Case Report

Pancreatic adenocarcinoma in a donkey. Use of laparoscopy to aid the diagnosis

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Summary

Pancreatic adenocarcinoma was diagnosed in a 15-year-old donkey that presented with signs of chronic laminitis, weight loss and chronic colic. An intra-abdominal mass was identified by exploratory laparoscopy, and this was subsequently confirmed to be a pancreatic adenocarcinoma at post mortem examination. Unlike most previously reported cases of pancreatic disease in equids, this donkey had no clinicopathological evidence of an associated hepatopathy.

Introduction

Pancreatic adenocarcinoma is an uncommon disease in equids. A review of the literature revealed fewer than 10 reported cases, in which the typical clinical signs were vague and nonspecific, including weight loss and mild intermittent abdominal pain (Kerr et al. 1982; Church et al. 1987; Carrick et al. 1992; Rendle et al. 2006). Clinical pathology evaluations in these cases have generally shown hypoalbuminaemia and elevated serum liver enzymes (Rendle et al. 2006).

This Case Report describes the presentation, diagnosis and pathological findings in a donkey with pancreatic adenocarcinoma. The identification of an abdominal mass was aided by the use of exploratory laparoscopy.

Case details

A 15-year-old female donkey was presented to Bell Equine Veterinary Clinic with a history of depression, weight loss, chronic laminitis over the past year, and intermittent mild abdominal pain of 2 days’ duration.

On arrival the donkey was dull and very reluctant to move, and had grossly overgrown hooves with increased digital pulse amplitude in all 4 feet. The donkey was in poor body condition, with a body condition score of 1–2/5 (Anon 2005) and bodyweight of 160 kg. The donkey was tachycardic (heart rate 60 beats/min) and tachypnoeic (respiratory rate 52 beats/min). Harsh lung sounds were auscultated diffusely over the entire lung fields on both sides of the thorax. Routine haematology, a serum biochemistry profile and serum electrolyte analysis revealed haemoconcentration (packed cell volume [PCV] 54%; normal reference range [rr] 32–46%), mild hyperfibrinogenaemia (plasma fibrinogen 4.6 g/l, rr 0–4 g/l), azotaemia (serum urea 10.0 mmol/l, rr 2.5–8.3 mmol/l) and hypercalcaemia (serum ionised calcium 1.79 mmol/l, rr 1.25–1.75 mmol/l). Concentrations of serum creatinine (99 µmol/l, rr 40–160 mol/l), serum triglycerides (1.6 mmol/l, rr <2.9 mmol/l) and plasma glucose (4.8 mmol/l, rr 4.4–5.5 mmol/l) were all normal. The serum concentrations of other biochemical parameters (total protein, albumin, globulin, alkaline phosphatase, gamma glutamyl transferase, glutamate dehydrogenase, aspartate aminotransferase, creatine kinase, bilirubin, bile acids) were all within the normal reference ranges for our laboratory. Abdominal paracentesis (performed under ultrasound guidance in view of the large amount of retroperitoneal fat) yielded turbid peritoneal fluid with an elevated total nucleated cell count (52.0 x 10⁹/l, rr <5.0 x 10⁹/l) and elevated total protein concentration (35 g/l, rr <25 g/l). Cytological examination of the peritoneal fluid revealed a preponderance of neutrophils (90%) with a smaller number of reactive mesothelial cells and large undifferentiated mononuclear cells. No microorganisms were identified. A faecal worm egg count was negative.

Lateral radiographs of all 4 feet showed significant distal rotation of the distal phalanx (capsular rotation up to 18°) and severe hoof overgrowth. Transcutaneous abdominl ultrasonography using a 5 MHz curvilinear transducer (Vivid 3 Expert) showed no significant abnormalities apart from distended but motile small intestine (maximum diameter of small intestinal loops...
7.8 cm, normal ≤4 cm). A small amount of hypoechoic peritoneal fluid was visualised.

Routine dental examination revealed no significant abnormalities. Only a limited rectal examination was possible in view of the donkey’s size, but this did not reveal any specific abnormalities. The donkey continued to pass faeces during the period of hospitalisation, but in reduced quantities.

**Initial treatment and additional diagnostics**

The results of initial examinations indicated hypovolaemia, azotaemia, aseptic peritonitis and chronic laminitis. The donkey was stabilised with i.v. Hartmann’s solution (Isolcet)2 administered via an indwelling i.v. jugular catheter (an initial bolus of 10 l administered over 3 h followed by a constant rate infusion of 1.5 l/h), and started on a course of i.v. sodium benzyl penicillin (Crystapen)3 (10 mg/kg bwt q. 8 h), gentamicin sulphate [Genta 100]4 (6.6 mg/kg bwt q. 24 h) and flunixin meglumine [Finadyne]3 (0.25 mg/kg bwt q. 8 h); a low dose of flunixin meglumine was used initially in view of the azotaemia. Supportive pads (Lily Pads)5 were placed on all 4 feet prior to corrective farriery being performed (resection of excessive toe and heel before re-placement of supportive pads). The donkey spent much of the time lying in sternal recumbency; this was attributed to foot pain and general depression. However, she appeared less lame when standing and moving around the stable following the application of supportive frog pads and subsequent corrective farriery. Acepromazine (Sedalin gel)6 (0.02 mg/kg bwt per os q. 8 h) was administered in an attempt to improve digital blood flow.

