Case Report

Hand-assisted laparoscopic nephrectomy in a standing horse for the management of renal cell carcinoma


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Summary

An 18-year-old Quarter Horse gelding was examined for haematuria of 6 weeks' duration. Rectal examination identified an enlarged left kidney and ultrasonographic examination of the kidney identified grossly abnormal renal architecture. Hand-assisted laparoscopic nephrectomy was performed following laparoscopic exploration of the abdomen for metastatic disease. A laparoscopic stapling device was successfully used to transect and ligate the renal vasculature and ureter. Histopathological examination of the kidney identified renal cell carcinoma. A 7 month survival was documented following surgery. Unilateral nephrectomy should be considered a therapeutic or palliative procedure for horses with renal cell carcinoma.

Introduction

Tumours of renal origin in the horse are rare (Haschek et al. 1981; Brown and Holt 1985) and due to the insidious onset and variability of their related clinical signs, disease is often far advanced by the time a definitive diagnosis is made (Hadjadj et al. 1995; Nakhjavani et al. 1997; Rhind et al. 1999). Treatment is rarely attempted due to the aggressive nature of the tumours commonly encountered and the fact that metastatic spread is often identified at the time of diagnosis. As a result, our understanding of the disease progression in such cases and the success of available therapeutic options remains limited.

This case report describes the presentation, diagnostic evaluation and novel surgical management of a horse with a unilateral renal cell carcinoma. A 7 month post surgical survival period is documented.

Case details

History

An 18-year-old Quarter Horse cross gelding presented to the Veterinary Medical Teaching Hospital at the University of California, Davis for the investigation of haematuria of 6 weeks’ duration. The gelding was fed a grass hay diet and a dietary supplement to increase red blood cell production (Red Cell) after a complete blood count performed by the referring veterinarian one week prior to presentation revealed a mild anaemia. Blood was present consistently throughout urination and no change in urinary output or habits had been seen.

Clinical findings

Initial physical examination was unremarkable. A rectal examination identified an enlarged and rounded left kidney; no pain was elicited on palpation of the kidney. No other abnormalities were detected within the urinary tract during this examination. Normal micturition was observed; the urine voided was red-brown and contained large amounts of clotted blood. Clinical laboratory abnormalities included mild anaemia (PCV 26.8%, reference range [rr] 32–52%), mild serum hypernatraemia (141 mmol/l; rr 125–137 mmol/l), hyperchloraemia (107 mmol/l; rr 91–104 mmol/l), hyperglycaemia (6.61 mmol/l; rr 2.7–5.9 mmol/l) and reduced total serum protein (55 g/l; rr 5.8–7.7 g/l). A free catch urine sample was submitted for urinalysis that revealed a specific gravity of 1.033 and a pH of 9.0. Microscopic analysis identified >100 red blood cells and 1–3 white blood cells per high power field. The sample submitted contained no cells of renal origin. A coagulation panel identified an increased partial prothrombin time (69.9 s; rr 31.5–48.5 s); fibrinogen and prothrombin time values were within normal limits.
Diagnostic evaluation and management

Transabdominal ultrasound revealed left renal enlargement (13.4 x 13 cm). The kidney had a spherical shape and near complete obliteration of renal architecture. The ventral 2/3 of the kidney had a solid heterogeneous appearance and the dorsal one-third was mostly anechoic (Fig 1). The right kidney had a normal size and the architecture was discernible; however, the corticomедullary junction was indistinct and pinpoint hyperechoic foci were diffusely scattered throughout the renal cortex and medulla. No metastases were apparent upon thorough examination of the entire abdomen; however, mild duodenal thickening and mild right hepatic enlargement with rounded margins was seen. Percutaneous ultrasound guided biopsy (Biopsy biopsy instrument and Bioply-Cut core tissue biopsy needle) of the right and left kidneys was subsequently performed. Thoracic ultrasound examination did not reveal further abnormalities. The gelding was started on a course of trimethoprim sulphamethoxazole at 30 mg/kg per os twice daily.

Histopathological examination of the biopsy sample from the right kidney revealed sclerotic changes in approximately 20% of the glomeruli examined with hyalinisation and thickening of the Bowman's capsule within the remaining glomeruli. These changes were consistent with a diagnosis of mild multifocal glomerulosclerosis. There was no evidence of bacterial infection or neoplasia. Examination of the tissue samples obtained from the left kidney showed fibroelastic tissue consistent with the muscular wall of an artery; at one end of the tissue submitted was an extensive region of necrosis interspersed with islands of haemorrhage and rare neutrophils. No renal tissue was present and there was no evidence of bacterial infection, inflammation or neoplasia.

