

Carcinomatosis of presumed prostate gland origin in an aged Standardbred stallion

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Abstract

A 23-year-old Standardbred stallion was examined because of hesitation to mount a breeding phantom, anorexia, weight loss, and a mass palpated within the pelvic cavity. The patient presented with moderate dehydration, tachycardia, marked abdominal distension, and edematous enlargement of the prepuce and scrotum. Serum chemistry demonstrated hyperfibrinogenemia. Ultrasound examination of the abdomen revealed a massive volume of anechoic peritoneal fluid, collapsed small intestine, diffusely thickened and edematous mesentery, and a thick and irregular omentum. Ultrasound examination of the thorax revealed displacement of the diaphragm and heart in addition to compression of the lung field. Ultrasound examination of the scrotum and prepuce confirmed edema and revealed irregular thickenings of the right spermatic cord, tunica vaginalis, and epididymis.

Human prostate-specific antigen (PSA) could not be detected in the patient's serum. Supportive care was provided for 48 hours until the horse became very weak and was euthanized. A postmortem examination was performed. Nodular masses were found throughout the abdominal viscera and pelvic accessory glands in addition to one pulmonary nodule. Histopathology examination revealed a poorly differentiated carcinoma suggestive of primarily prostatic origin.

This is the first reported case of accessory gland neoplasia in a stallion. Confirmation of a suspect case is difficult because existing diagnostics for prostatic cancer in humans and dogs rely on specific clinical findings, biopsy, and serum markers which are unavailable for horses. Prostate cancer should be considered as a rare cause of sexual dysfunction and pelvic mass in horses.

Keywords: Prostate, neoplasia, prostate specific antigen, accessory reproductive glands

Clinical report

A 23-year-old Standardbred stallion was presented to the Widener Hospital for Large Animals at the University of Pennsylvania School of Veterinary Medicine's New Bolton Center with a history of hesitation to mount a breeding phantom in the five to seven days prior to presentation. Further history revealed slight weight loss over the previous two weeks in conjunction with mild anorexia. The stallion was actively breeding in an artificial insemination program and had bred approximately 20 mares in the previous breeding season. The horse had been admitted to New Bolton Center approximately five years previously due to a suspected right spermatic cord torsion that had spontaneously resolved with no ensuing problems. Prior to the current admission, transrectal examination by the referring veterinarian determined that there was a palpable mass located within the pelvic cavity of the stallion. The horse was referred to the Clinical Reproduction Service at New Bolton Center for evaluation.

Upon presentation, the stallion was moderately dehydrated, had a resting heart rate of 88 bpm, normal respiratory effort, and marked abdominal distension. The prepuce and scrotum were mildly enlarged with pronounced pitting edema. There was an elevated serum fibrinogen (832 mg/dl) but all other serum chemistry values and complete blood count findings were within normal limits. Ultrasonography of the horse's abdomen revealed a massive volume (>10 cm fluid depth) of anechoic peritoneal fluid. Collapsed small intestine was visible floating within the fluid. The mesentery was

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diffusely thickened and edematous. The omentum was very thick and irregular in appearance ventrally. The periphery of the liver and spleen were visible and appeared normal and surrounded by anechoic fluid. The peritoneal fluid markedly displaced the diaphragm cranially and dorsally. Ultrasonography of the thorax revealed marked compression of the lung field secondary to massive ascites. The lung field on the right extended from the dorsal aspect of the eighth intercostal space to the fourth intercostal space above the point of the shoulder. In the ventral aspect of the fourth intercostal space on the right, the lung was irregular with hyperechoic and echogenic areas scattered within it. The heart was displaced into the cranial mediastinum.

