrome is characterized by cryptorchidism, upper and lower urinary tract dilation, and either absence or deficiency of the abdominal wall musculature. While much of the literature has focused upon urinary tract malformation and cryptorchidism, fertility is a crucial aspect of urologic evaluation and care in these patients. Initial reports suggested that men with PBS were necessarily infertile, though subsequent studies and the advent of assisted reproductive technology have challenged the conventional wisdom, suggesting that spermatogenesis and fertility may be preserved in select men with PBS (Table 1) [2]. Here we report a case of successful sperm retrieval in a man with PBS and a review of the pertinent literature.

A 31-year-old man with a history of PBS (Woodard category 2) and childhood orchidopexy (unknown approach) presented for fertility consultation. Physical examination revealed a 20 mL left descended testis of normal consistency and an empty right hemiscrotum. Laboratory evaluation was notable for testosterone 282 ng/dL (normal 200–800 ng/dL), follicle stimulating hormone (FSH) 7.6 mIU/mL (normal 1.3–19.3 mIU/mL), luteinizing hormone (LH) 6.0 mIU/mL (normal 1.2–9.0 mIU/mL), estradiol 20.4 pg/mL (normal ≤32 pg/mL), and serum creatinine 1.6 mg/dL (normal 0.6–1.3 mg/dL) (estimated glomerular filtration rate 55 mL/min/1.73 m²).

Semen analysis revealed low volume (<0.01 mL) azoospermia with fructose absent, and post-ejaculatory urinalysis revealed no sperm. He was treated with clomiphene citrate 25 mg daily, and repeat testosterone 1 month later was 942 ng/dL. Semen analysis again revealed low volume (<0.01 mL) azoospermia.

The patient was taken to the operating room for examination under anesthesia, scrotal exploration, and microdissection testicular sperm extraction (microTESE). Examination revealed a 12 mL right testis at the external inguinal ring without firmness or nodularity. A left microTESE was performed. The seminiferous tubules had a normal, dilated appearance, and there was no visible intratesticular scarring. Intra-operative microscopic evaluation revealed numerous sperm with normal morphology and occasional twitching. Final pathology revealed predominantly normal testicular parenchyma with mildly reduced spermatogenesis and focal areas (20%) with Sertoli cell-only pattern. Multiple vials of testicular tissue were cryopreserved, and in vitro fertilization (IVF) with intracytoplasmic sperm injection (ICSI) is intended in the future.

The potential barriers to fertility in PBS are numerous. First, cryptorchidism and/or ectopic testis is characteristic of PBS and is a well-established risk factor for infertility, though early orchidopexy can optimize future fertility. Lopes et al. [3] reported outcomes in 46 patients with PBS who underwent bilateral orchidopexy and found that 85% of testes remained normal in size and well-positioned within the scrotum at late follow-up. Three patients required repeat orchidopexy due to ascension of the testis, and three testes within the cohort were noted to be ectopic. Our case, wherein the right testis was found during examination under anesthesia in adulthood, demonstrates the importance of a thorough physical examination for assessment of ectopic testis and routine follow-up after orchidopexy.

Second, testicular histology may be inherently altered in PBS independent of cryptorchidism. Orvis et al. [4] reported significantly lower number of spermatogonia in testes of patients with PBS relative to controls. Additionally, these testes demonstrated marked Leydig cell hyperplasia relative to controls. The authors concluded that testis pathology in PBS is likely multi-factorial and cannot be attributed to cryptorchidism alone.

Third, prostatic and urethral anatomy is altered in PBS, resulting in prostatic secretory dysfunction and retrograde ejaculation [5]. These men can even present with Wolffian duct abnormalities resulting in agenesis of the seminal vesicles and vas deferens, thereby exacerbating secretory dysfunction [6]. Dénes et al. [2] performed pelvic magnetic resonance imaging in adolescent and adult men with a

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history of genitourinary reconstruction for PBS and found a hypoplastic or absent prostate in 55.6% and 22.3% of patients, respectively. Woodhouse and Snyder [7] assessed nine adolescent and young adult men with PBS and found that seven (77.8%) had retrograde ejaculation.

Despite these barriers, the current presentation builds upon prior cases in dispelling the notion that men with PBS are infertile. Fleming et al. [5] reported the first case of successful IVF/ICSI using ejaculated sperm in PBS. The patient had low volume (0.1 mL) ejaculate, however rare, motile sperm were present. Pregnancy with IVF/ICSI on two separate occasions resulted in the live births of two male infants, both of whom developed normally without PBS. Kolettis et al. [6] reported the first case of successful sperm retrieval with subsequent IVF/ICSI in 1999. Two men with PBS and azoospermia underwent successful microepididymal sperm extraction (MESA); vasography was performed in one of the two patients due to normal FSH and suspected potential for reconstruction, and findings were consistent with congenital vassal obstruction. Only one couple proceed with IVF/ICSI, resulting in twin live births. The current case adds to this small body of literature demonstrating successful sperm extraction in these men.

To date, there is no consensus regarding the genetic basis and inheritance in PBS. Ramasamy et al. [8] reviewed 11 cases of familial PBS, suggesting a sex-influenced autosomal recessive mechanism of inheritance. Subsequently, Boghossian et al. [9] performed genotype analysis on 34 patients with PBS, identifying novel pathogenic copy number variants in select genes related to muscle and urinary tract development. However, due to lack of parental DNA, the authors were unable to determine whether the identified mutations were de novo or inherited. Of the aforementioned live births reported in the literature, one girl displayed signs of hypotonia and micrognathia, which may or may not represent partial inheritance of PBS-related traits [6].

At an early stage, men with PBS should be referred to a reproductive urologist for counseling regarding the fertility implications of their disease, potential therapeutic avenues, and lack of clarity regarding inheritance of PBS and risk to offspring. Ultimately, further research is required to elucidate prognostic indicators of fertility, genetic basis and inheritance patterns for PBS, though these efforts will be limited by the universal challenges of studying any rare disease.

Conflicts of interest

The authors declare no conflict of interest.

Author contributions

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