

Case Report

Metastasis of a Prostatic Carcinoma along an Omental Graft in a Dog

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Received 17 February 2013; Accepted 11 March 2013

Academic Editors: S. M. Abutarbush, C. Hyun, R. M. Santos, and S. Stuen

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An 11-year-old male American Bulldog was presented for hematuria and tenesmus. It had been treated for chronic bacterial prostatitis with abscessation two years earlier and underwent castration and a prostatic omentalization procedure. There was no histologic evidence of prostatic neoplasia at that time. On physical examination, an enlarged prostate was found by rectal palpation, and it was characterized with ultrasonography and computed tomography. Surgical biopsies were obtained, and histopathology identified prostatic adenocarcinoma. It received carprofen and mitoxantrone chemotherapy in addition to palliative radiation therapy; it was euthanized six weeks later due to a progression of clinical signs. Necropsy findings included marked localized expansion of the prostatic tumor and dissemination of prostatic carcinoma cells throughout the peritoneal cavity along the omental graft with infiltration onto the serosal surfaces of most abdominal viscera and fat. This case represents a previously unreported potential complication of the omentalization procedure wherein carcinoma cells from a prostatic tumor that independently arose after omentalization may have metastasized along the surgically created omental graft.

1. Introduction

The surgical treatment of canine prostate abscesses was revolutionized by the application of an intracapsular prostatic omentalization technique first reported by White and Williams in 1995 [1]. In this procedure, an omental graft is tunneled through the parenchyma of the prostate after digitally breaking down any loculated abscesses and is sutured to the prostate. The omentum provides vascular and lymphatic drainage to cavitated sites of infection within the prostate gland. Along with systemic antibiotic therapy, prostatic omentalization has enabled the successful management of many refractory cases of prostatitis in dogs. No long-term complications have been reported with this technique.

Prostatic carcinoma in dogs is generally an aggressive malignancy characterized by local invasiveness and early

metastasis to regional lymph nodes, liver, lung, and bone [2–5]. Clinical signs are variable but typically include hematuria, stranguria, urinary incontinence, tenesmus, and pain, which may be localized if skeletal metastasis has occurred. The presence of an enlarged prostate in a neutered male dog may indicate malignancy; however, the prostate is not enlarged in all cases of prostatic carcinoma [4]. Radiography, ultrasonography, and computed tomography (CT) are useful imaging techniques to assess the prostate for the disease and to evaluate for evidence of metastasis. Diagnosis is confirmed by cytologic or histologic examination of prostatic fluid or tissue that is frequently obtained under ultrasonic guidance or by surgical biopsy. Oftentimes, the diagnosis is made at an advanced stage of the disease; therefore, the prognosis is guarded. Treatment options include surgery, radiotherapy, and chemotherapy [6–8]. Attempts at partial or complete

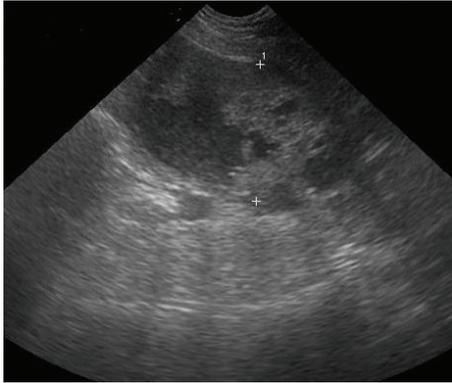


FIGURE 1: Sagittal ultrasound image of the prostate gland taken on initial presentation. Note the marked prostaticomegaly with large cavitory areas containing hyperechogenic fluid within the gland.

prostatectomy in dogs are usually avoided due to the risk of traumatizing neurovascular structures during dissection around the trigone of the bladder which may result in urinary incontinence or less commonly avascular necrosis [9]. Radiotherapy has the potential to achieve temporary local tumor control, but complications can include acute signs of urethritis and colitis or later the occurrence of urethral or colonic stricture and bladder fibrosis [10–12].