Transrectal examination revealed a prominent mass associated with the pelvic urethra caudodorsal to the neck of the urinary bladder. The bladder was surrounded cranially by peritoneal anechoic fluid in the abdominal and pelvic cavities (Figure 1a). The dorsal portion of the mass was freely movable transrectally but was anchored ventrally and broadly and could not be distinguished from the urethralis muscle. Ultrasonographic examination of the accessory sex glands using a 7.5mHz linear probe was performed and revealed normal ampullae and small seminal vesicles as would be expected in a non-aroused stallion. An amorphous mass approximately 12-14 cm in diameter was palpated and imaged ventrolateral to the pelvic urethra. The prostate gland was not palpable or imaged but the location of the pelvic mass encompassed the prostate gland region (Figure 1b). Ultrasonography of the scrotum and prepuce revealed superficial edema of the skin and subcutaneous tissues and numerous irregular thickenings of the right spermatic cord, tunica vaginalis, and epididymis (Figure 1c). A hydrocoele was imaged in the scrotum and appeared as nonechogenic fluid of approximately 2-4 cm in depth. The bulbourethral glands were normal in appearance. No abnormalities were noted on the echocardiogram. Evaluation of peritoneal fluid obtained by abdominocentesis revealed a relatively acellular transudate. Blood samples were drawn for determination of serum levels of human PSA, a circulating kallikrein-II, or acid phosphatase protein that is produced by neoplastic prostate tissue in human beings.

Supportive care was provided over the ensuing 48 hours with intravenous fluids, analgesics, anti-inflammatory drugs, and periodic drainage of the ascites in an effort to make the horse comfortable and stable. The horse became very weak and a grave prognosis for life was given to the stallion's syndicate. The decision was made to euthanize the stallion. The etiology of the ascites was thought to be most likely due to a neoplastic mass, since such a mass was palpable within the pelvic canal. Other differential diagnoses included heart failure and chronic liver disease, although there was no evidence to support these possibilities.

A cosmetic postmortem examination was conducted at the owner's request. Incision sites were limited to the right scrotum, ventral abdomen, and thorax. The abdominal viscera were thus exposed and visualized to reveal all surfaces studded with irregular-shaped firm white to yellow-tan nodules ranging 1-3 cm in diameter (Figure 2). The abdominal side of the diaphragm was covered with nodules embedded within a 5 mm sheet of fibrous tissue (Figure 2b). No carcinomatous lesions were observed in the thoracic cavity, although a single 1.5 cm nodule was observed within the lung parenchyma (Figure 2a). Most visceral organs also displayed carcinomatous lesions (Figure 2). The omentum and mesocolon was covered with nodular transplants and was profoundly thickened and fibrotic with a coarse fibrovascular core (Figure 3). Grossly, the pelvic accessory sex organs did not appear to be invaded by the neoplasm and the normal shapes were present (Figure 4). The right testis was soft and flaccid and numerous nodules were observed along the epididymis, spermatic cord, and cremaster muscle attachment to the spermatic cord. The left testis appeared normal with no associated lesions.

The histologic features of the neoplastic nodules were consistent with a poorly differentiated carcinoma. In the testis, mature spermatozoa were present within the seminiferous tubules and ductus deferens. Sperm granulomas, in addition to nodular masses, were observed in the loose connective tissue surrounding the vesicular glands. The lung neoplasm was least affected by autolysis and for this reason, the morphological description is based on this section. The masses were discrete and solid with abundant desmoplasia and showed little tendency to form lumina. Cells were monomorphic in composition in that they were small with scant granular eosinophilic cytoplasm and a centrally located, round to oval, moderately chromatic nucleus devoid of an obvious nucleolus. Cell shape varied from cuboidal to low

columnar. Some foci suggested spindle-shaped and stellate cell morphology. The mitotic indices in the most active sites were 3-4 mitoses per high-powered field. In the ampullae and prostate, which were not grossly distinguishable within the pelvic mass, the neoplasm extensively infiltrated the fibrous and smooth muscle elements of the tissue. The distribution of normal-appearing glandular acini suggests the mass to be primarily prostatic in origin, however, severe autolysis made distinction between neoplasm, native glands, and stroma difficult. Cytokeratin (AE1 and AE3) was weakly positive and vimentin (V9) staining of neoplastic cells was negative which suggests the neoplasm is epithelial in origin.