Differential diagnoses at this time included primary renal or metastatic neoplasia, renal trauma and chronic haematoma, verminous arteritis and atypical pyelonephritis. An exploratory laparoscopy was undertaken to further investigate the abnormalities found and rule out abdominal metastatic disease; a tentative plan to perform a laparoscopic hand-assisted left nephrectomy was made in the absence of visible dissemination. Blood was submitted for donor cross matching and the gelding was placed on a gradually reducing dietary intake; feed was withheld entirely for 36 h prior to surgery. The horse received antibiotics (Procaine penicillin G at 22,000 u/kg i.m. and gentamicin 6.6 mg/kg bwt i.v.) and anti-inflammatory medication (flunixin meglumine 1.1 mg/kg bwt i.v.) prior to preanaesthetic medication.

Surgical technique

The horse was sedated with 200 mg xylazine hydrochloride i.v., placed in surgical stocks and 45 mg morphine sulphate was administered into the caudal epidural space to provide sustained pain relief. Intravenous polyionic fluids were administered at a rate of 3 l/h for the duration of the procedure. Following surgical preparation of the left flank standing surgical sedation was induced with a 5 mg i.v. bolus of detomidine hydrochloride and maintained with an i.v. constant rate infusion of detomidine hydrochloride (5 mg/h). Continuous electrocardiography, direct arterial blood pressure measurement and sequential arterial blood gas analysis were used to aid in anaesthetic monitoring of the patient during surgery.

Following aseptic preparation and draping of the surgical site, flank analgesia was achieved as previously described (Keoughan et al. 2003). A 1.5 cm vertical skin incision was made and a threaded laparoscopic cannula (Endo TIP) was progressively advanced through the abdominal muscles and peritoneum and into the abdominal cavity. Visualisation through a 0° 30 cm laparoscope, partially inserted in the cannula during the process, aided in safe placement of the cannula within the peritoneal cavity.

Once within the abdominal cavity, a 30° 30 cm laparoscope was completely inserted through the cannula and the abdominal cavity was insufflated with CO₂ (Storz Laproflator) to a pressure of 12 mmHg. Abdominal exploration was performed as previously described (Galuppo et al. 1995). There was no gross evidence of metastasis on the structures visualised.
Following abdominal exploration and isolation of the left kidney as previously described (Keoughan et al. 2003), a laparoscopic stapling device (Endo GIA II with 3.5 x 60 mm cartridge)\(^4\) was introduced into the abdomen guarded by the hand of the surgeon. Under laparoscopic visualisation the ureter, renal vein and artery and the accessory branch of the renal artery were identified, isolated, stapled and transected using the stapling device. A sterile plastic bag was then introduced in the abdomen and the kidney was placed in it to facilitate its extraction. The kidney was retrieved from the abdomen with traction on the plastic bag. Laparoscopic visualisation of the vessel stumps did not reveal any haemorrhage.

**Histopathological findings**

The entire left kidney was submitted for histopathological examination. The organ was 2.7 kg measuring 20.0 x 15.0 x 15.5 cm in maximal dimension. Multiple nodular flocculent foci were present on the surface of the kidney; a well-circumscribed 15.0 x 13.5 x 6.0 cm white fibrous nodular mass was present on the peritoneal side of the kidney. Numerous smaller nodular masses emanated from this area. Several other masses were present on the caudal pole of the kidney, measuring from 6.0 x 5.5 x 5.0 cm to 1.0 x 1.0 x 0.3 cm with occasional black, subcapsular discoulouration. On cut section, the nodular masses were revealed to be cystic in nature and filled with blood and clotted blood. The largest cystic mass had an area of central necrosis and haemorrhage and measured approximately 10 cm in diameter (Fig 2). The renal mass, which grossly obliterated approximately 80% of the pre-existing renal architecture, had histological features consistent with an aggressive mixed papillary and tubular carcinoma (Fig 3). No evidence of lymphatic or intravascular tumour metastasis was observed in the sections examined. Other features noted histologically, including the marked peritumoural necrosis and fibrosis, tubular dilatation with cyst formation; haemorrhage and chronic inflammation were considered the likely result of local tumour growth with destruction of adjacent tissues.

**Post operative care**

The horse recovered uneventfully from surgery and post operatively was maintained on i.v. polyionic fluids at 2 l/h, flunixin meglumine, procaine penicillin G and gentamicin at preoperative doses for 3 days following surgery. Morphine sulphate (30 mg i.v.) was also used to control the considerable post operative pain and was initially administered at 6 h intervals. Due to reduced intestinal bordorpgymi and faecal output the gelding received mineral oil and water via a nasogastric tube on several occasions. Three days after surgery the frequency of morphine administration was reduced to twice daily; i.v. fluids, procaine penicillin G and gentamicin were discontinued and the horse was started on trimethoprim sulphamethoxazole at 30 mg/kg bwt per os as twice daily. The horse was discharged from the hospital 5 days following surgery on a tapering dose of oral flunixin meglumine and oral

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Fig 2: Cut section through the left kidney showing a large cystic mass with an area of central necrosis and haemorrhage measuring approximately 10 cm in diameter.