Chemotherapy utilizing mitoxantrone and cyclooxygenase inhibitors (COX-2) is frequently considered the most appropriate treatment option for both localized and metastatic diseases; however, limited responses are usually obtained, and median survival times are measured in months [6–8]. This report describes the occurrence of prostatic carcinoma with metastasis along an omental graft in a dog that had an omentalization procedure performed for a prior episode of bacterial prostatitis and abscessation.

2. Case Report

An 11-year-old castrated male American Bulldog was examined for signs of recent onset of hematuria with dyschezia. It had a chronic history of recurrent urinary tract infections with hematuria, prostaticomegaly, and bacterial prostatitis and was treated repeatedly with appropriate antibiotics. The dog underwent castration 20 months prior to presentation; however, the prostate enlargement was not resolved. Ongoing signs of hematuria led to reevaluation two months later. Abdominal radiographs and ultrasonography identified prostaticomegaly with multiple dilated cystic cavities within the prostate gland (Figure 1). During abdominal exploratory surgery, both lobes of the prostate gland were distended with multiple cystic cavities containing brown, cloudy fluid. Prostatic biopsies from four sites were obtained, and omentalization of the prostate gland was performed as previously described. Histology revealed severe lymphoplasmacytic prostatitis with regions of hemorrhage, necrosis, and fibrosis and no evidence of neoplasia. No further episodes of hematuria or urinary tract infection were observed for the next 18 months.

At presentation, firm symmetric prostaticomegaly with tenderness was found on rectal palpation. Urinalysis revealed

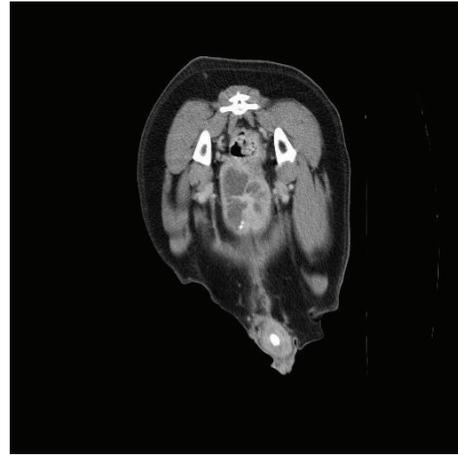


FIGURE 2: CT image of the prostate gland obtained prior to chemotherapy and radiotherapy. Note the prostatic enlargement and mineralization.

hematuria and proteinuria, and no bacteria grew on aerobic culture. The results of a complete blood cell count and serum biochemistry profile were unremarkable. Abdominal radiographs showed an enlarged prostate; spondylosis along the spine was noted; however, no evidence of bone metastasis was seen. Ultrasonography identified two small cystic cavities and focal hyperechoic regions within the parenchyma of the prostate as well as mineralization along the wall of the urinary bladder. Celiotomy was performed, and the prostate gland was examined. The omental graft was observed to be intact, entering and exiting the cranioventral aspect of the prostate gland, which was enlarged with mildly distorted contours but no obvious masses. There were no cystic calculi present and no appreciable thickening of the wall of the urinary bladder. Biopsies were taken from the urinary bladder and from two sites within the right lobe of the prostate. Aerobic and anaerobic cultures of the prostate yielded no growth. Histological examination of the bladder tissue revealed cystitis with mineralization. The prostatic tissue sample identified medium to large moderately pleomorphic polygonal epithelial cells with considerable variation in cell and nuclear size, a large nucleolus, and frequent mitoses. The histologic diagnosis was prostatic adenocarcinoma. Staging was undertaken utilizing three-view thoracic radiographs and CT scanning of the chest and abdomen. No significant abnormalities were found in the chest. Prostaticomegaly and mild iliac lymphadenopathy were found on the CT scan (Figure 2) along with mild mineralization of the prostate, bladder, and renal pelvis.

