

Squamous cell carcinoma of the urethral process in a horse with hemospermia and self-mutilation behavior

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- ▶ In horses, hemospermia may result from neoplasia of the urethral process; excision of the tumor is the treatment of choice and may resolve the hemospermia.
- ▶ Irritation of the urethral process may be a predisposing factor in development of self-mutilation behavior in stallions.

A 14-year-old Arabian stallion was admitted to the veterinary teaching hospital for evaluation of acute hemospermia. The stallion was being used for breeding in an artificial insemination program, and the first semen collection of the 1998 breeding season had yielded 40 ml of what appeared to be arterial blood. Under microscopy, some sperm cells were observed in the sample, indicating that the horse had ejaculated.

The stallion had a long-standing history of low-grade hemospermia. During a prepurchase breeding soundness examination at the teaching hospital in 1992, the horse was found to have normal sexual behavior and semen characteristics, but the first ejaculate contained a slight amount of blood. A minor irritation of the urethral opening was determined to be the origin of the blood. Treatment was not recommended at that time.

After the 1994 breeding season, the stallion began exhibiting self-mutilation behavior consisting of biting of the flanks and kicking out with one or both hind legs. The self-mutilation sequence included prolonged and excessive sniffing of feces, the walls of its stall (where body oil residues had accumulated), the windows of the stall, and its flanks, as well as the vocalizations characteristic of self-mutilation and inter-male investigation sequences.

Physical examination at that time revealed bite marks and a recent hematoma on one of the horse's flanks. The owner reported that the behavior may have started in conjunction with a change of location during the breeding season, which the owner believed to represent more stressful management conditions for the horse. At that time, it was recommended that a grazing basket muzzle and a blanket be applied to reduce the

chances of further bite wounds. It was recommended to change the diet to mostly grass and grass hay ad libitum, to provide continuous social companionship (eg, with a mare, donkey, pony, or goat), to provide regular exercise and turn-out, and to administer imipramine hydrochloride^a (500 mg, PO, q 12 h). In the experience of one of the authors (SMM), tricyclic antidepressants such as imipramine hydrochloride have some value in improving locomotor stereotypies as well as self-mutilation behavior in some horses.¹ The owner and manager were also advised to systematically vary housing and turn-out conditions in an effort to identify those that exacerbated or ameliorated the self-mutilation.

A breeding soundness examination performed at that time revealed normal sexual behavior and semen characteristics. However, hemospermia was once more evident in one of the ejaculates, and the owner reported that intermittent minor hemospermia had been a chronic finding. Examination of the urethral process revealed a small ulceration that was considered to be the origin of the blood. Once more, specific treatment for hemospermia was not recommended, but the breeding manager was advised to dilute the semen with an adequate semen extender to minimize the spermicidal effects of RBC in the sample.²

A follow-up on-farm behavior examination was performed at the beginning 1995. The self-mutilation behavior had been reasonably controlled, with only occasional minor biting of the flank. There was no evidence of recent skin or flesh wounds. Continued administration of imipramine for approximately 6 weeks, together with changes in housing, diet, and exercise, all appeared to have contributed to the reduced self-mutilation. At that time it was decided to discontinue treatment with imipramine and substitute treatment with L-tryptophan^b (1 oz, PO, q 12 h), as in the experience of one of the authors (SMM), L-tryptophan is more effective for long-term treatment of self-mutilation as well as less expensive and more convenient to administer.

At the time of admission following the episode of acute hemospermia at the beginning of the 1998 breeding season, the horse was in reasonable body condition, and results of a general physical examination were normal. A CBC was performed and fibrinogen concentration was measured; results were within reference ranges for our laboratory.

The stallion was sedated with xylazine hydrochloride^c (350 mg, IV) to facilitate examination of the penis and urethral endoscopy. A 0.5 cm diameter mucosal ulcer was evident in the distal portion of the urethra.

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†Deceased.



Figure 1—Appearance of the urethral process of a stallion examined because of hemospermia and self-mutilation behavior.



Figure 2—Appearance of the urethral process of the horse in figure 1, two days after excision of the urethral process. The suture line was intact but there was still some evidence of inflammation.

The ulcer was covered by blood (Fig 1), suggesting that it was the source of the recent hemorrhage. The right hemicircumference of the urethral process was markedly thicker than normal. On endoscopy, the urethra, including the openings of the bulbourethral glands and the coliculus seminalis, and the bladder appeared normal. There was no evidence of inflammation, masses, rents, lacerations, or calculi, all of which have been associated with hemospermia in stallions.^{3,6}

A biopsy sample of the affected mucosa was obtained the day of admission to rule out habronemiasis^{3,5,6} and neoplasm of the urethral process. The horse was sedated with xylazine (300 mg, IV) and butorphanol tartrate (5 mg, IV), and a ring block was performed at the base of the urethral process with 1 ml of 2% lidocaine.⁴ The urethral mucosa was sprayed with a local anesthetic solution containing benzocaine, butyl aminobenzoate, and tetracaine hydrochloride.⁵ An elliptical section of the affected urethral mucosa was excised and placed in neutral-buffered 10% formalin for histologic evaluation. The gap in the mucosa was sutured to urethral process epithelium with simple interrupted sutures of 5-0 polydioxanone.⁴ The histologic diagnosis was low-grade squamous cell carcinoma with organizing hematoma.

Six days after admission, when results of histologic examination of the urethral biopsy specimen were available, the urethral process was excised. The horse was anesthetized and placed in dorsal recumbency. The penis was extended and aseptically prepared, and the urethral process was completely excised at its junction with the penile urethra. Urethral mucosa was sutured to the surrounding epithelium with simple interrupted sutures of 5-0 polyglactin 9/10. Histologic examination of the urethral process revealed pseudoepitheliomatous hyperplasia. Histologically normal tissue surrounded the lesion.

