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CRYPTORCHIDISM

Developed by Paige Murphy and Dr. Kirsten Miller for PedsCases.com.

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Introduction:

Hello, my name is Paige Murphy and I am a third year medical student at the University of British Columbia in their Northern Medical Program. This podcast was developed with the help of Dr. Kirsten Miller, a pediatrician at the University Hospital of Northern B.C. Today I will be discussing cryptorchidism, which refers to undescended or absent testes. This is something that you could run into during a typical newborn exam or during well child checks, so it is important to have a good understanding of the condition.

Learning Objectives:

The learning objectives for this podcast are as follows:

1. Describe the epidemiology of cryptorchidism and the relevant risk factors
2. Be able to appropriately evaluate the condition with a targeted history and physical exam
3. List a differential diagnosis based on your clinical findings
4. Describe the rationale behind treatment and the principles of management

Clinical Case:

Let's begin with a case. You are examining a 1-day-old male infant prior to discharge. He was born at 36 weeks and had an average birthweight for his gestational age at 2800g. The pregnancy was uncomplicated and his newborn period up until now has been unremarkable. When you perform your newborn exam, you are unable to palpate

the left testis and think you might feel a lump in the inguinal canal. The right testis is palpable and there are no other genital anomalies. The rest of the exam is normal. You suspect cryptorchidism, but you want to review the topic before speaking with the parents. What risk factors did this baby have for undescended testes? What are you looking for on physical exam? Why is it important to properly diagnose this condition? And what follow-up and treatment will you discuss with the parents? Let's move on to some information to help you answer these questions.

Epidemiology:

Cryptorchidism is the most common urogenital anomaly in male infants. It refers to the state of an absence of one or both testes from their typical anatomical position in the scrotum (1). The word cryptorchidism comes from the Greek "kryptos", meaning hidden and "orchis", meaning testis. It occurs in 1-5% of full term male neonates and up to 45% of preterm male neonates (2). In many cases, the testes will spontaneously descend, so the prevalence reduces to 1% of all males at one year of age (2).

Risk Factors:

The main risk factors for cryptorchidism are preterm birth and babies who are small for gestational age at birth or have a birthweight of less than 2500g (3,4). It is usually an isolated condition but can be seen as a part of over 400 genetic syndromes (1). Two conditions where cryptorchidism is common are Prune Belly or Eagle Barrett syndrome and Klinefelter syndrome. Prune Belly Syndrome presents with undeveloped abdominal wall muscles, severe renal and urinary tract anomalies, and undescended testes which are usually intraabdominal. Klinefelter syndrome is a condition with an XXY karyotype which also commonly presents with cryptorchidism (5).

Embryology and Natural History:

Testicular descent represents a multifactorial process that involves genetic, hormonal and environmental influences. Testicular development begins in the abdomen when sexual differentiation occurs at 7-8 weeks' gestation (6). The gonads descend within the abdomen from 10-15 weeks and then they descend through the inguinal canal into the

scrotum between 25-35 weeks, assisted by a fibrous structure known as the gubernaculum (6,7).

After birth, some undescended testes will complete their descent by 4 months of age. After 4 months of age, testes are unlikely to descend spontaneously and require surgical intervention.

Treatment Rationale:

If you do suspect cryptorchidism in a child, it is important to refer them to a pediatric urologist or pediatric surgeon in a timely manner in order to avoid potential serious long-term consequences.

First, cryptorchidism is one of the main risk factors for testicular cancer. Testicular cancer makes up approximately 1% of cancers in Canadian males (10). Despite the low absolute risk, an individual with cryptorchidism is 2.75-8 times more likely to develop testicular cancer in their lifetime than a member of the general population (11). Patients who have surgical correction after puberty are 3-6 times more likely to develop testicular cancer than cryptorchid patients who undergo prepubertal orchidopexy (12). Surgical intervention may reduce the risk of developing testicular cancer, but these patients are still at increased risk throughout their lives. An important benefit of repair is being able to more accurately monitor for testicular cancer and detect it an earlier stage.

