

Seminomas and an interstitial cell tumor in an 8 year old male Husky

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Summary

An eight year old male Siberian Husky was presented for semen collection and assessment. Gross testicular asymmetry with an enlarged, firm, oval-shaped left testis and a small, atrophied right testis was found on palpation. There were no scrotal lesions or a history of any trauma involving the scrotal contents. The proportion of motile sperm in the ejaculate was 30%, and only 25% of his sperm were classified as morphologically normal. The predominant morphological defect present was proximal droplets. Testicular ultrasonography revealed a large mottled mass of mixed echogenicity in the left testis and a smaller mass in the right testis. A routine, bilateral closed castration procedure was performed and the testes were submitted for histopathologic assessment. The mass in the left testis was confirmed to be a seminoma and the mass in the right testis was diagnosed as an interstitial cell tumor. An intra-tubular seminoma was microscopically present as well in the right testis. Evidence of secondary testicular degeneration adjacent to both tumors was also observed.

Background

This case report describes a classic seminoma with an incidental finding of an interstitial cell tumor (ICT) in a dog. Although the presence of multiple tumors is not uncommon in the dog, this particular case had a different form of seminoma in each testis, in addition to an ICT. Although this case is not a novel topic, this is the first published indepth case report of multiple testicular tumors in bilaterally descended testes in a dog. Other thorough reports have been either retrospective histopathologic studies,¹⁻⁶ lesions in retained testes,⁷⁻¹⁰ or single testicular tumors.¹¹

There is significant variation in the literature in regards to the incidence rate of the different types of canine testicular tumors. The term “Leydig cell tumor” can be used interchangeably with ICT, but for the remainder of this paper, the tumor will be referred to as an ICT. In a study by Grieco et al, ICTs were the most commonly reported testicular tumors followed by seminomas.² D’Angelo et al reported that the seminoma was the most commonly diagnosed canine testicular tumor type followed by Sertoli cell tumors.⁶ Another retrospective study by Liao et al found that seminomas were the most common testicular tumor diagnosed in dogs followed by ICTs.³ The reason for this variation may be due to geographic differences and also breed and genetic differences between the populations involved in these studies. It can be concluded from all these reports and previous studies that the seminoma, Sertoli cell tumor, and interstitial cell tumor are the three most commonly diagnosed canine testicular neoplasms.^{2-4,6,12-14}

Seminomas originate from the spermatogenic cells of the seminiferous tubules. They are typically a soft tumor, measuring from one to ten cm in diameter.¹³ Usually they are benign, but 5-10% can metastasize to inguinal, iliac, and sub-lumbar lymph nodes.¹³ Other sites of metastasis include the lungs, liver, spleen, kidneys and pancreas with one case reported with aberrant metastases to the skin.^{11,13} Seminomas in the dog are reported to be found more often in scrotal testes than retained testes, but in regards to retained testes, they are more commonly found abdominally than inguinally. On the cut surface, they are colored cream to pinkish gray to tan-colored.¹² Although an uncommon presentation, paraneoplastic syndromes of seminomas consist of progressive, non-pruritic alopecia with hyperpigmentation of the trunk, prostate disease, and non-insulin dependent diabetes mellitus.^{12,13} Seminomas frequently begin as the intratubular form, in which the seminiferous tubules are overgrown with seminoma cells and multiple layers of neoplastic Sertoli cells may stretch across the tubule. This was the presentation of the seminoma found in the right testis in our case study. They can also spread to the “diffuse form,” in which tumor cells are not confined to the seminiferous tubules and instead form broad sheets.^{4,15} This form of seminoma was found in the left testis of our case report. In human literature, seminomas are classified as “classical” or “spermatogenic” based on morphology, histochemistry, and

immunohistochemistry findings. This classification system has not been uniformly adopted in the veterinary field but has been advocated as beneficial by some pathologists.^{1,15} Canine seminomas tend to resemble the human “spermatogenic” seminoma in that they are often benign and originate from post-pubertal germ cells, but they can also have the “classical” characteristics of cancerous *in situ* cells and inflammatory lymphocytic infiltrates, as seen in the left testis of this case.¹⁵ Due to the incongruity of the human literature, this paper will refer to seminomas as intratubular or diffuse.

