Theriogenology Question of the Month

**History**

A 63-kg (139-lb) 1-month-old Angus bull calf was examined because of gross enlargement of the scrotum, which had been evident since birth (Figure 1). Except for the scrotal enlargement, the owners had not detected any other abnormalities and reported that the calf was suckling its dam and gaining weight. The cow and calf were housed on a pasture that contained a mixture of grasses.

Physical examination revealed a firm, freely moveable mass within the scrotum. Palpation did not elicit signs of pain. Both spermatic cords were palpable, with the left spermatic cord larger than the right. The inguinal rings were considered to be normal during palpation. It was not possible to distinguish 2 separate testes in the scrotum. Scrotal circumference was 34 cm. No other abnormalities were evident during physical examination.

Ultrasonographic examination of the scrotum revealed hyperechoic areas surrounded by multiple hypoechoic regions beneath the skin. No normal testicular tissue or loops of bowel were detected.

**Question**

What are your differential diagnoses for the scrotal mass in this bull calf? *Please turn the page.*
Answer

Primary differential diagnoses included neoplasia (sustentacular [Sertoli] cell tumor, interstitial [Leydig] cell tumor, and vascular hamartoma), abscess, and hernia, with inflammation (orchitis, periorchitis, or epididymitis) or hematoma as less likely differential diagnoses.

Results

After consultation with the owner, bilateral castration of the calf was performed. The calf was anesthetized and placed in dorsal recumbency. The scrotum was clipped and scrubbed for aseptic surgery. The ventral third of the scrotum was removed, and a mass (approx 15 × 10 × 10 cm [6 × 4 × 4 inches]) was identified. The mass was attached to the left spermatic cord and appeared to be the left testis. The mass was removed by severing the spermatic cord with an emasculator; the excised tissues were placed in neutral-buffered 10% formalin and submitted for histologic examination. A small (approx 2 × 1 × 1-cm [0.8 × 0.4 × 0.4-inch]) testis was identified in the scrotum after removal of the mass; this testis was removed in a similar manner. The inguinal rings were palpated and considered to be normal. Scrotal skin was closed by use of No. 1 chromic catgut in an interrupted cruciate pattern. The middle 5 cm (2 inches) of the incision was left open to facilitate drainage. The calf was treated after surgery by administration of oxytetracycline (20 mg/kg [9.1 mg/lb], SC) and flunixin meglumine (0.5 mg/kg [0.23 mg/lb], IV).

The submitted tissue specimen was routinely processed, sectioned (thickness of 4 μm), and stained with H&E for microscopic examination. Immunohistochemical analysis was performed with mouse antivimentin monoclonal antisera and rabbit polyclonal antisera raised against GATA-4 of human origin. For GATA-4 staining, a commercially available kit was used to enhance immunospecificity and reduce background staining. For the negative control samples, nonimmune mouse or rabbit sera were used as a substitute for the primary antisera.

Figure 2—Photomicrograph of a section of tissue obtained from the left testicular mass of a 1-month-old Angus calf. Notice the islands of round to polyhedral tumor cells surrounded by fibrous connective tissue. Mitotic figures are evident (arrows). H&E stain; bar = 25 μm.

Figure 3—Photomicrographs of sections of tissue obtained from the left testicular mass of a 1-month-old Angus calf and stained to detect vimentin (A) and GATA-4 (B). Notice the positive reactivity for vimentin at the periphery of tumor cells and the positive reactivity for GATA-4 in the nuclei of tumor cells. Immunohistochemical staining with mouse antivimentin monoclonal antisera and rabbit polyclonal antisera against GATA-4 in panels A and B, respectively; bar = 25 μm.
Microscopically, the testicular mass was composed of large germinal cells arranged in islands and trabeculae surrounded by thin fibrous stroma (Figure 2). The neoplastic islands were often densely populated, but in a few, the center was cystic and formed tubules. Most tumor cells were round to polyhedral with round vesicular nuclei and vacuolated cosinophilic cytoplasm. There was mild variation in the size and shape of cells. There were a few slightly elongated tumor cells that formed palisades along and outlined the fibrous stroma. Mitoses were common (3 to 4 mitotic figures/400X field).

