

Case report: Do peripheral testosterone concentrations differ between dogs with abdominal testicles and scrotal testicles? Clinical implications

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Summary

Cryptorchidism is an important clinical problem and it is not fully known if testosterone production is affected because of the location of the testicles. Hence the peripheral concentrations of testosterone in a cryptorchid dog were measured and compared to dogs with scrotal testicles. Further, the response in testosterone production to human chorionic gonadotropin (hCG) was determined in this cryptorchid dog. Baseline testosterone concentrations (209 ng/dL) in the cryptorchid dog were comparable to those in dogs with scrotal testicles (246 ± 255.25 ng/dL). Testosterone concentrations increased to 400 ng/dL after hCG injection in this cryptorchid dog. Two structures that appeared to be testicles were removed during a laparotomy. Histologic examination of these structures indicated that one of these structures did not contain testicular tissue, but did contain epididymal and rete testis tissues. Peripheral testosterone concentrations determined five weeks after surgery were < 20 ng/dL suggesting that no testicular tissue remained. Pre- and post-injection testosterone concentrations were also < 20 ng/dL during a subsequent hCG stimulation test.

Background

Leydig cells, also known as interstitial cells of Leydig, are found adjacent to the seminiferous tubules in the testicles. They produce testosterone in the presence of luteinizing hormone (LH). Leydig cells are polyhedral in shape, display a large prominent nucleus, and have an eosinophilic cytoplasm with numerous lipid-filled vesicles. Mean baseline peripheral concentration of testosterone in non-castrated dogs is 2.44 ± 0.41 ng/mL.¹ Testosterone production may be influenced by factors such as testicular pathology and the location of the testicle in the body.²⁻⁴ Lower production of testosterone may result in reduced sexual function⁵ and possibly abnormal sperm production.⁶ Researchers have reported that there is no compensatory production of testosterone by a normal testicle when the contralateral testicle was abnormal⁴ or absent⁷. Testicular production of testosterone is measured by determining its concentration in peripheral blood.⁸ Testosterone concentrations may be influenced by the time of day when a blood sample is obtained,^{9,10} the breed of dog,¹¹ and the laboratory and type of assay utilized. Gonadotropin releasing hormone (GnRH) or hCG can be administered to test the presence of testicular tissue since these compounds stimulate Leydig cells to synthesize testosterone. Gonadotropin releasing hormone elicits this response by its ability to stimulate release of LH from the anterior pituitary gland followed by LH action on Leydig cells while hCG acts directly on the Leydig cells since it has LH-like activity. However, the response in testosterone synthesis by the Leydig cells to these compounds may be different¹² and further, it is not known if the response is influenced by the testicular histology.

Cryptorchid conditions have been reviewed and identified as an important clinical problem.¹³ It is not fully known whether testosterone production is affected in testicles because of their location. Some investigators found that the endocrine function in retained testicles is normal despite exposure to core body temperature.^{14,15} However, one study found that the testosterone concentrations were lower in unilateral cryptorchid dogs compared to dogs with scrotal testicles.¹⁶ Later these researchers reported that the testosterone concentrations were also lower in bilateral cryptorchid dogs compared to dogs with scrotal testicles.¹⁷ It was suggested that the higher temperature due to location of the testicle might decrease the conversion of cholesterol to androgen at the testicular level. A recent study found lower concentrations of testosterone in a bilateral cryptorchid dog.⁴

Hence in this present clinical study the peripheral concentrations of testosterone in a cryptorchid dog were measured and compared to dogs with scrotal testicles. Further, the response in testosterone production to hCG stimulation was determined in this cryptorchid dog.

Case Presentation

A five-year-old male boxer was adopted by a client three years prior to presentation from a local humane society. The original owner of the pet informed the humane society that the dog has not been castrated nor had they noticed evidence of testicular descent. After being adopted, the dog was given a complete physical examination in a local veterinary hospital and the client was informed about the potential complications of bilateral cryptorchidism. No further diagnostic tests were performed.

The dog had normal behavior and there was no evidence of aggression. However, it was noted that the dog lifted one of its hind limbs while urinating and also marked the fence or the cage. The scrotal and inguinal areas were palpated while the dog was conscious and anesthetized and there was no evidence of testicle(s). The client was informed that abdominal testicle(s) can become neoplastic and also informed that a stimulation test is available to determine if a testicle is present. The client decided to have the test conducted. No attempt was made to collect semen for evaluation. The dog weighed 85 lbs.

Two blood samples were obtained in the early afternoon, one before and one 60 minutes after 1,000 IU hCG^{8,18} (Chorulon[®], Intervet/Schering-Plough Animal Health, Millsboro, DE) was administered intravenously. Serum testosterone concentrations were determined in a commercial laboratory (Clinilab, Valparaiso, IN) by chemiluminescent enzyme immunoassay (Immulite, Diagnostic Products Corporation, Los Angeles, CA). The testosterone concentrations were 209 and 400 ng/dL before and after injection, respectively.