Interstitial cell tumors are derived from the interstitial cells adjacent to the seminiferous tubules in the testes. They are typically small, discrete (0.1-0.2 cm in diameter) masses that are difficult to palpate and are often an incidental finding. When palpation is possible, they are soft and nodular. They are typically yellow to brown in color. They are almost always benign.^{13,14} Unlike some of the other testicular tumors, cryptorchidism is not a predisposing factor for ICTs. An associated paraneoplastic syndrome has been reported with the presence of ICTs. Clinical signs seen are associated with hyperestrogenism (bone marrow suppression, pale mucous membranes, prolonged bleeding, bilateral symmetric flank alopecia) or hypertestosteronism but most often, clinical signs are absent.¹²

Case presentation

An eight year old male Siberian Husky was presented for semen collection and assessment for artificial insemination at Glenbred in Matamata, New Zealand. He was a reproductively proven dog, having sired a litter three years previously. On physical examination, he was bright, alert, and responsive with a body condition score of 5/9. He had pink mucous membranes with a capillary refill time of less than two seconds. Skin and coat were clean and in good condition. Chest auscultation was within normal limits. No enlarged peripheral lymph nodes were palpated. Abdominal palpation and the rest of the physical examination were unremarkable. There was no evidence of paraneoplastic syndrome.

On reproductive examination, a significantly enlarged left testis and a soft, smaller atrophied right testis were detected on palpation. The entire scrotal circumference measured nine cm. The left testis was large, firm in consistency, and oval-shaped. The left epididymal tail and spermatic cord were difficult to palpate. The right testis was soft in consistency and smaller in size compared to the left testis. A prominent but not enlarged right epididymal tail was palpated. There were no scrotal lesions or evidence of trauma. His non-erect penis and prepuce appeared anatomically normal with no evidence of inflammation, masses or trauma.

Manual collection of an ejaculate was performed using the open hand technique. The ejaculate was fractionated into the pre-sperm, sperm-rich and post-sperm fractions. The dog demonstrated a good libido with the presence of a bitch in standing heat. Samples were taken from the sperm-rich (“raw”) fraction of the ejaculate immediately after collection for microscopic assessment. Total motility was subjectively assessed on a warm stage under X100, X200 and X400 magnification. This evaluation was repeated after tris-based extender was added as well. Sperm motility was classified as poor with only 30% of sperm in the ejaculate demonstrating progressive motility. A dry smear was made from a semen sample taken from the sperm-rich fraction and was stained using Wright’s Giemsa stain (Diff-Quik: New Zealand Veterinary Pathology, Hamilton NZ). Assessment under X1000 magnification with oil emersion and differential interference contrast (DIC) found only 25% of sperm were classified as morphologically normal with 49% of the abnormal sperm having proximal droplets, 15% with coiled tails, 8% with detached heads, and 3% with distal midpiece reflex tail defects. Less than five inflammatory cells (neutrophils) per high-powered field (HPF) were seen and no abnormal cells (round, Sertoli, Leydig, or epithelial cells) were detected. The sample volume was 1.5 mL with a concentration of 105×10^6 spermatozoa/mL for a total of only 157.5 million spermatozoa in the ejaculate.

Ultrasonographic examination of the scrotal contents was carried out in B-mode using an Esaote MyLab™30 VET Gold ultrasound with a variable frequency (9-3MHz) micro-convex transducer. Sedation with acepromazine (0.01 mg/kg SQ) and morphine (0.4 mg/kg SQ) was given prior to the ultrasonographic examination. The smaller right testis dimensions were 4.22 cm x 1.62cm x 1.93cm. An ovoid mass with the dimensions 1.10 cm x 0.76 cm was visible within the testicular parenchyma at the caudal pole of the testis (Figures 1a and 1b). The mass had smooth borders and was homogenous and

hypoechoic compared to the surrounding normal homogenous testicular parenchyma. Dilation of the vessels of the right pampiniform plexus was apparent. There were no obvious changes to the right epididymis.

The larger left testis dimensions were 5.31 cm x 3.48 cm x 3.61 cm. A large mass with the dimensions 4.11 cm x 3.44 cm x 3.54 cm was visualized within the testis. Its size was such that only a thin rim of normal homogenous appearing testicular tissue was present around the periphery of the mass (Figures 2a and 2b). The mass had irregular borders and a mixed echogenicity but it was mostly hypoechoic. There was significant dilation of the vessels of the left pampiniform plexus. There were no apparent ultrasonographic changes to the left epididymis.