Fig 3: Rafts of tumour cells showing marked nuclear atypia with prominent nucleoli and vesiculated chromatin. Note the numerous mitoses in this high power field. H&E stain, x400.

Fig 4: Ultrasonographic appearance of omental nodules found in the cranioventral abdomen 7 months post nephrectomy. Masses measured 1–2 cm diameter. Image obtained with a 4.0 MHz curvilinear transducer at a scanning depth of 9 cm.
trimethoprim sulphamethoxazole for a further 5 days. Telephone conversations revealed that the horse appeared normal and comfortable. Furthermore, there were no more episodes of haematuria and the owner successfully resumed a normal exercise routine (trail riding) within 3 weeks of the surgical date.

Outcome

Seven months post surgery, the horse was presented to our institution with a 3 week history of lethargy and shallow breathing. The horse was bright and alert with a body condition score of 5/9; physical examination abnormalities included mild fever (38.3°C; rr 37–38.2°C), tachycardia (48 beats/min; rr 28–40 beats/min) and tachypnoea (56 breaths/min; rr 8–16 breaths/min). Clinical laboratory abnormalities included mild anaemia (PCV 26.4%; rr 30–46%), neutrophilia (9.43 x 10^9/l; rr 2.6–6.8 x 10^9/l) with slight toxicity and left shift (bands 245/μl), hyperfibrinogenaemia (7 g/l; rr 1–4 g/l) and mild proteinuria on a dipstick. Abdominal fluid was copious and appeared red and cloudy with a total protein (48 g/l; rr up to 20 g/l) with a total nucleated cell count of 7.48 x 10^9/l (rr up to 2.5 x 10^9/l). There were moderate numbers of erythrocytes, markedly increased numbers of nucleated cells and atypical epithelial cells with numerous mitotic figures. These findings were consistent with metastatic carcinoma with haemorrhage and low-grade purulent inflammation. Transabdominal ultrasound revealed a small (1.4 x 2.1 cm) hypoechoic mass in the region of the left kidney, a 4.6 x 4.3 cm heterogeneous mass between the stomach and spleen, multiple hypoechoic omental nodules in the cranioventral abdomen (Fig 4), scattered small peritoneal masses and moderate peritoneal effusion. Moderate pleural effusion was evident on thoracic ultrasonography and radiography. Euthanasia was undertaken due to poor prognosis.

Post mortem findings

A full body necropsy showed carcinomatosis of the diaphragm, mesentery, omentum, serosal surfaces, spleen, liver and lymph nodes. The lungs had multifocal scattered intravascular metastatic carcinoma and mild eosinophilic bronchitis and scattered pneumonia. The right kidney had moderate interstitial fibrosis with severe multifocal tubular cyst formation, moderate multifocal papillary ductal epithelial hyperplasia, and moderate tunica intimal and tunica medial hypertrophy of arcuate arteries.

Discussion

Primary renal tumours are uncommon in horses (Haschek et al. 1981; Brown and Holt 1985). Of the relatively small number reported, renal cell carcinoma (RCC) has been the most commonly identified (Brown and Holt 1985). This condition occurs most frequently unilaterally but has been reported to affect both kidneys (West et al. 1987). Common clinical features include weight loss, reduced appetite, haematuria and the presence of a palpable mass per rectum (Haschek et al. 1981; van Amstel et al. 1984; Brown and Holt 1985; Owen et al. 1986; van Mol and Fransen 1986; West et al. 1987). Clinical pathological abnormalities described include anaemia, neutrophilia, hypoglycaemia, thrombocytopenia, hypoalbuminaemia, and increases in blood urea nitrogen and serum creatinine concentrations.

