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Primary Testicular Failure with Unilateral Cryptorchidism

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ABSTRACT

Background: Primary Testicular Failure (PTF) in men with unilateral cryptorchidism is a rare case, which might be the first time reported.

Case: A 34-year-old man came with infertility and azoospermia. Signs of secondary sex found. FSH levels: 60.68 mIU / ml, LH levels: 15.96 mIU / ml, T levels: 336.14 ng / dl, E2 levels: 27.81 ng / dl. Ultrasound showed the left testis in the left inguinal +/- 2,4x1,1x3,6 cm in size, with decrease vascularization; +/- 4.1 cm from the base of the penis. The right testis size +/- 2,8x1,1x2,2 cm in the right scrotum accompanied by spermatocele. The patient was referred to the Urology department for orchidopexy of the left testis in the inguinal.

Discussion: Primary testicular failure, in this case, may occur due to idiopathic but does not rule out the mosaic type of Klinefelter syndrome. The patient has unilateral cryptorchidism for 20 years, there will be a risk of testicular cancer. Management of cryptorchidism must be performed orchidopexy the first year after birth. After orchidopexy, monitoring is needed every year until at least 5 years.

Conclusion: PTF occurs when the parenchymal tissue contained in the testes is no longer able to produce sperm or testosterone. PTF diagnosis is only possible through pathology and testicular cytology, but the combination of FSH and Inhibin B examination remains the best recommendation as a biomarker for patients with PTF.

Keywords: Primary Testicular Failure, Cryptorchidism, Azoospermia

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INTRODUCTION

Primary Testicular Failure (PTF) occurs when parenchymal tissue contained in the testes is no longer able to produce sperm or testosterone, even though hormonal levels from the pituitary are sufficient. PTF is the most common cause of non-obstructive azoospermia and oligozoospermia. These cases account for 1% of all men and about 10% of men with infertility.[1] PTF is classified into four different subtypes, including Sertoli cell only syndrome (SCOS), germ cell/maturation arrest (GCA/MA), hypospermatogenesis (HS) and tubular fibrosis (TF) according to histopathological/cytological findings although accurate categorization is only possible with multiple fine needle aspiration (FNAC) biopsy testis/cytology. PTF shows normal or low testosterone levels, whereas follicle-stimulating hormone (FSH) levels have increased.[1–3]

Although the diagnosis of PTF is only possible through testicular pathology and cytology, we can predict this condition through biomarker analysis. Some biomarkers that can be examined include FSH, Inhibin B, Anti-mullerian hormone (AMH), and Lactate. FSH is the best biomarker of SCOS and tubular fibrosis (TF). Inhibin B is a relatively better marker of maturation arrest (GCA / MA), hypospermatogenesis (HS). AMH and Lactate examination did not provide additional benefits, whereas the role of LH and testosterone were minimal because biochemical hypogonadism was rarely found in PTF cases.[1–4]

PTF can occur congenitally or acquired abnormalities. Congenital PTF can occur due to chromosomal disorders (Klinefelter syndrome, Y chromosome microdeletions, single-gene mutations, cryptorchidism, etc.) While the acquired PTF may occur due to mumps orchitis, drugs (alkylating agents, anti-androgens, high-dose androgens, and anabolic steroids, etc.), high doses of radiation (above 6 Gy), environmental factors (heavy metals, organic solvents, pesticides) can act as gonadotoxins, and chronic diseases (chronic renal failure, liver cirrhosis, etc.)[1]

PTF must be distinguished from azoospermia caused by other diseases. Some differential diagnoses for PTF include Klinefelter syndrome, viral orchitis (such as Mumps, Coxsackie virus), testicular autoimmune orchitis, testicular tumors, and autoimmune polyglandular syndromes, blood vessel abnormalities (repetitive torsion, ischemic conditions due to systemic hypotension), testicular trauma, testicular tumors, and autoimmune polyglandular syndromes, blood vessel abnormalities (repetitive torsion, ischemia condition due to systemic hypotension), testicular trauma, testicular tumors cancer, chemotherapy (radiation, alkylating agents), anorchia (both congenital and post-surgery) and idiopathic.[5]

CASE

A patient, 34 years old, came to the Andrology clinic complaining of wanting to have children. The patient has been married to his wife for a year and four months. The patient brought sperm analysis with azoospermia results. The patient claimed that libido, erection, ejaculation, and orgasm function remained good. Changes in voice and hair growth that indicate puberty occur around the age of 17 years. The patient has never experienced drug use, exposure to gonadotoxic substances, orchitis, or chronic diseases. The patient has never smoked or exposed to radiation.

