Case Based Urology Learning Program

Resident's Corner: *UROLOGY*

Case Number 16

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Case Based Urology Learning Program

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A 32-year-old-male presents with a 1-year history of infertility. His wife has normal menstrual cycles and had a normal fertility evaluation from her Gynecologist. The couple has been timing their intercourse with ovulatory predictor kits for the past six months and use no lubricants for intercourse. The patient has also noticed a mild decrease in libido and reduced quality of erections over the last 2 years. The referring Gynecologist obtained a semen analysis prior to the visit.

Semen Analysis:

Volume	2.5 (2 – 5 mL)
pH	7.4 (7.2 – 7.8)
Concentration	0
Motility	0
Morphology	0
Round cells	0
WBC	0

What other history is particularly relevant?

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The patient underwent puberty at age 13, and has always been taller than all of his friends. He denies any history of undescended testicles, mumps, orchitis, or testicular trauma. He relates occasional fatigue. His past medical/surgical/family/social history is negative. He takes no medications. He denies drug use or exposures.

What physical examination findings are particularly relevant?

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General: tall, slender male

Height: 6 foot 5 inches

Long arms and legs

Chest: gynecomastia

Tanner stage: 5

Groin exam: No hernia

Testicular exam: atrophic (5 cc volume bilaterally), firm testicles, no masses

Normal vas deferens and epididymis bilaterally

No varicocele

DRE: small prostate

What is the differential diagnosis for this patient with azoospermia and bilateral severely atrophic testes?

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Klinefelter's syndrome is most likely

Other considerations include:

- Bilateral undescended testicles s/p orchidopexy
- Mumps orchitis after puberty
- Bilateral testicular atrophy

What other diagnostic testing should be considered?

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Repeat semen analysis: Normal volume azoospermia

Endocrine testing:

FSH	21 (1 – 10 mU/mL)
LH	12 (1 – 7 mU/mL)
Total testosterone	180 (220 – 1000 ng/dL)
Estradiol 17B	11 (0 – 60 pg/mL)
Prolactin	5 (2 – 14 ng/mL)