Metastatic disease is a common feature with dissemination of the neoplasm to the peritoneum and abdominal organs, liver and lungs, regional lymph nodes, thyroid gland, bone and the oral cavity (Haschek et al. 1981; Brown and Holt 1985; Servantie et al. 1986; van Mol and Fransen 1986; West et al. 1987; Rhind et al. 1999; Rumbaugh et al. 2003). Human RCCs are recognised to have unusual and unpredictable metastatic patterns resulting in clinically detectable metastases without symptoms relating to the primary tumour (Hadjadj et al. 1995; Nakjavan et al. 1997). Treatment in horses is usually symptomatic until such time as a diagnosis is made. Disease is often so advanced at the time of definitive diagnosis that euthanasia is commonly performed. The primary role of surgery in the treatment of RCC is related to the low radio and chemosensitivity of this tumour (Ficarra et al. 2002). Partial or radical nephrectomy, usually in combination with pre- or post surgical immunotherapy or radiotherapy is the current treatment of choice in man (Oya 2006; Ulutin et al. 2006). In the horse, unilateral nephrectomy has been used in the management of renal trauma (Mitchell et al. 2004), ectopic ureters (Sullins et al. 1988), renal abscession (Trotter et al. 1984), nephrolithiasis (Iuzwia et al. 1988) and pyelonephritis (Irwin and Howell 1980). Traditionally this procedure has been performed under general anaesthesia with the horse in lateral recumbency. Recently however, a hand-assisted laparoscopic surgical technique has been described for removal of the left kidney in the standing horse (Keoughan et al. 2003). Given that laparoscopy was employed in this case to aid in the exclusion of regional metastatic or invasive disease, in addition to the inherent risks associated with general anaesthesia and the minimised surgical trauma, this approach was a logical method with which to attempt removal of the abnormal left kidney. The lack of ultrasonographic evidence of metastasis to thoracic and other abdominal structures was an important consideration prior to surgical intervention.

The technique used in this case employs a similar approach to that described previously (Keoughan et al. 2003). The surgical technique was modified in the present case to allow for the extensive abdominal exploration needed to identify possible metastatic disease. This led to the creation of 2 laparoscopic portals before the large abdominal incision and also created the need for insufflation of the abdomen.

We used a blunt-tipped threaded cannula (Endo TIP)3 to initially penetrate the abdomen. It is used without a trocar and is introduced by rotation rather than with direct pressure, usually under visualisation with the endoscope. By dissecting and moving tissue and fascia instead of cutting those tissues it allows controlled penetration into the abdomen reducing the risk of iatrogenic injury to the abdominal organs (Ternamian 1997, 1998). It has been used successfully without
preinsufflation (Hickey and Rendon 2006) in man and it is the technique of choice for penetration of the equine abdomen without preinsufflation at our institution.

The use of a laparoscopic stapling and cutting device, such as the Endo GIA II stapler\(^2\), has become routine in human surgery for donor nephrectomy (Meng et al. 2003). Such devices, which consist of 2 rows of staples either side of an incision, greatly reduce surgical time and have been shown to be effective in achieving haemostasis in arteries of up to 17 mm in diameter and veins up to 22 mm in diameter (El-Hakim and Galuppo 2005). This stapling device has been used successfully for laparoscopic ovarioectomy in mares (van Hoogmoed and Galuppo 2005), but to the authors’ knowledge its use has not been described in nephrectomy surgery. In this case the use of this device was time-saving and provided excellent haemostasis.

The use of a plastic bag facilitated the extraction of the enlarged kidney, as the incision size would not have allowed the passage of both the surgeon’s hands and the enlarged kidney. In addition it may also help to diminish direct friction between the kidney and the abdominal wall at the time of extraction, which may result in exfoliation of tumoural cells as has been reported in human cases of RCC (Chen et al. 2003). Examination of washings from the laparoscopic retrieval bag for malignant cells has been used as a prognostic factor in human surgery (Ankem et al. 2006).

The aggressive nature of RCC is reflected by 20–40% recurrence rate following nephrectomy for clinically localised disease in human studies (Janzen et al. 2003) and underscores the importance of post surgical disease surveillance (Chin et al. 2006). Surveillance protocols aim to minimise low yield studies without reducing patient prognosis. For this reason, stage-based surveillance systems have been employed in man. Anatomic staging systems based on the tumour, nodes, metastasis (TNM) system have been the mainstays in RCC prognosis; integrated staging systems in which the TNM system is combined with nuclear grading (Fuhrman grading) has improved prognostic accuracy (Shuch et al. 2006). Serial serum alkaline phosphatase and serum liver enzyme levels may be used as indicators of osseous and hepatic metastatic disease, respectively (Chin et al. 2006).

Nephrectomy may increase life expectancy in horses with renal cell carcinoma and should be considered as a therapeutic or palliative option. In the authors opinion the hand-assisted laparoscopic approach provided a safe and practical method for nephrectomy that negated the necessity for general anaesthesia in this high risk horse population (Robertson et al. 1985).

Manufacturers’ addresses

1Horse Health Products, Massillon, Ohio, USA.
2C.R. Bard, Covington, Georgia, USA.
3Karl Storz Endoscopy America, Goleta, California, USA.
4United States Surgical, Norwalk, Connecticut, USA.

References