An exfoliative cytology of the preputial mucosa was taken for cytological assessment. Non-cornified, nucleated squamous epithelial cells were seen. There was no cytological evidence of the presence of estrogen. Measurements of plasma estrogen and inhibin concentrations were not carried out.

Thoracic and abdominal radiographs and bloodwork were not performed due to financial constraints and the reported low incidence of metastatic spread of testicular neoplasia in the dog.¹²⁻¹⁵

As both testes had detectable masses on ultrasonography the owner elected to carry out a bilateral castration. A closed castration procedure was performed, leaving the parietal vaginal tunic intact as to avoid potential seeding of the tumor and not incise through neoplastic tissue. A local incisional block of bupivacaine was injected and a subcutaneous meloxicam injection (0.2 mg/kg) was given. The dog recovered uneventfully from anesthesia. He was sent home on meloxicam 0.1 mg/kg PO every 24 hours for pain management.

Differentials

Differentials for testicular asymmetry include neoplasia, trauma, inflammation, infection, spermatoceles, and sperm granuloma.^{12,13} After ultrasonographic examination of the testes, neoplasia was the most likely cause of the testicular asymmetry palpated with the most likely type of tumor present being a seminoma, Sertoli cell tumor, and/or interstitial cell tumor. Other tumors considered but less likely included benign epidermoid cysts, fibrosarcoma, hemangioma, neurofibrosarcoma, anaplastic carcinoma, gonadoblastoma, embryonal carcinoma, sarcoma, lymphoma, and granulosa cell tumor.^{12,13,15}

Treatment

The treatment of choice for a canine testicular neoplasm is orchiectomy, which was performed in this case. A unilateral orchiectomy or hemicastration was considered as he was a valuable breeding dog.¹²⁻¹⁴ However, the presence of multiple tumors affecting both testes, his older age, poor semen quality, and the degree of testicular degeneration present on ultrasound made hemi-castration a poor treatment option. Bilateral orchiectomy is the treatment of choice in cases with bilateral neoplasia.¹² However, unilateral orchiectomies have resulted in litters even with persistently low total sperm numbers ejaculated with the aid of breeding management and artificial reproductive technologies.¹² Chemotherapy is adjunct therapy for seminomas if metastasis is present, which is uncommon.¹²⁻¹⁵

While bilateral or unilateral orchiectomy is the treatment of choice,¹²⁻¹⁵ an area that potentially could be explored further for poor anesthetic candidates would be chemical ablation. Intra-testicular injections exist currently for chemical castration¹⁶ and may provide an option in the future for testicular tumor treatment though an obvious concern would be leaving behind cancerous cells.

Outcome

Gross analysis of both the testes was performed immediately after surgical removal (Figure 3). Both testes were then sent to the pathology laboratory in a 10% formalin solution for histopathology.

Microscopically, the left testis contained a discrete, round, fleshy white mass measuring approximately 35 mm x 25 mm in diameter. Within the testis was a discrete, expansile, partially encapsulated nodular proliferation of neoplastic round cells that formed sheets and lobules and were supported by fine, fibrovascular stroma. The cells had discrete cell borders and moderate amounts of eosinophilic cytoplasm and a central nucleus with stippled to vesicular chromatin and a single nucleolus.

There were frequently multinucleated cells with up to five nuclei and scattered aggregates of lymphocytes. There was moderate anisocytosis and anisokaryosis and the mitotic rate ranged from 6-8/HPF. Surrounding seminiferous tubules had reduced numbers of spermatids and there were rare spermatid multinucleated giant cells (Figures 4a and 4b).

The right testis contained a discrete, multilobulated, tan nodule within the proximal part of the testes that was approximately 10 x 7 mm in diameter. Within the testis was a discrete, multinodular proliferation of neoplastic polygonal cells forming nests and cords, entrapping atrophic seminiferous tubules and supported by a fine, fibrovascular stroma. The cells had moderate to large amounts of pale eosinophilic granular to vacuolated cytoplasm and a central nucleus with stippled chromatin and a single nucleolus. There were occasional intranuclear cytoplasmic invaginations. There was mild to moderate anisocytosis and anisokaryosis and the mitotic rate was approximately 1/5 HPFs. Adjacent to the neoplastic proliferation were a few, closely associated seminiferous tubules that were effaced by a population of neoplastic cells morphologically similar to those in the left testis. Surrounding seminiferous tubules had reduced numbers of spermatids (Figures 5a and 5b).