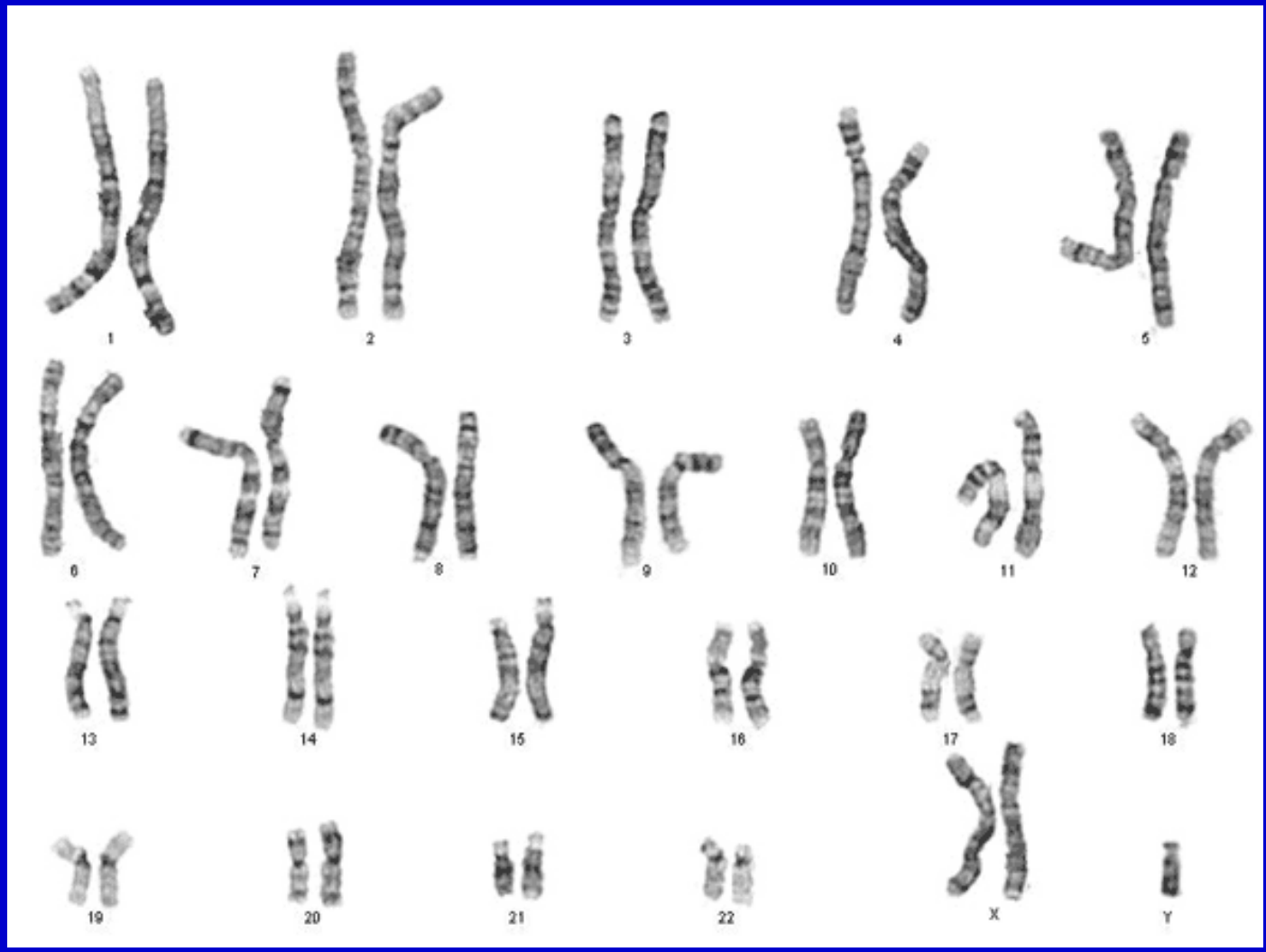
Genetic testing:

Karyotype	47,XXY (Figure 1)
Y-linked microdeletion	Negative for AZFa, b, or c deletion

Testicular US:

- Small atrophic testes with homogeneous appearance
- Normal symmetric blood flow
- No masses
- No varicoceles

Figure 1



Klinefelter’s syndrome. Karyotype = 47,XXY.

What is the diagnosis?

What is the diagnosis?

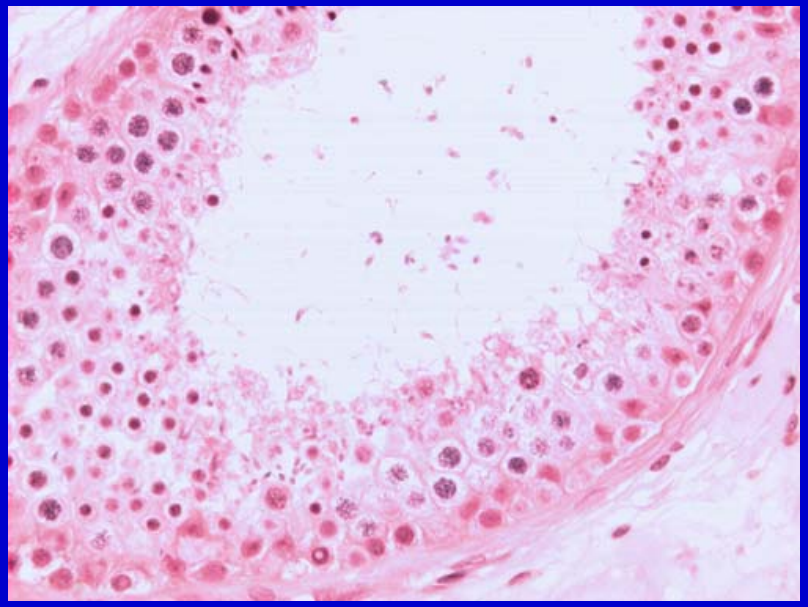
Klinefelter's syndrome with primary testicular failure. The markedly elevated FSH indicates primary testicular failure.