Treatment

A decision was made to conduct an exploratory laparotomy. Prior to induction of anesthesia, the patient was given atropine (1.6 mg SC) and carprofen (150 mg PO). Anesthesia was induced with ketamine (200 mg IV) and diazepam (10 mg IV). The dog was intubated and maintained on isoflurane for the duration of the procedure. A ventral midline incision was made from the umbilicus to the pubis. The right testicle was visible immediately when the abdomen was opened. The testicular vessels and ductus deferens were clamped and double ligated. Tissue that appeared to be the left testicle was more difficult to locate but was visible after the urinary bladder was moved to the right and the intestines were moved cranially. The ductus deferens was visible along with a narrow small white to pale blue object (approximately 1.5 x 1.5 x 0.5 cm). It had a visible ductus deferens cranially and a fibrous band of tissue caudally. The fibrous tissue and ductus deferens were clamped and ligated and the tissue excised. The abdominal incision was closed routinely and postoperative recovery was uneventful.

Outcome

The histopathology report indicated that the specimen obtained from the right side contained testicular, epididymal, and rete testis tissues. There was a diffuse loss of seminiferous epithelium and the tubules were lined by Sertoli cells. The Leydig cells were found to be mildly hyperplastic. The specimen from the left side contained epididymis and rete testis tissue but lacked testicular tissue. The testosterone concentration determined five weeks after surgery was < 20 ng/dL which was consistent with the absence of testicular tissue. The dog continued to lift its leg while urinating and also marked with urine.

To compare baseline testosterone concentrations blood samples were obtained in the early afternoon from seven dogs with scrotal testicles. Their ages ranged from 1.5 to 7 years and their weight ranged from 24 to 72 lbs. They belonged to different breeds (1 boxer, 1 beagle, 1 Boston terrier, 1 pit bull and 3 mixed breed) and their average testosterone concentrations ranged from 50.3 to 750 (mean 246 ± 255.25) ng/dL.

Discussion

To minimize the influence of diurnal variation in serum testosterone concentrations, blood samples were collected in the early afternoon. Baseline serum concentrations in this cryptorchid dog and in the dogs with scrotal testicles were similar. In other words, the amount of testosterone produced by one abdominal testicle was similar to dogs that had two scrotal testicles. It should be pointed out that three of the control dogs had lower testosterone concentrations (50.3, 58.9, 80.8 ng/dL) than this

cryptorchid dog. However, it is not known whether these dogs with lower testosterone production had normal testicular histology or poor sperm production. Despite the abnormal histopathology of the abdominal testicle, testosterone production was similar to scrotal testicles. It is interesting to note that there is a possibility of reduction in testosterone production by an abdominal testicle¹⁹. The correlation between histopathological changes in Leydig cells and testosterone production in abdominal testicles needs to be characterized. There was evidence of mild hyperplastic changes in Leydig cells in the abdominal testicle. It is not known whether these changes contributed to normal baseline testosterone concentrations in this dog. Since only one dog was used in the present study, cautious interpretation of findings is necessary. Further studies with adequate number of cryptorchid dogs are warranted.

The positive response in testosterone production to an hCG stimulation test suggested the presence of abdominal testicle(s). Given the cost of testosterone assays, an hCG stimulation test was not conducted in control dogs. Although this test has been used in studies,^{8,18} reports of its application to detect the presence of retained testicles in clinical cases are scarce. One study found that there was no difference in response to hCG in a bilateral cryptorchid dog.²⁰ In another study GnRH was used in the place of hCG,²¹ however, the efficacy of one compound over the other is not known. It is not clear how much of an increase in testosterone concentrations one can expect and the best time to detect such an increase. Further, it is not known whether this increase will be the same whether the animal has one or two testicles. A clinical investigation is necessary to address these issues.

Although we did not determine the type of sperm production in this dog prior to surgery, an existing report²² indicated that testosterone concentrations may be lower in azoospermic dogs. These workers reported that the response to GnRH stimulation was delayed and lower in azoospermic dogs compared to dogs with normal sperm production.²³ Since the histopathology findings of this abdominal testicle suggested that there was a diffuse loss of seminiferous epithelium one can speculate that there would not have been any sperm production. Failure to notice changes in urinating and marking behavior despite the removal of testicle is an important clinical observation. While it is not known whether castrated dogs would continue to lift their legs while urinating it is known that some castrated dogs will continue to have marking behavior.²⁴

Learning points

Based on these findings it is evident that an abdominal testicle can produce testosterone concentrations similar to those produced by scrotal testicles even in the presence of histological evidence of lack of sperm production. It is possible to detect the presence of abdominal testicle(s) by determining testosterone concentrations before and after a challenge test using hCG. An important clinical observation was that the urination and marking behavior remained despite removal of the abdominal testicle and after testosterone concentrations reached those of neutered dogs.

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