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Review

Veterinary interventional oncology: From concept to clinic

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ABSTRACT

Interventional radiology (IR) involves the use of contemporary imaging modalities to gain access to different structures in order to deliver materials for therapeutic purposes. Veterinarians have been expanding the use of these minimally invasive techniques in animals with a variety of conditions involving all of the major body systems. Interventional oncology (IO) is a growing subspecialty of IR in human medicine used (1) to restore patency to malignant obstructions through endoluminal stenting, (2) to provide dose escalations to tumors without increasing systemic chemotherapy toxicities via superselective transarterial chemotherapy delivery, (3) to stop hemorrhage or reduce blood flow to tumors via transarterial embolization or chemoembolization, and (4) to provide therapies for those cancers with no safe or effective alternative options.

This review provides a brief introduction to a few of the techniques currently available to veterinarians for cancer treatment. For each technique, the concept for improved palliation, patient quality of life, or tumor control is presented, followed by the most current veterinary clinical information available. Although promising, more studies will be necessary to determine if veterinary IO will provide the same benefits as has already been demonstrated in oncology care in humans.

Introduction

Interventional radiology (IR) involves the combination of minimally invasive approaches and contemporary imaging modalities to gain access to specific organs in order to deliver a variety of devices or medications for therapeutic purposes (Rösch et al., 2003). First developed over 50 years ago, IR techniques have expanded considerably with both vascular and non-vascular procedures being performed routinely in humans (Rösch et al., 2003). Specifically, IR techniques are being increasingly utilized to help manage humans with cancer (interventional oncology or IO) in which traditional therapies have failed or have been shown to provide little benefit. IO has been previously referred to as the 'fourth pillar' of oncological care along with medical, surgical, and radiation therapies (Geschwind and Soulen, 2008). The techniques are particularly useful in cases of regional disease in order to maximize local effectiveness and minimize systemic toxicity or complications.

Non-resectable and metastatic tumors present a difficult challenge for veterinarians and pet owners. Surgery is rarely indicated when resections have a high likelihood of subsequent complications and low likelihood of improved survival times. The relatively limited efficacy of intravenous (IV) chemotherapy for macroscopic disease, and the cost, occasional morbidity, and tumor resistance associated with radiation therapy have stimulated the search for additional therapeutic options. Initial results have been promising and regional techniques, such as palliative stenting for malignant obstructions, intra-arterial chemotherapy, trans-catheter arterial embolization/chemoembolization, and percutaneous tumor ablation, are becoming increasingly investigated.

In the veterinary oncology community we have been evaluating the use of these therapies in pets with cancer, and this review provides a brief introduction to the concepts behind the most commonly used regional tumor therapies, and the current clinical applications and results obtained to date.

Palliative stenting for malignant obstructions

Concept

Animals are often euthanased due to the local effects of a tumor rather than the systemic impact associated with a large cancer burden. While these conditions can occur in any lumen, such as those of the respiratory, gastrointestinal, and cardiovascular systems (Fig. 1), one of the more common examples is malignant obstructions of the urinary tract associated with transitional cell carcinomas (TCCs) or prostatic tumors. These may result in life-threatening signs associated with complete urinary tract obstruction and often lead to owner-elected euthanasia, even when the disease remains otherwise localized.

Minimally invasive endoluminal urethral stenting and endoscopic or percutaneous ureteral stenting have been performed in humans to relieve both lower and upper tract obstructions (Chitale

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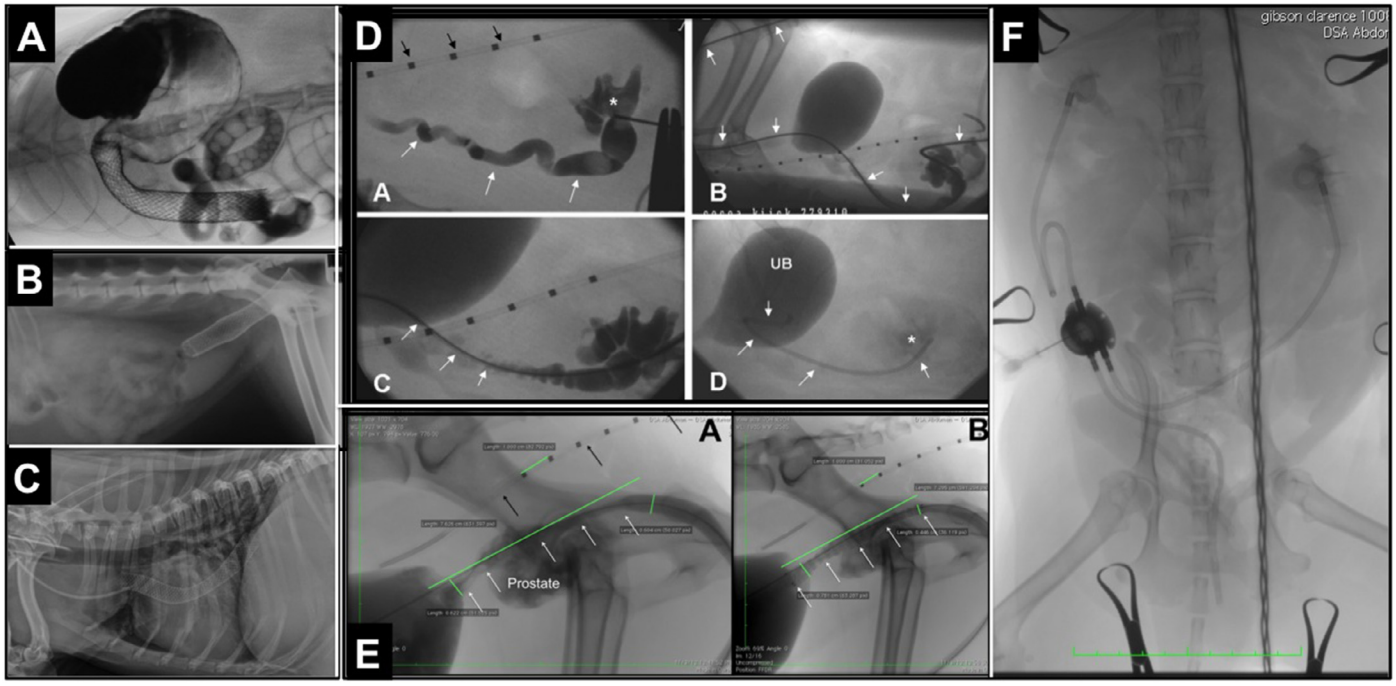