How should this patient be managed?

How should this patient be managed?

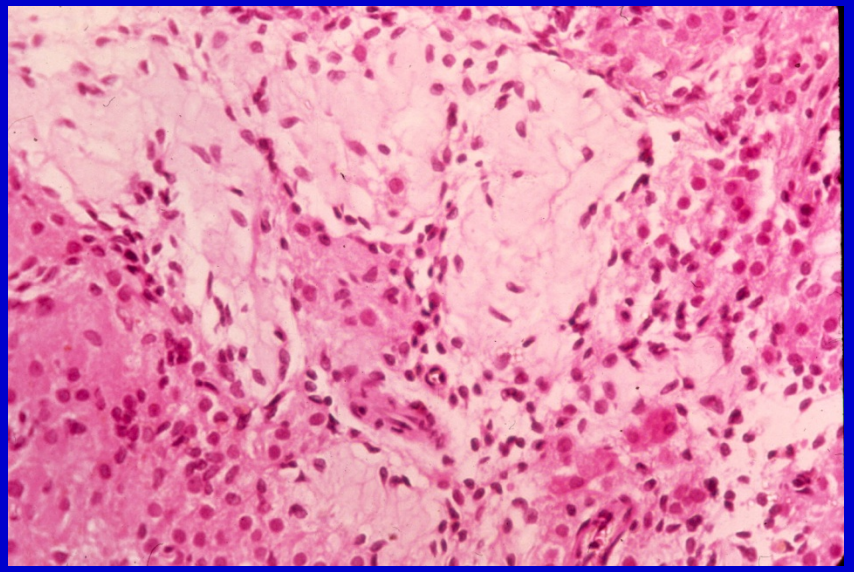
Even though the patient demonstrates azoospemia on two separate semen analysis, sperm may be successfully found in approximately 2/3 of males with Klinefelter's syndrome undergoing testicular sperm extraction (TESE – **Figure 2a & b**) or microdissection TESE (**Figure 3 & 4)**. This sperm can be used for IVF/ICSI to achieve pregnancy.