Treatment options were discussed with the owners, and chemotherapy with palliative tomotherapy was selected. Carprofen (Rimadyl; Pfizer, Exton, PA) (4 mg/kg P.O. q 24 hr) and mitoxantrone (Mitoxantrone Injection; Hospira, Lake Forest, IL) (5 mg/m² IV once) were administered. One week later, the first of the four planned doses of coarsely fractionated radiotherapy directed at the prostate gland, 6.5 Gray (Gy), was given under general anesthesia. Appropriate analgesic, antiemetic, and antidiarrheal medications were provided as needed. The dog experienced a febrile neutropenia (494/ μ L)

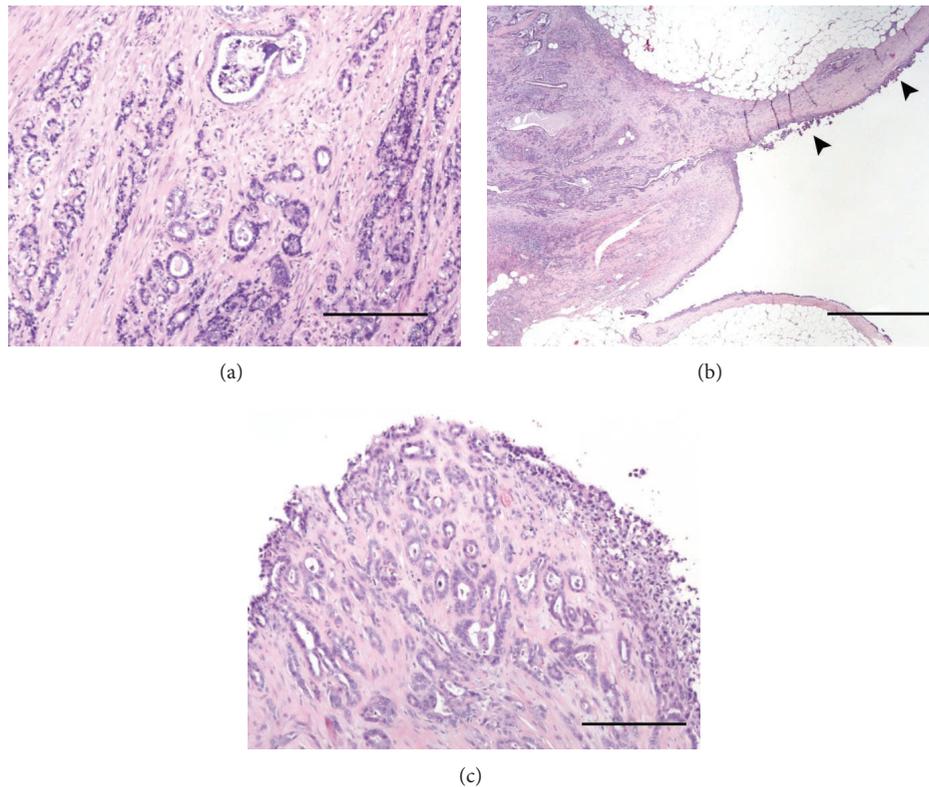


FIGURE 3: (a) Prostate gland: prostatic adenocarcinoma. Note the neoplastic cells arranged in nests and variably sized acinar structures amidst a dense fibrovascular stroma. Hematoxylin and eosin stain. Bar = 200 μm . (b) Omentum: note the metastatic spread of prostatic adenocarcinoma cells on the serosal surfaces forming small papillary fronds (arrowheads) and within the omental adipose tissue (carcinomatosis). Hematoxylin and eosin stain. Bar = 1000 μm . (c) Omentum: note the metastasis of prostatic adenocarcinoma cells on the serosal surface. Hematoxylin and eosin stain. Bar = 200 μm .

one week after mitoxantrone was given that responded to supportive intravenous fluids and broad-spectrum antibiotics; the mitoxantrone was then discontinued. A methicillin-resistant *Staphylococcus intermedius* urinary tract infection developed and was resolved with chloramphenicol (50 mg/kg P.O. *q* 8 hrs for 7 days). Three additional radiation treatments of 6.5 Gy with tomotherapy were completed, to a total dose of 26 Gy, over the next four weeks. The radiotherapy was well tolerated, but signs of tenesmus and abdominal discomfort persisted. One month after the final radiation treatment, progressive signs of dyschezia, hematochezia, anorexia, weight loss, and abdominal pain developed. The patient was euthanized three months after the diagnosis of prostatic carcinoma, and a complete necropsy was performed.