A morphologic diagnosis of a seminoma in the left testis and an interstitial cell tumor with an intra-tubular seminoma in the right testis was reported.

Since surgery, the dog has recovered well with no postsurgical complications.

Discussion

This case report highlights the importance of carrying out a complete diagnostic workup if a testicular tumor or tumors are suspected. The dog in this case report initially presented for semen collection for an artificial insemination, and the owner had hopes of future breeding. The owner had no previous concerns for the dog. When a tumor was suspected after testicular palpation and semen evaluation, serious consideration was given to carrying out a hemicastration procedure with the objective of restoring his inherent fertility. However, further diagnostics (testicular ultrasonography) revealed a non-palpable tumor present in the contralateral testis, leading to bilateral castration as the best treatment option for the dog's future health combined with the poor prognosis for future fertility. Had further investigation not been performed after finding the enlarged left testis, and removal of only the left testis by hemicastration was performed in an attempt to preserve fertility, there would have been considerable frustration and potential economic loss for the owner to find an ICT detectable by ultrasonography as well as a microscopic seminoma present months later.

Although this case is not a novel topic, this is the first published in depth case report of multiple testicular tumors in bilaterally descended testes in a dog. Canine testicular tumors are the second most common type of tumor to occur in the dog second to skin tumors.¹² They are generally a disease of older dogs with different ages reported at the time of first diagnosis (mean age range: 9-11 years old; actual range: 2-19 years).¹² Testicular tumors occur more often in undescended testes and retained testes are 10-13 times more likely to develop neoplasia.^{12,13} Tumors can present unilaterally or bilaterally. The presence of multiple cell types as in our case is not uncommon with the occurrence of two or more tumor types reported in 11-35% of cases.^{4,12,13} A study by Peters et al found a 30% incidence in apparently normal dogs that was not palpable on examination.⁴

Often the only clinical sign associated with testicular neoplasia is testicular asymmetry. Atrophy in the contralateral testis is common, due to negative hypothalamic-pituitary-testicular feedback from hormone production by the tumor of estrogens or androgens. Furthermore, increased intrascrotal temperature, and pressure atrophy inflicted on the contralateral testis can result in asymmetry.^{12,13} With multiple potential causes of asymmetry, further diagnostic testing should be performed, especially if the owner is considering hemicastration as clearly demonstrated in this case study.

Learning points

- Palpate testes at every semen collection as owners are often unaware of any abnormalities.
- In all cases of testicular asymmetry an ultrasonographic examination should be performed as neoplastic lesions may be undetectable by palpation alone.

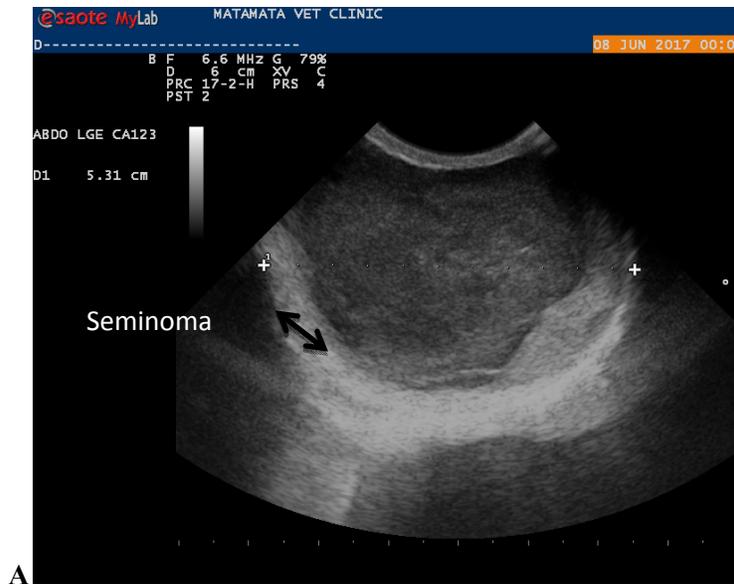
- Submit testes for histopathology as there may be multiple tumor types that are not appreciable on ultrasonography or grossly visible.
- Malignancy for canine testicular tumors is low.
- If hemicastration is performed due to the value of the breeding stud, a recheck semen evaluation every 6 to 12 months should be performed to assess return to fertility given the potential for microscopic tumors to be present.