Immunohistochemically, the tumor cells had positive results when tested for vimentin and GATA-4. Vimentin is the main intracytoplasmic intermediate filament protein. Immunohistochemical analysis for vimentin yielded diffusely positive results on the cytoplasm of tumor cells (Figure 3). In contrast, GATA-4 is a DNA-binding protein, so the nuclei of the tumor cells stained positively. Sertoli cells stain diffusely for vimentin, similar to the results for the tumor reported here; however, staining of germ cells is focal.1 Only Sertoli cells express GATA-4 in the testes.2 On the basis of histologic examination and immunohistochemical analysis, the mass was diagnosed as a Sertoli cell tumor.

Discussion

Testicular neoplasia appears to be rare in cattle. A survey of 147 bulls culled in the state of New York during the late 1950s identified 12 bulls (> 7 years old) with Leydig cell tumors, which were commonly bilateral and not accompanied by metastases.3 A subsequent study4 in the United Kingdom revealed 4 animals with tubular adenoma of the testes (Sertoli cell tumor) among 293 tumors of cattle, but 3 of the 4 tumors were in newborn calves. Similarly, Sertoli cell tumors were found in 2 related newborn Shorthorn calves in another study.5 In a study in India, 2 of 3 tumors recorded during postmortem examination of an unspecified large number of animals were Sertoli cell tumors, with the other tumor being a Leydig cell tumor. In an abattoir study6 in Australia, 6 Sertoli cell tumors were identified in 1,598 mature (> 3.5 years old) bulls from North Queensland, with 5 of the 6 tumors developing in Shorthorn bulls. In another study7 in India, a slaughterhouse survey of domestic cattle between 9 and 14 years of age revealed that most testicular neoplasms were Sertoli cell tumors, with a single seminoma being recorded. Other neoplasms associated with the bovine testes include mesothelioma, vascular hamartoma, and lymphosarcoma. Hence, Sertoli cell tumors appear to be the most prevalent tumor of bovine testes and also appear to be the tumor type most commonly found in neonates, although vascular hamartoma and Leydig cell tumor have been recorded. In addition, Shorthorn cattle appear to be predisposed to the development of Sertoli cell tumors, with a single seminoma being recorded. Other neoplasms associated with the bovine testes include mesothelioma, vascular hamartoma, and lymphosarcoma. Hence, Sertoli cell tumors appear to be the most prevalent tumor of bovine testes and also appear to be the tumor type most commonly found in neonates, although vascular hamartoma and Leydig cell tumor have been recorded. In addition, Shorthorn cattle appear to be predisposed to the development of Sertoli cell tumors.

Three of 5 bulls in which the affected testis was recorded had involvement of the left testis, and in 2 of those bulls, there was no evidence of a right testis.8 In the Angus bull reported here, the right testis was identified only after removal of the neoplastic left testis. Testicular tumors in other domestic species most often are detected in adult animals, and there are few reports of congenital testicular tumors in other species.

Sertoli cell tumors, seminomas, and interstitial cell tumors are the most common testicular tumors in dogs, with a mean age of 10 years for affected animals. In general, these tumors are benign with a low rate of metastasis. In horses, teratomas appear to be the most common testicular tumor of young stallions, with seminomas being the tumor type most commonly reported in stallions and Sertoli cell tumors being rarely reported.

Diagnosis of a Sertoli cell tumor is based on histologic examination of a biopsy specimen. In the bull described here, immunohistochemical analysis was used in addition to histologic examination to confirm the diagnosis. Sertoli cell tumors that primarily consist of round cells arranged in solid cellular sheets cannot always be easily differentiated from germ cell tumors by use of routine histologic examination alone. The transcription factor GATA-4 has been implicated in the regulation of gene expression and differentiation in a number of tissues, is abundantly expressed in the nuclei of Sertoli cells, and may be used as a specific marker for the identification of Sertoli cells in prepubertal and postpubertal bulls.2 To our knowledge, the information reported here is the first described use of GATA-4 as an aid in the diagnosis of a Sertoli cell tumor in a bull.

Treatment in the bull calf reported here involved bilateral castration. In the 2 Shorthorn bulls of another report,2 removal of the affected tissue also appeared to be curative. Treatment of Sertoli cell tumors in dogs primarily centers on orchietomy, although chemotherapy or radiation therapy has been used. Orchiectomy also appears to be the treatment of choice for Sertoli cell tumors in horses, although cryotherapy has also been reported.

Outcome

The calf recovered without complications from surgery and was discharged to the owners on the same day. Three months after the surgery, the owners reported that the calf appeared healthy and was gaining weight normally.

References