Figure 2a



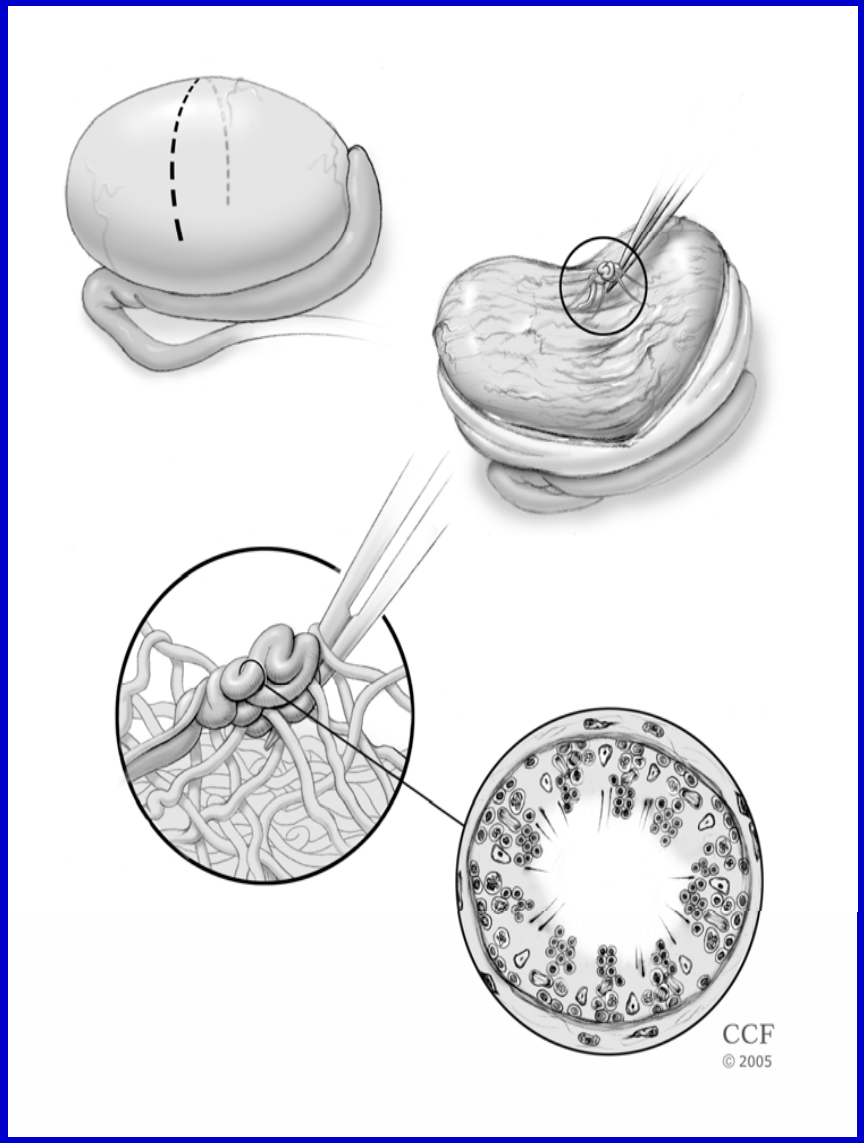
Normal testicular tissue

Figure 2b



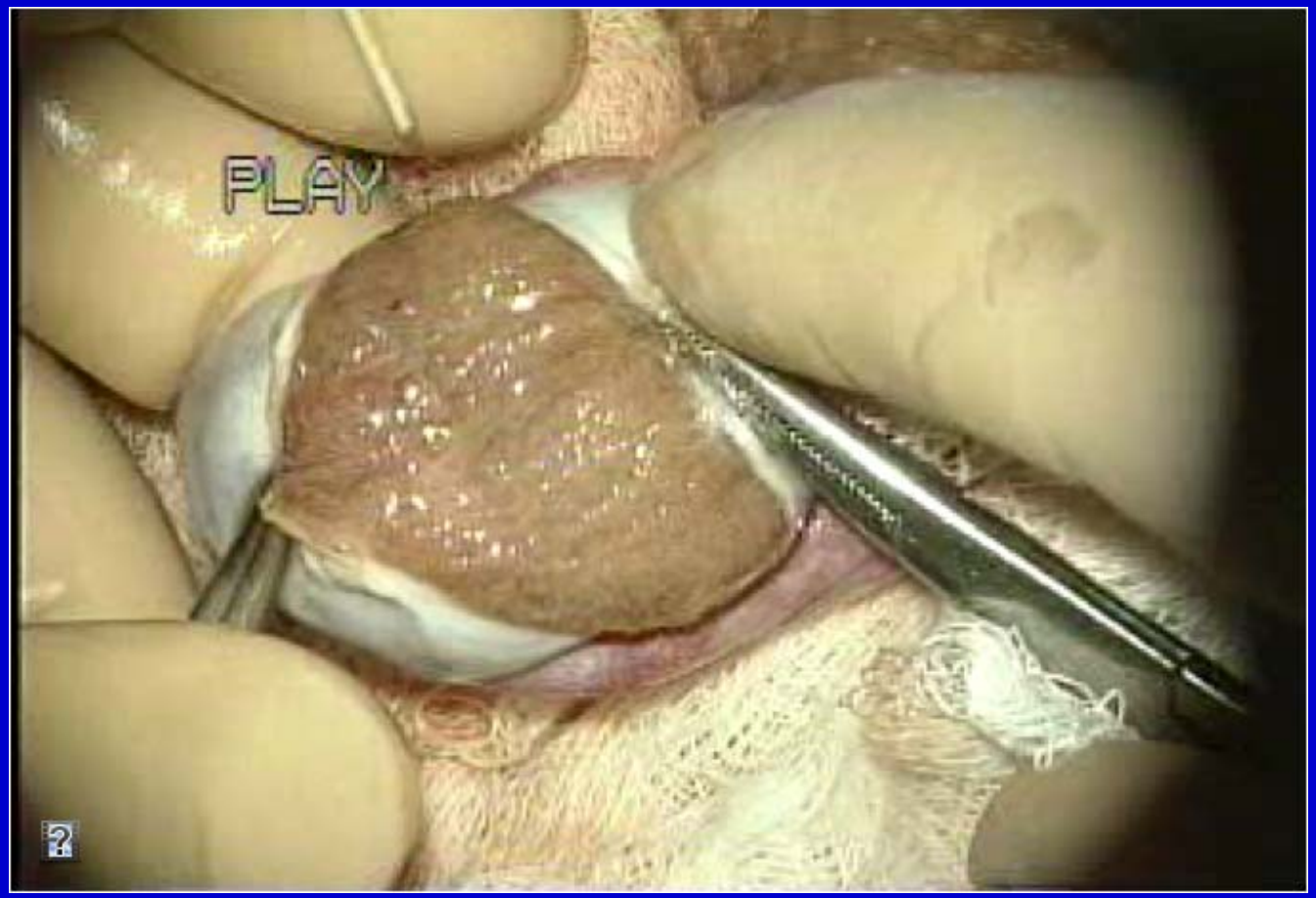
Klinefelter’s testicular biopsy with sclerotic tubules