The stallion was treated with trimethoprim-sulfamethoxazole (25 mg/kg [11 mg/lb] of body weight, PO, q 12 h) for 15 days and phenylbutazone (1 g, PO, q 12 h) for 6 days. Stall rest for 1 week after surgery was recommended. Two days after surgery, there was

evidence of blood staining the hind limbs. The surgical site was examined, and the suture line was intact although there was still some evidence of inflammation of the surgical site (Fig 2). The owner did not report any further hemorrhage from the incision site after discharge of the horse from the hospital. During a follow-up examination 8 weeks after surgery, the urethral mucosa appeared completely healed. Semen collection was performed successfully, and there was no evidence of RBC in the ejaculate.

During the remainder of the 1998 breeding season, the stallion was used to breed 9 mares naturally, and semen was collected 4 times, using an artificial vagina. A small amount of blood was noticed at dismount during 1 of the natural breedings, but hemospermia was not detected at other times. During the 1999 breeding season, the stallion was used to breed 4 mares naturally, and semen was collected twice, using an artificial vagina. Episodes of hemospermia were not observed, and the owner reported that the surgical site appeared less reddened and inflamed than during the previous breeding season.

To the authors' knowledge, this is the first published report of hemospermia in a stallion secondary to neoplasia of the urethral process. Previously described causes of hemospermia in stallions include bacterial urethritis, rents in the urethral mucosa that communicate with the corpus spongiosum, damage to the urethra during placement of stallion rings, lacerations or habronemiasis of the urethral process, lacerations and penetrating wounds of the penis, and inflammation of the accessory sex glands.^{3,6} Red blood cells are spermicidal; therefore, treatment of hemospermia is targeted at resolving the primary problem causing bleeding. Low-grade hemospermia may be managed by adding an extender to the semen to dilute the effect of RBC on the spermatozoa.²

Squamous cell carcinoma is the most common neoplasm of the external genitalia of horses.^{7,8} Squamous cell carcinomas usually involve the skin of the glans penis or prepuce and are most common in older horses and in areas of depigmented skin. Chronic

irritation with smegma may predispose horses to develop squamous cell carcinomas. Treatments include cryosurgery, topical chemotherapy, hyperthermia, local excision, reeving operations (if the prepuce is involved), and phallectomy, depending on the character and extension of the lesion.^{6,9,10} In 1 study,⁸ 64.5% of horses that underwent partial or complete penile amputation were still alive 18 months after surgery. Squamous cell carcinomas may metastasize to regional lymph nodes, and death may result from metastases of the tumor or complications of radical surgery.⁸ In the horse described in the present report, the size and character of the mass allowed complete resection of the tumor, resulting in resolution of the hemospermia.

The diagnosis of squamous cell carcinoma was made on the basis of results of histologic examination of the biopsy specimen. Chronic ulceration and constant irritation at the level of the urethral process may have triggered development of this lesion, as other reports have described development of cutaneous squamous cell carcinomas in association with chronic wounds or scarring of the affected area.^{11,12} Although, after complete excision of the urethral process, histologic examination revealed only pseudoepitheliomatous hyperplasia, we think that this lesion may have proceeded to malignant transformation if left untreated. It is likely that most, if not all, of the neoplastic tissue was removed at the time of biopsy.

The cause of self-mutilation syndrome in horses is presently unknown, although management, physiologic, and genetic factors have been linked to this disorder.^{12,13} In our experience, the onset of similar self-mutilative behavior in some horses has been associated with potentially uncomfortable or painful conditions such as inguinal location of the testes, scrotal hernia, testicular torsion, jejunal abscess, and gastric ulcers. We speculate that irritation of the urethral process may have been a predisposing factor in the development of self-mutilation behavior in the stallion described in the present report. This may be supported by the fact that this behavior started when this stallion was already 10 years old, whereas one report found that for most self-mutilating stallions the behavior started at younger ages.¹³ Retrospectively, it also appeared that the owner of this stallion recognized an apparent association of periods of increased self-mutilation and periods of hemospermia. In addition, for several months before the first semen collection of the 1998 season, during which the massive hemorrhage occurred, the severity of self-mutilation had been less than at any time since the onset of the problem. Upon dismount following the massive hemorrhage, the stallion immediately began self-mutilating, and the behavior continued at low to moderate levels during hospitalization and subsided as the lesion healed. One year after surgery, the owner reported that the stallion still occasionally displayed elements of the self-mutilating sequence, but of a markedly muted character and frequency, compared with its behavior before the penile surgery. Although this might support the idea that the lesion was the root cause of the self-mutilation, certainly other changes in management during the period of hospitalization and recovery may also have contributed to changes in the severity of self-mutilation. Over the years of self-mutilation, the sequence consistently included considerable sniffing of body secretions and excrements as apparently provocative events, suggesting possible involvement of more complex social factors in addition to physical irritation or pain.

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¹Imipramine, Schein Pharmaceutical Inc, Florham Park, NJ.

²EZ-Kalm, Horse Health Products Inc, Mundelein, Ill.

³Xylazine hydrochloride, Bayer Corp, Shawnee Mission, Kan.

⁴Lidocaine 2% injectable, The Butler Co, Columbus, Ohio.

⁵Cetacaine, Cetylite Industries Inc, Pennsauken, NJ.

⁶PDS II monofilament, Ethicon Inc, Somerville, NJ.

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