Postmortem examination revealed that all gross pathology was confined to the abdominal cavity. The prostate gland was enlarged (5 \times 5 \times 4 cm) with a markedly irregular surface and bilateral cystic cavities up to 2.5 cm diameter containing brown fluid and nodular tissue and surrounded by firmly adhered adipose tissue containing multiple white firm nodules. The prostatic urethra was patent but narrowed. The caudal and midabdominal fat was firm and variably infiltrated with white nodules; no peritoneal effusion was

present. One kidney had an uneven capsular surface and foci of cortical thinning (infarctions), and the spleen had an irregular capsular depression. Sections of lung, liver, kidney, spleen, abdominal fat, and the entire prostate and urinary bladder were submitted in neutral buffered formalin and processed routinely for histology. On histological examination, the prostate gland contained a poorly demarcated, unencapsulated, and invasive mass composed of cuboidal to columnar cells arranged in variably sized, disorganized tubules, acini, and nests separated by a dense fibrovascular stroma, with 2–4 mitotic figures observed per ten high-power (400x) fields (Figure 3(a)).

In the kidney sample, subacute renal infarctions were associated with interstitial/intravascular nests of similar neoplastic cells. The neoplastic cells were also found within the splenic capsular depression, along many serosal surfaces, and within bands of scirrhous tissue throughout the abdominal fat, including the omentum (Figures 3(b) and 3(c)).

No metastatic sites were discovered in the liver or lung. The urinary tract had lymphoplasmacytic cystitis and pyelonephritis. The pathologic diagnosis was prostatic adenocarcinoma with metastasis to the spleen, kidney, abdominal fat including omentum, and serosal surfaces (carcinomatosis).

3. Discussion

Based on necropsy studies, the incidence of prostatic carcinoma in dogs is estimated to be 0.2%–0.6% [4, 13]. It is seen most often in older, castrated dogs, and while its pathogenesis is unknown, canine prostatic carcinomas are thought to originate from ductal epithelium in an androgen-independent process [13–15]. Recent molecular studies suggest that many prostatic tumors are transitional cell carcinomas arising from the prostatic urothelium [14, 16]. In contrast, prostate cancer is very common in older men, and its carcinogenesis is believed to be a multistep process involving androgens in the malignant transformation of acinar cells with inflammation and sexually transmitted diseases identified as risk factors [17]. Dogs with prostatic carcinoma typically have a high-grade malignancy, and the disease is generally multicentric at the time of diagnosis [6, 7]. A metastatic rate of 80% was found in one necropsy study of canine prostatic carcinomas, most commonly to lymph nodes, lung, and bone with rarer spread to the liver, colon, kidney, heart, adrenal gland, brain and spleen [15]. Direct extension of the tumor may occur, cranially into the urinary bladder, caudally into the urethra, or dorsally into the lumbar vertebrae [6, 8]. Regional metastasis to lumbosacral or iliac lymph nodes occurs frequently, and many dogs have a considerable pain during defecation due to lymphadenopathy and prostatomegaly [4, 6]. Radiographically, the finding of prostatomegaly with mineralization or bony reaction of the ventral surface of the caudal lumbar vertebrae is suspicious for prostatic carcinoma [18]. Surgical treatment of dogs with prostatic carcinoma is rarely recommended; however, selected cases have benefited from transurethral partial prostatectomy, urethral stenting, and/or tube cystotomy [9, 19–21]. Protocols for radiotherapy of dogs with prostate tumors are currently being investigated, but few reports have been published. A recent pilot study utilizing coarsely fractionated radiotherapy along with piroxicam and mitoxantrone for the treatment of dogs with transitional cell carcinoma of the bladder found that doses of 5.75 Gy were well tolerated and largely ameliorated clinical urinary signs [22]. Tomotherapy, a newly emerging technology, combines precise three-dimensional helical CT imaging with intensity-modulated radiotherapy (IMRT) to try to contour the radiation field to conform to the shape of the tumor [23]. Chemotherapy with piroxicam or other nonsteroidal anti-inflammatory drugs (NSAIDs) and mitoxantrone has become a standard of care for dogs with prostatic carcinomas based largely on studies showing partial efficacy in the management of transitional cell carcinomas of the urinary bladder [22, 24]. A recent study demonstrated the expression of COX-2 in nearly 90% of dog prostatic carcinomas, and a statistically significant survival advantage in 16 dogs given NSAIDs (14 treated with piroxicam and 2 treated with carprofen) compared with untreated controls [25].