The free and total human PSA concentrations in blood serum samples were measured using both the fPSA and PSA enzyme immunoassay (DRG International, Mountainside, NJ). Prostate specific antigen was not detected in any samples, including normal control serum taken from two geldings, two mares, and two stallions. Additionally, immunohistochemistry was performed on formalin-fixed and frozen tissue sections of neoplastic nodules and the accessory gland mass. No crossreactivity was detected on these equine tissues using six different human PSA antibodies whereas human positive control serum and tissues were strongly positive in the same assays.

Discussion

In this case, gross pathology findings of effacement of the ampullae and prostate gland, carcinomatosis, pulmonary metastasis, and nodules in the right testis are strongly indicative of a carcinoma arising from the region of the accessory sex glands. Since neoplasia of the accessory sex glands is so rare in male large animals, few clinical descriptions have been published. No other source of a primary tumor was observed in any tissue. One author described one case each of prostatic cystadenoma and leiomyosarcoma involving the prostate gland in geldings.¹ Although the deferent ducts, ampullae, seminal vesicles, bulbourethral glands and ejaculatory ducts can potentially be invaded by metastatic neoplasia, there are no reported cases of primary neoplasia in these structures in any animal species.²⁻⁵ In humans, several authors have reported seminal vesicle invasion by prostatic carcinoma as well as urothelial carcinoma of the bladder, but the seminal vesicle has not been identified as a primary site for accessory gland neoplasia.⁶⁻⁷ Therefore, a primary carcinoma in the region of the accessory sex glands likely originates from either the prostate or the prostatic part of the urethra.

Dogs and humans are the only mammals with a significant incidence of prostate neoplasia, although a few cases have been reported in cats.⁸⁻¹² Although the majority of prostate neoplasms in dogs are prostate adenocarcinomas and transitional cell carcinomas of the prostatic urethra, rare cases of lymphoma, primary leiomyosarcoma, primary sarcomatoid carcinoma, primary hemangiosarcoma, and metastatic epithelioid hemangiosarcoma have also been reported.^{3, 13-15} Of the above tumor types, the histopathologic description in this equine case of a poorly differentiated carcinoma with abundant desmoplasia and diffuse normal-appearing glandular acini is most consistent with a prostate adenocarcinoma. However, due to the paucity of information on equine prostatic neoplasia, clinicians should keep these other potential tumor types in mind as initial differential diagnoses when presented with a suspected equine prostate neoplasia case.

Canine prostate adenocarcinoma is poorly differentiated and expression patterns of various markers compared to normal canine prostatic tissue indicate that it most likely originates from the collecting ducts rather than from the peripheral acini.¹⁶⁻¹⁷ Histopathology in this equine case showed variation in neoplastic cell shape from cuboidal to low columnar which could be consistent with the adenocarcinoma originating from collecting ducts. For epithelial tumor progression to malignancy as seen in canine prostate adenocarcinoma, a change in cell phenotype from an epithelial to a motile mesenchymal phenotype occurs and this phenotypic alteration may be characterized by the acquisition of mesenchymal markers such as vimentin.¹⁸⁻¹⁹ In one study, 46% of canine prostate adenocarcinomas showed positive expression of vimentin on immunohistochemistry in the neoplastic epithelial cells while not expressing vimentin in adjacent non-neoplastic or pre-neoplastic epithelial cells.²⁰ Although vimentin was negative in the lesions of this equine case, it should be noted in future cases that expression of vimentin can still be consistent with epithelial origin of a prostatic neoplasm.