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Figure 1a. Ultrasonographic image of the right testicle with a hypoechoic mass (ICT) seen at the caudal pole of testicle.
Figure 1b. Gross image of the cut surface of the interstitial cell tumor found in the right testicle. Note the classic small, tan colored mass protruding from the interstitium of the testicle.



A



B

Figure 2a. Ultrasonographic image of the left testicle which contains a large, irregular hypoechoic mass centrally (seminoma). Only a small rim of normal testicular tissue remains (black arrows).

Figure 2b. Gross image of the cut surface of the seminoma located in the left testicle. Note the classic pink colored, large protruding mass encompassing the center of the testicle.

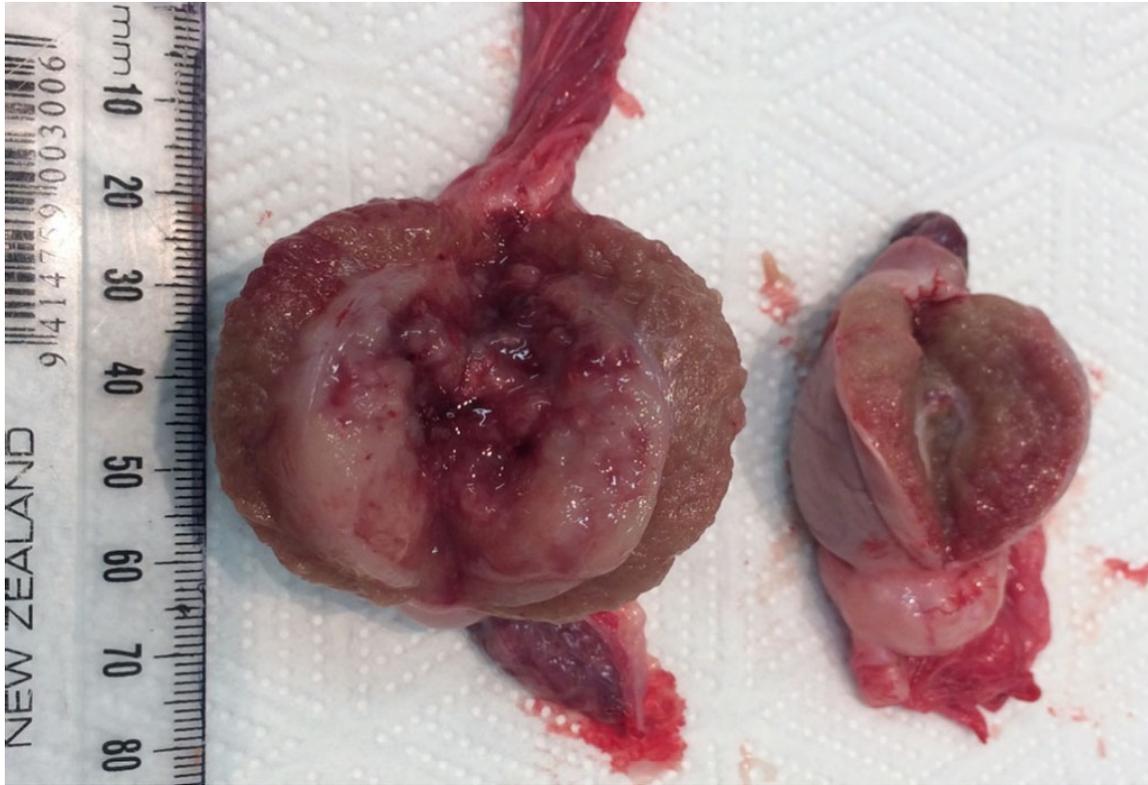


Figure 3. Gross image of the two adjacent testicles. Note that the left testicle containing the seminoma is larger than the right testicle containing the ICT and microscopic seminoma.