Figure 3



Microdissection testicular sperm extraction (MicroTESE). Larger tubules are identified under 25X magnification and extracted. They are more likely to contain sperm.

Figure 4



Microdissection TESE. The testicle is bivalved and the seminiferous tubules are examined under high magnification (20 – 25X).

How common is Klinefelter's syndrome?

How common is Klinefelter's syndrome?

Klinefelter's syndrome (47,XXY) occurs in 1/500 to 1/1000 live births. It is found in approximately 10% of men with azoosperimia and is the most common genetic cause of non-obstructive azoospermia. It is important to send these couples for genetic counseling prior to any fertility intervention. Live births of children with normal 46 XX or XY karyotype have been reported. However, there is a slight increase in sex-chromosomal abnormalities (0.9%) and autosomal disomy (7.5%).

Are men with Klinefelter's syndrome at risk for other medical problems?

Are men with Klinefelter's syndrome at risk for other medical problems?

Men with Klinefelter's syndrome need lifelong follow-up. They are at risk for osteoporosis, heart disease, and metabolic syndrome due to the hypergonadotrophic hypogonadism. However, testosterone replacement therapy should not be started until any fertility issues have been addressed and treated. In addition, these patients have an increased risk of developing breast cancer, non-Hodgkin's lymphoma, and mediastinal germ cell tumors.

How often is Klinefelter’s syndrome associated with the prototypical body habitus: tall, long arms and legs, etc.?

How often is Klinefelter's syndrome associated with the prototypical body habitus: tall, long arms and legs, etc.?

Most men with Klinefelter's syndrome do not have this phenotype. Any man with severely atrophic testes, particularly if associated with azoospermia or severe oligospermia, should be considered for having this syndrome.

Selected Reading

Lanfranco F, Kamischke A, Zitzmann M, Nieschlag E. Klinefelter's syndrome. *Lancet* 2004;364:273-83.

Ramasamy R, Ricci JA, Palermo GD, Gosden LV, Rosenwaks Z, Schlegel PN. Successful fertility treatment for Klinefelter's syndrome. *J Urol* 2009;182:1108-13.

Topic:

Male Fertility/Benign Testis

Subtopics:

Azoospermia, Klinefelter’s Syndrome