Forty-eight hours after admission, the respiratory rate and effort remained increased although the respiratory rate had dropped to 28 breaths/min. On auscultation of the thoracic cavity, diffuse crackles were heard over the lung entire fields. Repeat abdominocentesis produced a turbid fluid sample with a total nucleated cell count of 30.0 x 10^9/l. Cytological appearance was similar to the previous sample. Intravenous fluid therapy was discontinued on the third day of hospitalisation; the PCV was 40% at this stage, and serum urea and creatinine levels were within the normal range. The administration of flunixin meglumine was also stopped, and analgesia with i.v. phenylbutazone (Equipalazone)7 (3.1 mg/kg bwt i.v. q. 12 h) started. Intravenous antimicrobial therapy was continued. By the third day, the respiratory rate and effort had returned to normal.

On the fourth day of hospitalisation the donkey appeared to be much more comfortable on her feet, and was standing for longer periods of time. The digital pulse amplitude had returned to normal, and the heart rate had reduced to 48 beats/min. A detailed transcutaneous abdominal ultrasound scan revealed an increased volume of hypoechoic peritoneal fluid with fibrin tags associated with visceral surfaces. The vascularisation associated with the caecum and colon appeared diluted.

Following discussion with the owner, it was elected to perform exploratory laparoscopy in an attempt to diagnose the cause of the peritonitis. This was undertaken on Day 6 of hospitalisation. A standard exploratory laparoscopic procedure [Galuppo et al. 1995] was performed within both sides of the abdomen with the donkey standing and sedated with 40 µg/kg bwt romifidine (Sedivet)8 and 25 µg/kg bwt butorphanol (Torbugesic)9. Laparoscopy revealed an increased amount of sero-sanguinous peritoneal fluid; the serosal surfaces of the small and large intestine appeared mildly hyperaemic with dialted vasculature (especially on the caecum). A mass was visualised in the right cranial abdomen, adjacent to the duodenum, caecal base, pancreas and right lobe of the liver (Fig 1). The precise size and limits of the mass were difficult to appreciate, but it was approximately 6–8 cm in diameter, multinodular, and had a smooth, glistening white surface. Laparoscopic biopsy of the mass was attempted, but was found to be difficult due to the surrounding small intestine, which obscured the field of view, and the firm, smooth surface of the mass. However, a small biopsy from the periphery of the mass was eventually obtained, and submitted for histopathological examination; this was considered to be fibrovascular tissue. No other significant abnormalities were detected during the laparoscopic examination.

In view of the laparoscopic findings of a mass in the region of the pancreas, analysis of the serum and peritoneal fluid obtained prior to laparoscopy was undertaken for measurement of amylase and lipase activities. These were normal (serum amylase 30 iu/l, rr 5–50 iu/l; serum lipase 55 iu/l, rr 40–80 iu/l; peritoneal amylase 10 iu/l, rr 0–13 iu/l; peritoneal lipase 28 iu/l, rr 0–36 iu/l).

Further evaluation of the mass by exploratory laparotomy under general anaesthesia was recommended, but the owner declined this option and...
elected to take the donkey home. At the owner's request the donkey was discharged from the hospital on oral antibacterial and analgesic treatments (trimethoprim 5 mg/kg bwt and sulphadiazine [Noradine] 25 mg/kg bwt q. 12 h, enrofloxacin [Baytril 10% oral solution] 7.5 mg/kg bwt q. 24 h, and phenylbutazone [Equipalazone] 0.45 mg/kg bwt q. 24 h). Despite these treatments, the donkey's clinical condition showed a continued deterioration with progressive depression and worsening inappetence, and the owners elected for euthanasia 5 days after discharge.

Gross pathological findings

Post mortem examination revealed copious amounts of turbid sero-sanguinous fluid in the peritoneal cavity. The mass previously visualised by laparoscopy was identified (Fig 2). The mass was adherent to the proximal duodenum and the distal pancreas; it was 8 x 9 x 5 cm in size, white in colour and gritty on palpation. The cut surface was grey-white in colour with small (2 x 2 mm) areas of translucency throughout. The pancreas was enlarged (approximately 30 cm in length), extending over the majority of the proximal duodenum and to the right liver lobe, and was grey-yellow in colour. Examination of the gastrointestinal tract showed erythematous intestinal walls with dilated vasculature. The serosal surface of the caecum was diffusely congested and there was an area of discoloured necrotic tissue at the base. The ascending, transverse and descending colons had congested serosal surfaces with numerous fibrin tags.