In this case report, prostatic omentalization was successful in treating the dog's prostatic abscess two years prior to presentation; however, on subsequent biopsy nearly two years later, prostatic carcinoma had developed. Although chronic inflammation is considered a risk factor for human prostate cancer [17, 26, 27], this process remains uninvestigated in

veterinary medicine. Metastasis of prostatic cancer can occur by hematogenous or lymphatic routes as well as by direct attachment of tumor cells onto the peritoneal lining. There are rare reports of human prostatic carcinomas metastasizing to the omentum [28, 29]. Carcinomatosis is the seeding of a body cavity by malignant carcinoma cells, sometimes leading to a malignant effusion. Carcinomatosis in dogs most often is associated with ovarian or gastrointestinal neoplasia; however, one study reported evidence of carcinomatosis in 15% of dogs with prostate tumors [14]. Transitional cell carcinomas of the bladder are recognized for their ability to seed the abdomen during aspiration or surgical procedures [30]. Based on the pathologic findings in this case, the presence of the omental graft within the prostate presented a potential pathway for the tumor to expand beyond the prostate throughout the abdomen; however, hematogenous and intraperitoneal spread was also a factor in metastasis of this neoplasm. Appreciating the possibility of omental involvement, the owners were presented with the option of surgical removal of the omental graft prior to definitive radiotherapy. They declined this option and selected palliative tomotherapy. Unfortunately, the prostatic tumor was refractory to the radiotherapy and chemotherapy, resulting in rapid dissemination of the cancer within the peritoneal cavity and a progression of the clinical signs.

In conclusion, prostatic omentalization, although useful for draining prostatic abscesses and cysts, may inadvertently serve to facilitate the spread of neoplastic lesions throughout the peritoneal cavity. To the author's knowledge, this case represents the first report of the dissemination of a canine prostatic carcinoma along the omentum after a prior prostatic omentalization procedure. Dogs undergoing prostatic omentalization may be at a higher risk for metastasis along this pathway if prostatic carcinoma develops at a future date, and surgeons should be aware of this potential complication when considering the procedure.

Conflict of Interests

The authors declare that there is no conflict of interests with respect to their authorship or publication of this paper. There was no financial support provided.

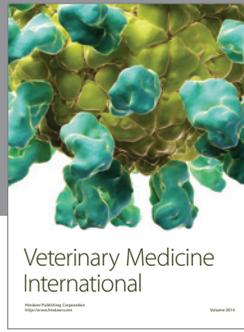
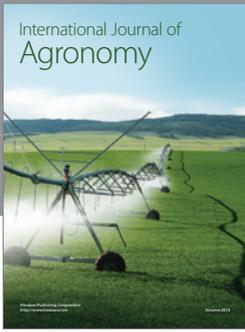
Acknowledgments

The authors would like to thank the Department of Medical Oncology and the Department of Radiation Oncology at the School of Veterinary Medicine, University of Wisconsin for their assistance with chemotherapy and tomotherapy.

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