Second, there is an increased rate of infertility in men with cryptorchidism (8). This is thought to be due to loss of both Leydig and germ cells when they are in abnormal anatomic locations. While most men with unilateral cryptorchidism are still fertile, they do have higher rates of infertility than the general population. Bilateral undescended testes have a significant risk of infertility. This effect is amplified when treatment is delayed or when the gonads develop intraabdominally (9). Treatment prior to 2 years of age likely improves outcomes, but some men with cryptorchidism may have subfertility throughout their lives.

There are other risks of cryptorchidism which include testicular torsion and trauma in some ectopic locations, due to their proximity to the pubic bone (1).

Differential Diagnosis:

When considering the differential diagnosis for cryptorchidism, first determine whether the testis is palpable or not.

If it is palpable it could be one of three diagnoses:

1. The first is a **true undescended testis**, which is palpable in the inguinal canal up to the external ring. This diagnosis refers to the fact that the testis is located somewhere along the normal anatomical path of descent, but not within the scrotum (1).
2. The second option is an **ectopic testis**, which means that the gonad has developed somewhere outside of the normal path of descent. The most common sites are in the suprapubic, perineal or femoral areas (13)
3. The third consideration with palpable cryptorchidism is a **retractile testis**. This occurs when the testis is absent from the scrotum due to an overly strong cremasteric reflex but can be brought into the correct position by overcoming that reflex during your physical exam. It can often be difficult to distinguish between a true undescended testis and a retractile one. Retractile testes are not associated with the same complications as undescended testes.

If there is a unilateral non-palpable testis, keep undescended or ectopic testes on your differential, but also consider the possibility of an absent testis. This can occur due to testicular agenesis or intrauterine vascular compromise.

While cryptorchidism usually presents unilaterally, up to one third of cases are bilateral (14). If the testes are not palpable bilaterally in the newborn or if there are other physical abnormalities such as hypospadias, where the urethral opening is on the ventral surface of the penis, the infant should be evaluated for a disorder of sex development, or DSD. Gender assignment should be deferred. An important diagnosis to consider in an infant

with ambiguous genitalia is Congenital Adrenal Hyperplasia, which presents with virilization in 46XX infants, and can be associated with adrenal insufficiency and life threatening salt wasting crises (1). Other DSDs are not as urgent and can be further evaluated by Pediatric Endocrinology or Genetics.

Evaluation:

It is important to diagnose cryptorchidism in a timely fashion in order to proceed to the appropriate treatment. A proper evaluation consists of both a thorough history and a focused physical exam, keeping in mind the differential diagnosis we have just discussed.

During the history, you should ask about any abnormalities during the pregnancy, the gestational age at birth, the birth weight and any documentation of palpable testes during the standard newborn exam and subsequent checks. You should also inquire about the child's medical history and surgical history.

The physical exam should take place in a warm, comfortable room, and should begin by removing all clothing from the lower half of the child. Begin by inspecting the scrotum for any asymmetry or signs of hypoplasia. Look for any evidence of ambiguity and the presence of hypospadias. You should also look for any qualities suggestive of a genetic syndrome such as dysmorphic features or midline defects. Before palpating, warm up your hands. When palpating, ensure that the child is in a frog leg position, with the thighs abducted as this helps to dampen the natural cremasteric reflex. Place one hand over the inguinal canal, gently sweep that hand towards the scrotum, and position the other hand over the scrotum to feel if the testis becomes palpable. If you are able to bring the testis into the scrotum, hold it there for one minute to fatigue the cremasteric muscle. If it remains in the scrotum after this maneuver it is more likely to represent a retractile testis whereas if it immediately springs back to its original position this is more likely to indicate a true undescended testis. If you are unsure of the diagnosis, it is reasonable to refer the patient to a pediatric urologist or surgeon who can better differentiate the two conditions. If you are able to palpate the testis, take note of the

size, position, mobility and consistency, compared to the contralateral side. Hypertrophy can be seen in the normally located testis and indicates a higher chance of an absent or atrophic cryptorchid testis. You should also examine the child for the presence of any hernias or hydrocele to complete your exam. If the testis is not palpable in the scrotum or inguinal canal, then you should proceed to evaluate the perineal or femoral areas for an ectopic testis (15)

The Canadian Urological Association, or CUA, does not recommend imaging in the standard workup of cryptorchidism (1). MRI and CT modalities should be avoided due to the necessity of anesthesia and risks of cumulative ionizing radiation, respectively. Ultrasound imaging is also not useful, because the results are not always congruent with physical exam findings and wait times can delay referral (16).