On physical examination, the patient has a height of 164 cm and a bodyweight of 64 kg. Facial hair and armpits grow well. The hand span is 170 cm. The penis is 15 cm in length and 10 cm in circumference. Pubic hairs grow well. Right testicle measuring 6-7 cc. While the left testis is not present in the left scrotum, but there is a palpable lump suspected as a testicle in the left inguinal (Figure 1).

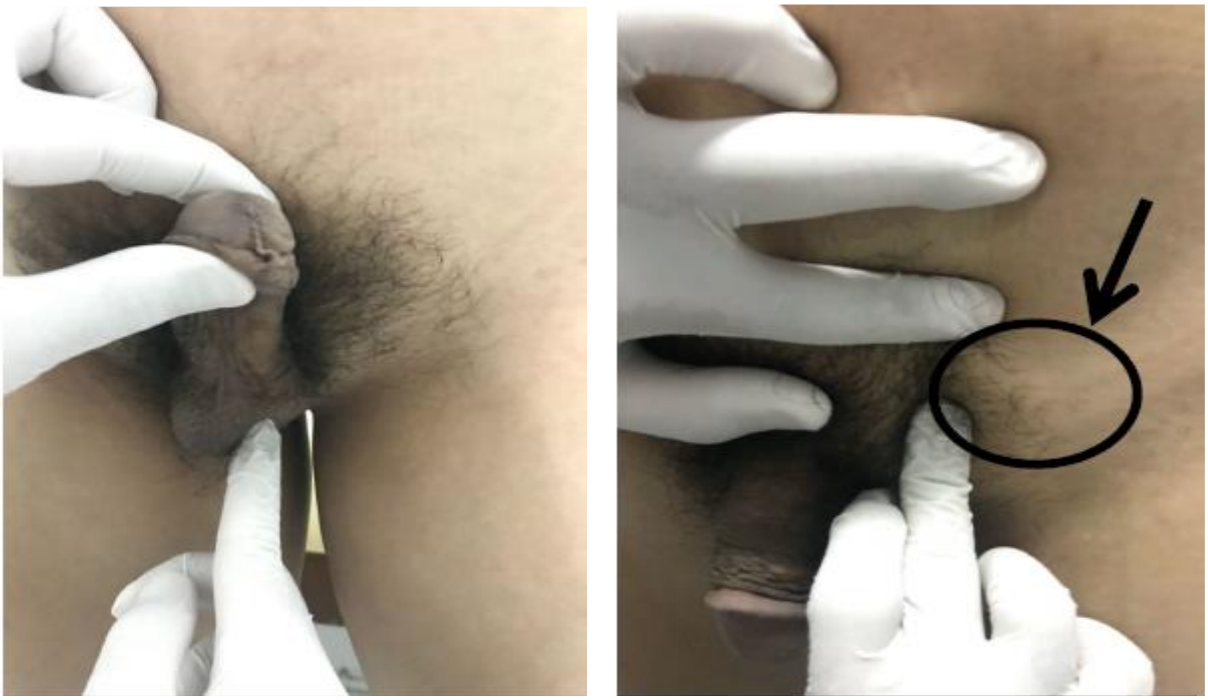

Figure 1. Left: No testis found in the left scrotum, Right: There is a palpable mass in the left inguinal, suspicious of the left testis (black arrow).

Sperm analysis is carried out twice at different times. Post-centrifugation sperm analyses result in azoospermia. Hormonal examination showed FSH levels: 60.68 mIU / ml (normal range of men 13-70 years: 1.4-18.1 mIU / ml), LH levels: 15.96 mIU / ml (normal range of men 20-70 years : 5-9.3 mIU / ml), Testosterone levels: 336.14 ng / dl (normal range: 241-827), Estradiol levels: 27.81 ng / dl (normal range: 0-52). Ultrasound results showed the left testis appeared in the left inguinal +/- 2,4x1,1x3,6 cm in size, with vascularization appearing to decrease; distance from the base of the penis +/- 4.1 cm. Whereas the right testicle measures +/- 2,8x1,1x2,2 cm in right scrotum accompanied by spermatocele (Figures 2 and 3). The patient is referred to the Urology department for orchidopexy of the left testis in the left inguinal.