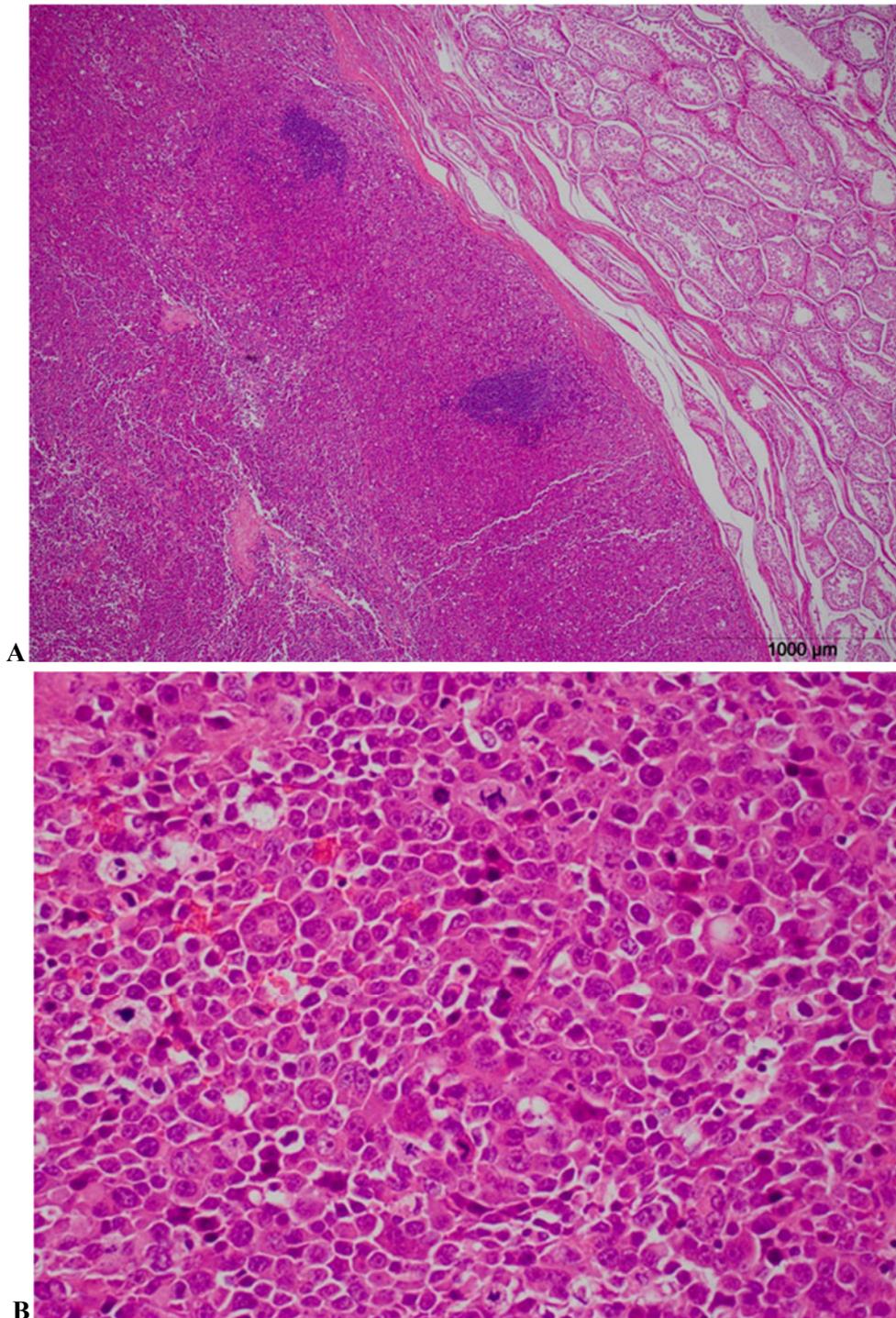


Figure 4a. Histologic image (H&E; ×4 magnification) of a sample taken from the left testicle which contained the seminoma. Note the surrounding seminiferous tubules containing reduced numbers of spermatids. There is proliferation of neoplastic round cells forming sheets and lobules which are supported by fine, fibrovascular stroma.

Figure 4b. Histologic image (H&E; ×40 magnification) of a sample taken from the left testicle containing the seminoma. Note the eosinophilic cytoplasm and multinucleated cells. The cells have a central nucleus with stippled to vesicular chromatin and a single nucleolus.