Routine karyotype analysis is not recommended because the rate of genetic abnormalities in boys with persistent cryptorchidism is only between 5-8%. However, it could be considered if other features of a DSD are present (1).

Management:

Now let's move on to management. The CUA has an excellent flowchart for management that is based on your findings in the newborn exam. If you would like further information on this topic, their publication titled "Guideline for the Diagnosis, Management, and Follow-up of Cryptorchidism" is a useful guide. In the meantime, I'll walk you through the steps you should take given these different findings.

1. If a child initially has a normal genital exam, they should have routine exams during well child checks, but require no further follow up (1).
2. If the testes are retractile, the infant should be re-evaluated between six months and one year of age. If the exam is normal at that time, the infant can return to routine well child checks. If the exam at that time is consistent with cryptorchidism, they should be referred to a pediatric urologist for surgical consultation (1).

3. If the child is found to have cryptorchidism during their initial newborn exam, they should be re-examined at 3-6 months based on their adjusted age. If the diagnosis persists at that time, they should also be referred to the pediatric urologist (1).

Hormonal therapies are not recommended as a first line treatment. You may see that HCG and LHRH therapies have been used to promote gonadal descent and GnRH has been used to improve fertility, but both lack clear therapeutic standards and efficacy data (1).

The mainstay of treatment for cryptorchidism is surgery, with the goals of reducing the risk of torsion or injury, maintaining fertility, and reducing the risk of testicular cancer.

If the gonad ***is*** palpable, an orchidopexy is performed. This procedure relocates the gonad to the correct anatomic position where it is at lower risk of injury, and more conducive to future self-examination, in the context of testicular cancer risk (1). This procedure should take place between 6 and 18 months, to avoid long term sequelae, as most gonads will not spontaneously descend after 4 months (1). The decision of whether to use an inguinal approach or a scrotal approach should be individualized based on the patient and surgeon.

If the gonad is ***not*** palpable at 6 months, further exploration of the inguinal canal and abdomen are required to locate the testis. Then an orchidopexy can be performed to bring it to the correct location, or it can be excised if necessary.

If cryptorchidism is first diagnosed after puberty, orchiectomy, surgical removal of the testis, may be recommended as this cohort has an increased risk of testicular cancer (1).

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In the case of a child with a genetic syndrome such as Trisomy 21 who requires an orchidopexy, it is reasonable to wait until they are optimized for anesthesia and surgery rather than adhering to a strict timeline (1).

Case Wrap-up:

Let's return to our case. After learning about cryptorchidism, you realize that this baby was born prematurely, and therefore had one of the risk factors we discussed. Now that you are more informed about the natural history of the condition, its long term effects and treatment approaches, you are able to talk to the parents of this baby to arrange an appropriate follow up plan. You agree to see the child again at 3-6 months adjusted age. At this second appointment you are able to palpate the testis within the scrotum and believe that his previously undescended testis has resolved. You will recheck in 6-12 months and if his exam is unchanged, you will progress to routine monitoring during well child checks. If the testis remains properly located, he will not require surgery which his parents are very relieved to hear.

Summary:

That concludes our podcast. As a summary, here are five key takeaway points:

1. Cryptorchidism is the absence of one or both testes from their normal anatomic position and is very common at birth.
2. Risk factors for cryptorchidism are low birth weight, prematurity and being small for gestational age.
3. Infertility and testicular cancer are two potential adverse outcomes if the condition is not diagnosed and treated in a timely manner.
4. The differential diagnosis for cryptorchidism includes undescended, retractile and ectopic testes, and each has their own clinical findings and management. If you are ever unsure you should seek a pediatric urology or surgery consult to confirm.
5. Surgery is the main treatment modality for cryptorchidism and orchidopexy is a procedure to relocate the testes to the scrotum. It is ideal to perform this surgery between 6-18 months so a timely referral to a pediatric urologist is essential.

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Thank you for listening to this podcast. I hope it helped give you a basis of understanding of cryptorchidism that you can use on your rotations and in your future practice. And thank you to Dr. Miller and the PedsCases team for their help in developing this podcast!

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