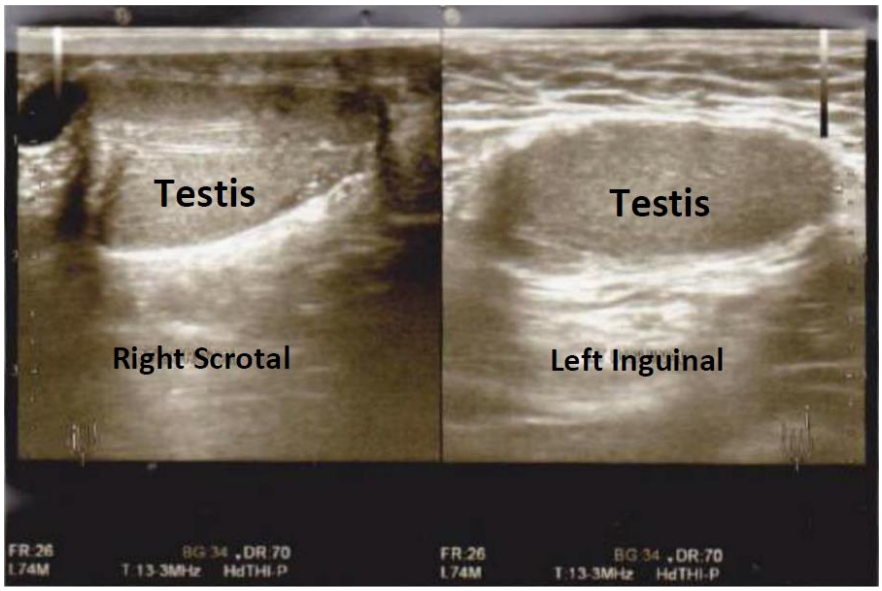

Figure 2. The ultrasound finding showed the right testis located in the right scrotum, while the left testis located in the left inguinal.

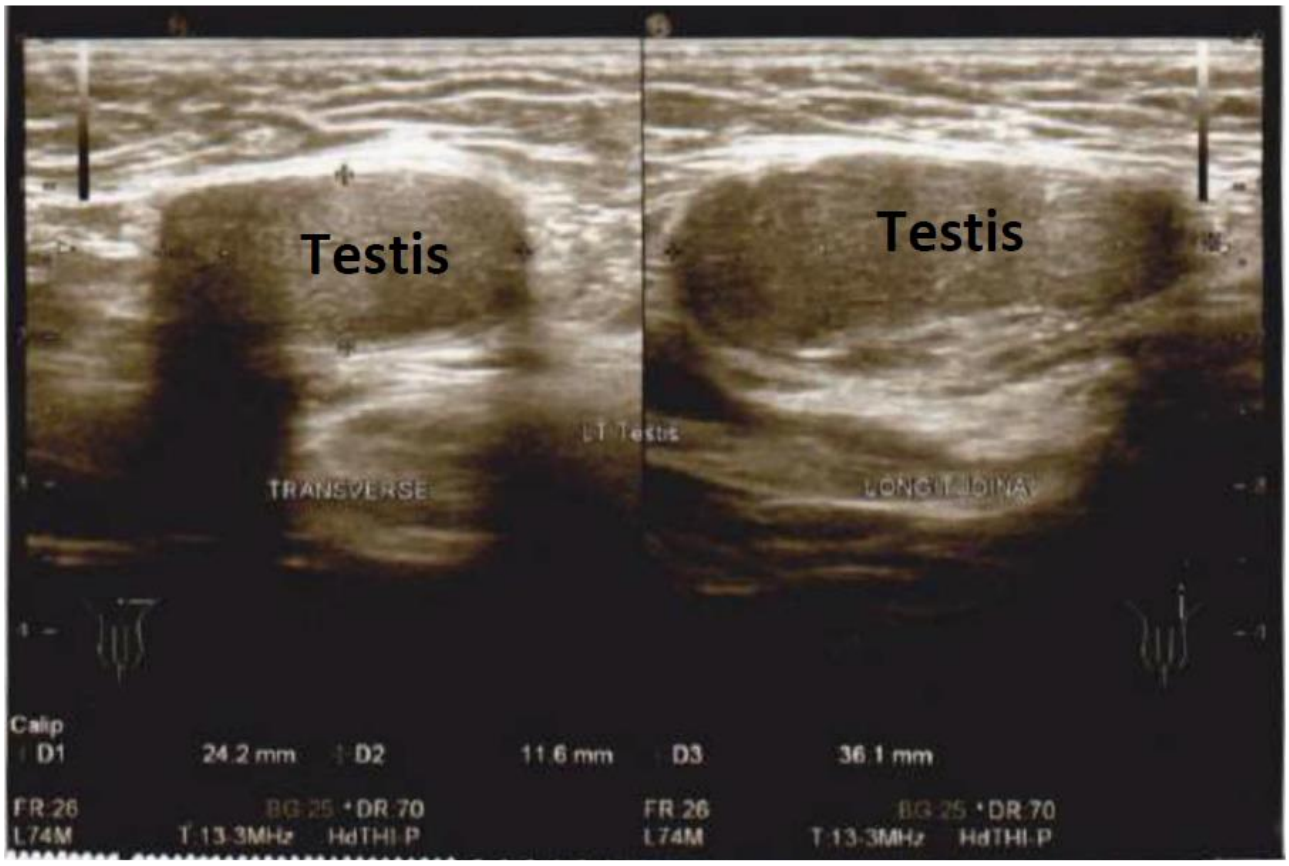

Figure 3. Transverse and Longitudinal view of the left testis located in the inguinal.