Fig. 1. Serial radiographic images of stenting for malignant obstructions. (A) Ferret with oral placement of a pyloric stent for gastrointestinal carcinoma. (B) Cat with a colonic stent for colonic adenocarcinoma. (C) Dog with a trans-atrial stent spanning from the cranial vena cava to the caudal vena cava for a cardiac neuroendocrine tumor. (D) Dog with percutaneous placement of a pigtail stent for a ureteral obstruction secondary to a transitional cell carcinoma (TCC). Insert A: needle placement in renal pelvis (*) with contrast ureterogram (white arrows). Insert B: guide wire (white arrows) advanced down the ureter and out the urethra. Inserts C and D: pigtail stent advanced over the guide wire spanning obstruction. (E) Canine prostatic tumor with urethral obstruction (white arrows) before (insert A) and immediately following (insert B) stent placement. (F) Dog following total cystectomy and partial bilateral ureterectomy and urethrectomy due to a large TCC after subcutaneous ureterovesicular bypass (SUB) device placement.

et al., 2002; Chao et al., 2011). It should be noted that while endoscopic-guided laser ablation is a common therapy for the typically superficial TCCs found in humans, this is not recommended for the less common and more aggressive muscle-invasive TCCs (which are the most common form of canine TCC). In considering the complications of TCCs in dogs, namely, laser ablation (L'Eplattenier et al., 2006; Cerf and Lindquist, 2012), cost, extended hospitalization times, need for repeat procedures (~47%), possible limitation to females, and other similar outcomes, stenting appears to compare favorably.

Clinic

Veterinary IO techniques involving the placement of intraluminal stents to palliate malignant obstructions have now been described for the respiratory, gastrointestinal and cardiovascular systems, as well as for the urinary tract, which seems to be the most commonly affected body system in our clinic (Fig. 1) (Hume et al., 2006; Weisse et al., 2006, 2011; Culp et al., 2007; Schlicksup et al., 2009; Berent et al., 2011; Hansen et al., 2012; McMillan et al., 2012; Weisse et al., 2012; Blackburn et al., 2013; Brace et al., 2014). These procedures are performed through natural orifices (or small percutaneous holes) under fluoroscopic guidance, and often as outpatient procedures.

IO techniques involving the urinary tract are generally rapid, safe, minimally invasive, and effective, and complications (such as tumor ingrowth into the stent or stent migration) are minor or uncommon. Stented malignant urethral obstructions were reported to have been relieved immediately in 97% of patients, with mild to absent stranguria in 75% of patients (Weisse et al., 2006; McMillan et al., 2012; Blackburn et al., 2013). Animals receiving chemotherapy and non-steroidal anti-inflammatory drugs (NSAIDs) in addition to stenting demonstrated prolonged survival times (250 days) in partially to completely obstructed patients with low morbidity (i.e., limited to 25% major incontinence rates) (Blackburn et al., 2013). The technique is generally performed as an outpatient procedure at many of the major oncology veterinary centers in the USA and appears to be one of the favored techniques for minimally invasive management of acute malignant urinary obstructions in dogs. Recently, similar positive outcomes, characterized by low morbidity and similar incontinence rates, have been reported with urethral stenting in cats with benign or malignant urethral obstructions (Brace et al., 2014).

Similar techniques can also be used in upper urinary tract obstructions through an 18 G renal puncture performed under ultrasound guidance, followed by fluoroscopic guide wire, catheter, and stent manipulations. In a recent series of canine malignant ureteral obstructions treated with percutaneous ureteral stent placement, the techniques were successful in 11/12 dogs with all azotemic dogs demonstrating reduction in blood urea nitrogen (BUN) and serum creatinine concentrations, and a reduction in the degree of hydronephrosis in the 10 dogs that were evaluated post-operatively (Berent et al., 2011). This procedure is typically outpatient and remains technically demanding; however, it can also be performed via a small open surgical technique for those without prior interventional training.

While euthanasia for local obstruction is often no longer necessary due to the advent of intraluminal stenting, management of subsequent metastases is becoming more critical to control. Local surgical resection is often incomplete due to the common trigonal location, or is non-durable when apical tumors are removed due to skip metastases or de novo TCC tumors elsewhere within the lower urinary tract. Recently, a combination interventional/surgical procedure has been described (in an abstract format) outlining how to facilitate en block resection of the distal ureters, bladder, and