Histopathology

The histopathological appearance of the pancreatic tissue revealed replacement of the normal exocrine pancreas architecture by a pleomorphic exocrine pancreatic adenocarcinoma. Anaplastic cells forming acini resembling exocrine pancreatic tissue were separated by scirrhous stroma. Neoplastic cells were large, pleomorphic with scant eosinophilic, finely granulated cytoplasm and large oval nuclei with a prominent nucleolus. There were extensive areas of coagulative and lytic necrosis (Fig 3). The adjacent mass consisted predominantly of scirrhous stroma with extensive areas of lytic necrosis, characterised by complete loss of architecture and cellular detail and focal osseous metaplasia. Pleomorphic epithelial cells forming acini-like structures were found scattered within the scirrhous stroma. In addition there was a necrotising steatitis within the peripancreatic tissues with multifocal mineralisation/saponification.

The muscularis of the caecum was extensively replaced by fibrovascular tissue and contained areas of extensive necrosis with scattered anaplastic cells arranged in nests (Fig 4).
Discussion

Common causes of weight loss and depression in donkeys (including dental diseases, colon impaction, hyperlipaemia and parasitism) were ruled out in this case during the initial clinical and clinicopathological evaluations. Previous cases of pancreatic adenocarcinoma in equids describe clinical signs attributable to hepatopathy with elevations in serum concentrations of aspartate transferase, alkaline phosphatase and gamma glutamyl transferase. Kerr et al. (1982) described a case of pancreatic adenocarcinoma in a donkey stallion, and concluded that pancreatic and hepatic neoplasms should be included as differentials when there is a suspicion of ragwort poisoning due to the similarities seen between these conditions. Two cases of pancreatic adenocarcinoma described by Church et al. (1987) showed severe biliary dilation and hepatic fibrosis secondary to obstruction of the common bile duct.

In the present case there was no clinical or pathological evidence of hepatic disease. No biochemical derangements in liver enzymes were identified, and gross and histopathological examinations of the liver were unremarkable. The primary presentation of this case was aseptic peritonitis and intermittent abdominal pain. The peritonitis was probably a sequel to the inflammation and necrosis of the surrounding fat and viscera, including the caecum. Histopathology of the mass, revealed marked necrosis of adjacent adipose tissue. Such necrotising steatitis has been recognised in other species in association with pancreatic disease, including exocrine pancreatic carcinoma in dogs and cats (Munster and Reusch 1988; Brown et al. 1994). This is believed to be due to the leakage of lipolytic enzymes into the peripancreatic adipose tissue. Additionally, more widespread inflammation of fat (panniculitis) (probably due to systemic circulation of pancreatic enzymes) has been recorded in association with pancreatic carcinoma in the cat (Fabbriini et al. 2005) and pancreatitis in the dog (Mellanby et al. 2003). There is also a recent report of peripancreatitis, pancreatic fibrosis, abdominal steatitis and panniculitis in a horse that presented with signs of acute colic and subcutaneous nodules (Waitt et al. 2006). In the present case, the steatitis was limited to the adipose tissue adjacent to the pancreas.

Histopathological examination of the caecum revealed extensive mural necrosis with nests of neoplastic epithelial cells within the intestinal wall, embedded in scirrhous stroma. This was considered most likely due to coelomic metastatic spread from the pancreatic carcinoma. Beside their aggressive behaviour and infiltrative growth, metastasis of pancreatic tumours in other species is a frequently observed feature, with the most common sites being mesentery and adjacent gastrointestinal organs; metastasis to the lungs is also frequently observed (Meuten 2002). The caecal lesion was, therefore, considered to be probably due to metastasis.

On presentation the donkey was also affected by chronic laminitis. This disease is not uncommon in the aged donkey, and may have been an entirely unrelated clinical entity (Reilly 1997). However it is reasonable to assume that pancreatic adenocarcinoma will cause damage to the endocrine cells of the islets of Langerhans and therefore changes to glucose metabolism. Although no previously reported cases of pancreatic adenocarcinoma in donkeys have noted clinical signs relating to endocrine disturbances, circulating insulin concentrations do not appear to have been recorded. Laminitis is a common and recurrent disease in equids (especially ponies) with endocrine disorders such as pituitary pars intermedia dysfunction (equine Cushing’s syndrome) and equine metabolic syndrome (Johnson 2002; Donaldson et al. 2004; Keen et al. 2004; Treiber et al. 2006), and recent experimental studies have shown a role of insulin in the pathogenesis of the disease (Asplin et al. 2007). It is possible that the chronicity of this donkey’s laminitis was contributed to by endocrine disorders secondary to pancreatic dysfunction due to the adenocarcinoma, but no specific endocrinological tests were performed. However, the plasma glucose concentration at admission to the hospital was normal suggesting that the donkey was not affected by diabetes mellitus.