DISCUSSION

Primary Testicular Failure in men with unilateral cryptorchidism is a rare case. This case may be the first time reported. We reported a patient who complained of infertility with azoospermia in post-centrifugation sperm analyses. The patient history experiences puberty with secondary sex growth around the age of 17 can rule out the classic type of Klinefelter Syndrome (46, XXY), but the mosaic type is still possible. Autoimmune orchitis with characterized by pain localized to the testicles during palpation, can be without or accompanied by fever. The patient has never experienced these symptoms and signs so we can rule out autoimmune orchitis. The patient had experienced parotitis when he was 11 years old, but the patient did not remember whether there was swelling and pain in the testicles at that time so that viral orchitis might also be ruled out. Trauma, tumors of the testes, or ischemic conditions due to torsion testis or systemic hypotension never occurred.[5–7]

Normal voice, posture, hair distribution (face, armpits, and pubic), penis size, and scrotal rugae indicate hypogonadism after puberty.[8] Hypergonadotropic hypogonadism in this patient can be seen from the small size of the scrotal testes (6-7cc) supported by low testosterone level (336.14 ng / dl), high FSH (60.68 mIU / ml) and LH (15.96 mIU / ml) level. Spermatocele found on ultrasound examination. Cryptorchidism is associated with defects in connection of the ductuli efferentes and ductus epididymidis. In the incomplete form of defect, some of the 5 to 30 ductuli efferentes in the epididymis are short and end blindly. Spermatocele usually arises from blind-ending ductuli efferentes and contains spermatozoa.[9]

Based on the patient history, physical examination, laboratory, and ultrasound findings, primary testicular failure with unilateral cryptorchids is confirmed. In this case, PTF may occur due to idiopathic but

does not rule out the mosaic type of Klinefelter syndrome. Scrotal testicular histology with unilateral cryptorchidism was considered normal in the early 20th century. Scrotal testis was used as a normal control in evaluating undescended testis. Many authors agree with this concept.[10,11] However, currently, various studies mention changes in the development of germ cells in the scrotal testis in patients with unilateral cryptorchidism.[12] The scrotal testis has a slightly increased risk of developing cancer.[13] The increased risk of scrotal testicular cancer is around 1.74 times in patients with unilateral cryptorchidism, and the incidence of azoospermia is 13%.[11,14,15] But testicular failure in unilateral cryptorchidism has no data.

In this case report, the patient has high levels of FSH and LH accompanied by low levels of testosterone with small right scrotal testicular size. FSH level itself is the best biomarker in SCOS and tubular fibrosis (TF).[4] Inhibin B is a relatively better marker of maturation arrest (GCA / MA), hypospermatogenesis (HS). For this reason, the combination of FSH and Inhibin B examination remains the best recommendation for patients with PTF.[1] A Karyotyping examination may also be recommended for this patient. The presence of azoospermia and cryptorchidism accompanied by a range of arms more than height does not rule out the mosaic-type of Klinefelter. However, to suggest a high-cost karyotyping and Inhibin B examination in this patient with very high FSH levels (60.68 mIU / ml) is certainly debatable whether the result will affect the follow-up and outcome. High FSH levels (above 19.4 mIU / ml) indicate no success for sperm retrievals.[16] Management of cryptorchidism must be performed orchidopexy the first year after birth. The American Urological Association recommends surgery for cryptorchidism to be completed by one year in infants who do not experience spontaneous testicular decline until six months (corrected by gestational age).[17] However, the patient has unilateral cryptorchidism for 20 years (from birth), there will be a risk of testicular cancer. Testicular cancer is a type of solid tumor most often occurs in young men aged between 15-34 years.[18] After orchidopexy, monitoring is needed every year until at least 5 years.[19] Physical examination monitoring, especially palpation of the testis, can detect early changes of the scrotal testicular texture. Ultrasound monitoring can be performed if a malignant suspicion is found.

CONCLUSION

Primary Testicular Failure (PTF) occurs when the parenchymal tissue contained in the testes is no longer able to produce sperm or testosterone. Testosterone levels will be normal or low, while FSH levels have increased. PTF diagnosis is only possible through pathology and testicular cytology, but the combination of FSH and Inhibin B examination remains the best recommendation as a biomarker for patients with PTF. Primary Testicular Failure in men with unilateral cryptorchidism may be the first time reported.

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