This case is based on post-mortem findings and diagnosis. Unfortunately, ante-mortem diagnosis in animals is difficult. Prostatic neoplasia is not often diagnosed in dogs until clinical signs develop, at which time metastasis has already occurred.^{4-5,13} The overall incidence of canine prostate cancer metastasis was 64% in one study with incidences for specific metastatic locations of 43% lymph node, 32% pulmonary, 25.5% skeletal, 15% carcinomatosis, and low incidences of metastasis to other sites.²¹ This equine case displayed pulmonary metastasis, and abdominal and scrotal carcinomatosis; the lymph nodes and skeleton were not evaluated for metastasis due to owners' wishes. In humans, PSA is the best available serum marker for diagnosis and prognosis of prostate cancer.²² However, evaluation of PSA, acid phosphatase, and canine prostate specific esterase as potential serum markers for use in canine prostate adenocarcinoma diagnosis has so far been unrewarding – human PSA could not be detected and canine prostate adenocarcinoma does not appear to be associated with changes in serum activities of either acid phosphatase or canine prostate specific esterase.²³ Human PSA similarly could not be detected in this equine patient's serum nor was crossreactivity detected using PSA for immunohistochemistry evaluation of the tissues. Since this case presented, however, an equine homologue of human PSA has been isolated, horse prostate kallirein (HPK).²⁴ As crossreactivity between species may have contributed to our not detecting human PSA in this stallion, the possibility remains that HPK could be used in future cases as a probe for prostate function once an antibody to HPK is developed.

Although this case could not be definitively confirmed as a metastatic prostate neoplasm, the high index of clinical suspicion, supportive histopathology results, and biologic behavior of the neoplasm consistent with that of canine prostate neoplasia make metastatic prostate adenocarcinoma the presumptive diagnosis in this case. This study points out the clinical usefulness of ultrasonography for imaging accessory sex glands in stallions. This technique should be performed routinely on breeding stallions to screen for any pathology of the internal genitalia, including prostatic pathology.

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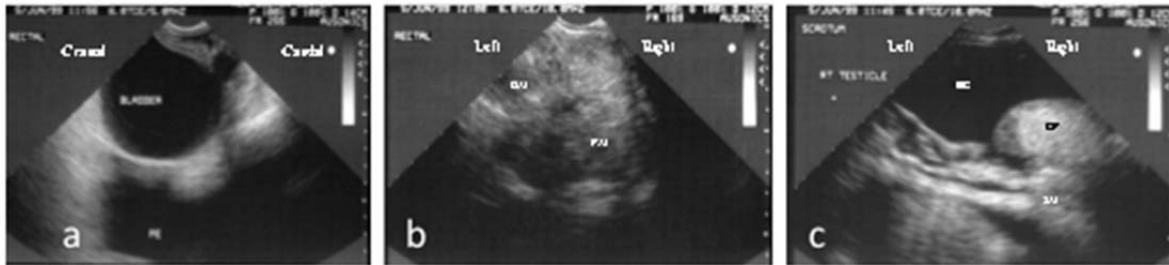


Figure 1: Ultrasonographic examination of a stallion with abdominal distension, pelvic mass palpable on transrectal examination, and a mildly enlarged scrotum. (A) Sagittal transrectal ultrasonogram of cranial peritoneal effusion (PE). (B) Transverse transrectal ultrasonogram of a pelvic mass (PM) associated with the prostate gland (normal prostate was not observed by palpation or ultrasound examination), surrounding the urethralis muscle (UM), and extending beyond the ultrasonographic field of view in this image. (C) Transverse right scrotal ultrasonogram of an intrascrotal mass (SM) and hydrocele (HC) associated with the tail of the epididymis (EP).