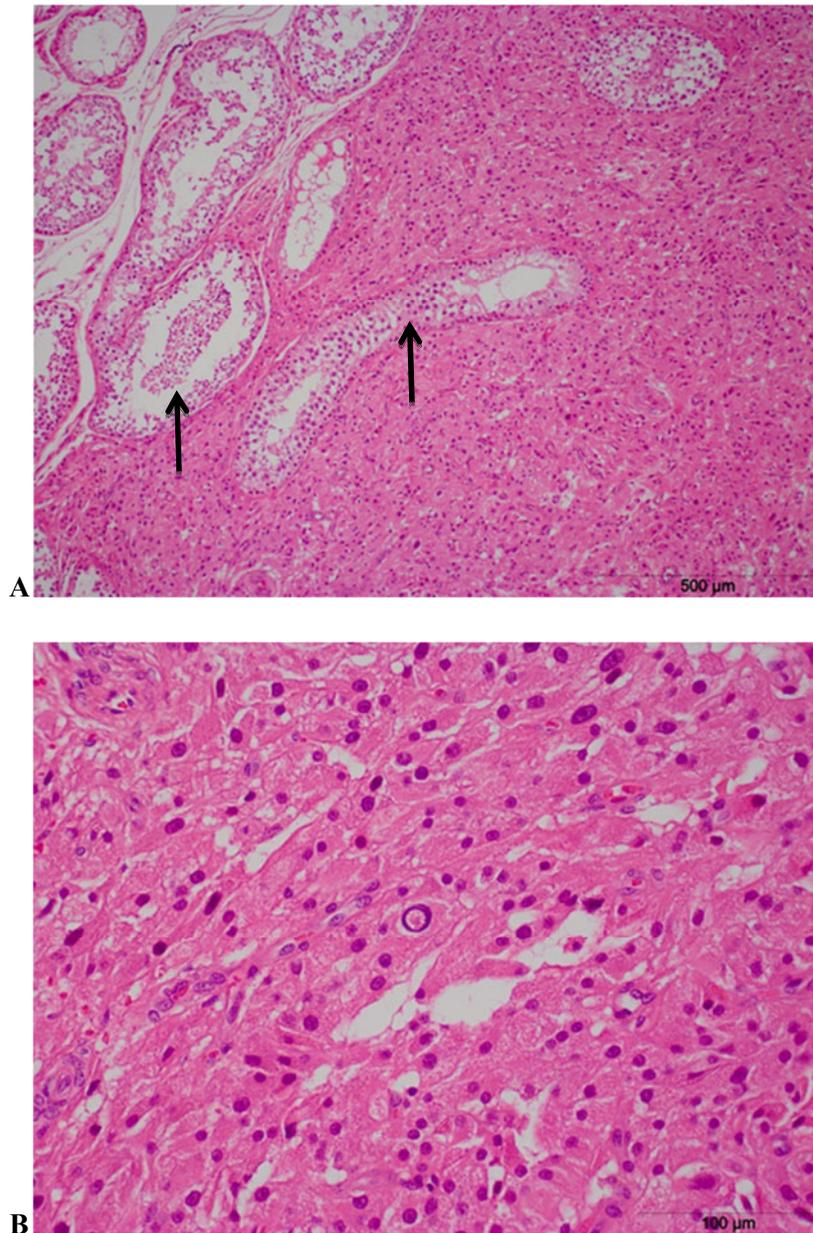


Figure 5a. Histologic image (H&E; $\times 4$ magnification) of a sample from the right testicle containing the interstitial cell tumor and intra-tubular seminoma. Note the unencapsulated, multinodular proliferation of neoplastic polygonal cells forming nests and cords, entrapping atrophic seminiferous tubules and supported by a fine, fibrovascular stroma. Adjacent to the neoplastic proliferation were a few, closely associated seminiferous tubules (arrows) that were invaded by a population of neoplastic cells morphologically similar to those in the left testicle.

Figure 5b. Histologic image (H&E; $\times 40$ magnification) of a sample from the right testicle containing the interstitial cell tumor and intra-tubular seminoma. The neoplastic interstitial cells had moderate to large amounts of pale eosinophilic granular to vacuolated cytoplasm and a central nucleus with stippled chromatin and a single nucleolus. There were occasional intra-nuclear cytoplasmic invaginations.

(Editor's Note: Photographs in this manuscript are available in color in the online edition of *Clinical Theriogenology*.)