Whilst there is an abundance of literature regarding lameness assessment in the domestic horse, a lack of comparable evidence exists for the donkey (Ashley et al. 2003). Donkeys may not demonstrate the typical postural changes associated with foot pain seen in horses, and thus laminitic pain may go unrecognised. As in the present case, the only alteration in behaviour associated with laminitis may be an increase in periods of time spent lying down (Trawford and Crane 1995). The donkey did, however, appear to walk around the stable more freely following the administration of flunixin meglumine (a low dose was used initially in view of the azotaemia in an attempt to minimise the risk of renal toxicity), and the application of frog supports. The latter technique has been questioned in view of the different foot anatomy in the donkey compared to the horse (Reilly 1997); it has been suggested that frog support may exaggerate distal phalangeal rotation. However, our clinical experience has been that frog supports can result in significant clinical improvement in some donkeys with chronic laminitis (as appeared to be the case in this donkey), and we may use this treatment initially followed by careful re-evaluation. The dosage of phenylbutazone chosen was also based on the clinical response of the donkey. Clearance of phenylbutazone is higher in donkeys than horses (Mealey et al. 1997) because hepatic metabolism appears to be more rapid in donkeys. As a result, phenylbutazone may require more frequent administration in donkeys than in horses. However, in the present case, dosing with phenylbutazone twice a day appeared to have the desired clinical effect, so more frequent administration was not considered necessary.
Due to financial constraints certain diagnostic procedures were omitted from the work-up of this case. The respiratory tract was never investigated in detail despite the initial episodes of tachypnoea and the auscultatory abnormalities. The clinical improvement in the respiratory rate and effort meant that further diagnostics could not be justified. Rendle et al. (2006) described a mare with tachypnoea and pleural effusion with metastatic pancreatic adenocarcinoma. The case described here had evidence of metastatic spread within the abdominal cavity, but no evidence of thoracic metastasis was identified.

The atypical presentation of this case meant that pancreatic adenocarcinoma was not initially considered. However, abdominal neoplasia is an important differential for peritonitis (Zicker et al. 1990; East and Savage 1998; Mair 2002). The index of suspicion was increased when analysis of the peritoneal fluid revealed an increased total nucleated cell count with the presence of large undifferentiated mononuclear cells, although no conclusive evidence of neoplasia was identified. Normal peritoneal fluid has an approximate ratio of 2:1 of neutrophils to mononuclear cells, and cases of peritonitis are generally characterised by high numbers of degenerate and nondegenerate neutrophils (Taylor 2002). Accurate diagnosis of abdominal neoplasia by cytological examination of peritoneal fluid is dependant on the exfoliation of neoplastic cells into the peritoneal cavity, which only occurs in a proportion of cases (Zicker et al. 1990). Exploratory laparoscopy was invaluable in the work-up of this case, despite the inability to obtain a representative biopsy, as it identified an abdominal mass. We were unable to identify this mass by transcutaneous abdominal ultrasonography (due to the presence of overlying intestine) or transrectal palpation (due to the small size of the patient). This case demonstrates the value of laparoscopy as a diagnostic procedure (Walmsley 1999), and the ability for it to be performed in even small patients. The value of laparoscopy in the diagnosis of pancreatic disease in dogs and cats has recently been highlighted (Webb and Trott 2008).

In conclusion pancreatic adenocarcinoma was diagnosed as the cause of intermittent abdominal pain and continued clinical deterioration in this donkey. This Case Report demonstrates that pancreatic adenocarcinoma should be considered as a differential diagnosis in cases with vague nonspecific abdominal signs, and that hepatopathy and associated signs are not always present with pancreatic problems. The use of laparoscopy as a diagnostic aid for clinical signs relating to the abdomen is highlighted here.

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Manufacturers’ addresses

1 GE Medical Systems, Chalfont St Giles, Buckinghamshire, UK.
2 Ivex Pharmaceuticals, Lane, Co Antrim, UK.
3 Schering-Plough Animal Health, Welwyn Garden City, Hertfordshire, UK.
4 CP Pharma, Burgdorf, Germany.
5 BL Farriers Ltd, Middlewich, Cheshire, UK.
6 Vetoquinol, Bicester, Oxfordshire, UK.
7 Arnolds Veterinary Products, Shrewsbury, Shropshire, UK.
8 Boehringer Ingelheim, Bracknell, Berkshire, UK.
9 Fort Dodge Animal Health, Southampton, Hampshire, UK.
10 Norbrook Laboratories, Carlisle, Cumbria, UK.
11 Bayer Health Care, Newbury, Berkshire, UK.

References