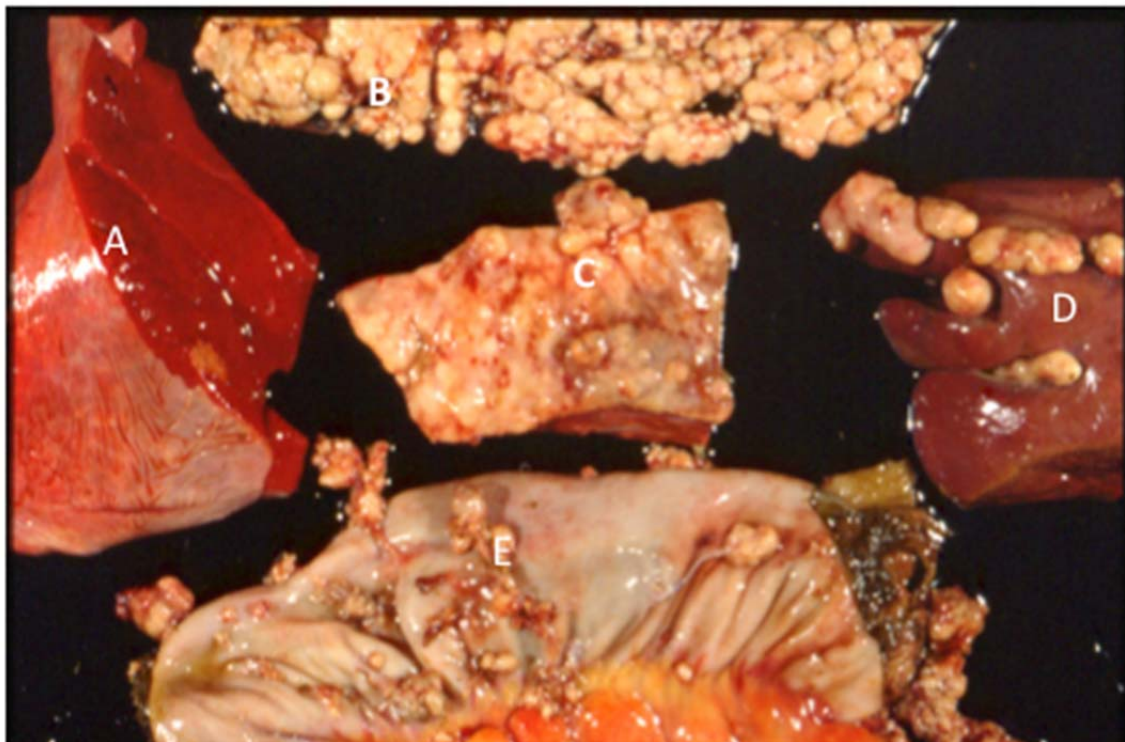


Figure 2: Excised pulmonary metastatic (A) and peritoneal carcinomatosis lesions of the diaphragm (B), abdominal wall (C), liver (D), and small intestine (E) noted during postmortem examination of the stallion.



Figure 3: Mesenteric carcinomatosis lesions noted during postmortem examination of the stallion on the dorsal aspect of the ascending mesocolon (A) between the left dorsal colon (B) and left ventral colon (C).

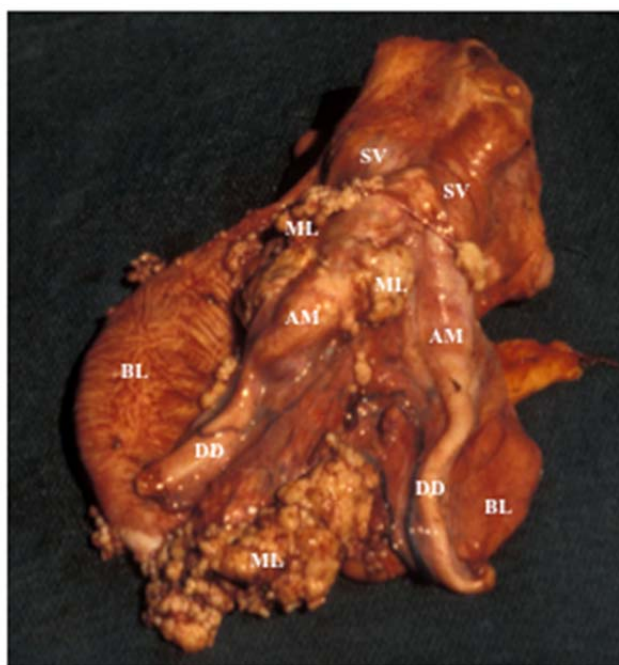


Figure 4: The pelvic nodular mass lesion (ML) excised during postmortem examination of the stallion is ventral to the ampullae (AM) and ductus deferens (DD), dorsal to the bladder (BL), and extends from the seminal vesicles (SV) to the apex of the bladder (BL). Normal prostatic tissue was not observed and no infiltration of other accessory sex glands was noted.

(Editor's note: The photographs in this manuscript are available in color in the online edition of Clinical Theriogenology.)