Rare presentation of a squamous cell carcinoma originating from gastric compartment 1 in an alpaca

Bijzondere presentatie van een squameus celcarcinoom afkomstig van compartiment 1 van de maag bij een alpaca


1Dierengezondheidszorg Vlaanderen, Industrielaan 29, B-8820 Torhout
2Veterinary Practice for Alpacas, Dadizelestraat 32, B-8940 Geluwe
3Department of Pathology, Bacteriology and Poultry Diseases, Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, B-9820 Merelbeke

ABSTRACT

A twenty-year-old, male, intact alpaca with a history of anorexia, progressive weakness and recumbency was euthanized because of a poor prognosis and clinical deterioration. The animal was submitted for necropsy at the pathology department of Dierengezondheidszorg Vlaanderen (DGZ) diagnostic lab. A full necropsy was performed and showed a large firm white mass measuring 18x8x10 cm attached to the dorsal wall of gastric compartment 1 (C1) and expanding to the abdominal aorta. Miliary small white metastatic nodules were present on the pleura and peritoneum (carcinomatosis). Multiple small white metastatic nodules were also present in the parenchyma of the liver. On histological investigation, this neoplasia was characterized as squamous cell carcinoma (SCC).

INTRODUCTION

Alpacas and llamas belong to the group of new world camelids. They are hardy animals that are able to adapt to a wide range of management situations (Smith, 1989). Anatomically, the anterior digestive tract is the most exceptional feature in camelids. Although camelids are foregut fermenters, they are not true ruminants as they lack the four well-defined stomachs of the ruminants. The anatomy of their three chambered stomach is markedly different from that of ruminants. Unlike ruminants, all of the compartments have glandular regions and none have papillae. C-1 fills the left abdomen and is divided into cranial and caudal sacs by a transverse pillar. The majority is non-glandular and is lined by unkeratinized stratified squamous epithelium (De la Vega, 1952; Luciano et al., 1980) but the ventral surfaces contain smaller glandular sacs lined by a mucinous glandular epithelium. C-2 has a glandular mucosal surface over the...
greater curvature, which is subdivided by intersecting
crests that create a retiform pattern not analogous to
the pattern seen in the reticulum of ruminants. The
lesser curvature shows a small area called the esophageal
or ventricular groove (Vallenas, 1970). The primary
crest margins are covered by stratified squamous
epithelium extending from the ventricular groove, the
secondary crests are covered with glandular mucosa
(Vallenas, 1970). C-3 is lined entirely by glandular
epithelium and secretes mucus and digestive enzymes
(Vallenas et al., 1971; Cornick, 1988). The proximal
four-fifths consists of a mucinous glandular epithelium
similar to the saccules in C-1 and C-2 (PH 6.5).
The terminal one-fifth of C3 is lined by true gastric
glands, which secrete digestive enzymes and acid (PH <2) (von Engelhardt et al., 1979). Neoplasia is not
common in camelds, with relatively few reports in
the literature (Smith, 1989; Fowler, 2010). However,
in a review by Valentine et al. (2007) on the prevalence
of neoplasia in llamas and alpacas submitted for
necropsy at a diagnostic laboratory, the prevalence in
llama’s was 11% and in alpaca’s 4.9%. In that study, a
difference in prevalence of neoplasia, tumor types and
age at diagnosis between llamas and alpacas was also
indicated (Valentine et al., 2007). Lymphosarcoma is
the most commonly reported tumor in llamas and
alpacas (Cebra et al., 1995; Irwin, 2001; Underwood
et al., 1993; Sartin et al., 2004; Shapiro et al., 2005;
Valentine et al., 2007; Rosa et al., 2013). Gastric squamous cell carcinoma has been previously reported in
various animal species including a few cases in llamas
(Cornick, 1988; Sartin et al., 1997; Valentine et al.,
2007). However, to the authors’ knowledge, no
reports on the occurrence in alpacas have been published.

Clinical symptoms are non-specific and consist of
weight loss, anorexia, vomiting and lethargy (Pat-
naik et al., 1980; Wester et al., 1980; Mc Kenzie et
al., 1997). Squamous cell carcinoma of the forestomachs has been reported in the bovine rumen and ovine
omasum and reticulum but are extremely rare (Doige,
1983; Bertone et al., 1985). Bovine ruminal squamous cell carcinoma is associated with consumption of
bracken fern and could be the result of a mutagenic
effect caused by interaction of the ptaquiloside car-
cinogen of bracken fern and bovine papillomavirus
(Bertone et al., 1985).

In the present study, a rare presentation of a prima-
ry squamous cell carcinoma is reported in a twenty-
year-old alpaca originating from gastric compartment
C1 without evidence of mucosal lesions but expanding
from the surface of the dorsal wall of C1 to the ab-
dominal aorta and metastasizing to the liver and mes-
entery.

Case history and necropsy

A twenty-year-old male intact alpaca was present-
ed to the attending veterinarian with chronic weight
loss, anorexia for already five days and an increased
frequency of recumbency during the past fourteen
days. The animal was kept for breeding purposes until
the age of sixteen. He was born in Australia and sub-
sequently stayed in New-Zeeland, England, France
and Belgium. He did well until symptoms started
four weeks prior to presentation to the veterinarian.
Because of the poor prognosis, the animal was euthanized. The animal was submitted to the diagnostic
laboratory DGZ Vlaanderen (Dierengezondheidszorg
Vlaanderen), where a full necropsy was performed.

At necropsy, the animal was found to be thin
and weighed 48 kg (reference mean 55 kg) (Fowler,
2010). The lower incisors were missing. The abdomi-
nal cavity contained a striking amount of clear yellow
serous fluid (approximately 1200 ml). The mediasti-
nal lymph nodes were enlarged, white and firm on cut
section. The pleura was covered with multiple super-
ficial small, white, well-circumscribed, slightly raised
areas measuring approximately 0.3 cm. The coronary
grooves of the heart showed cachectic serous fat at-
rophy. The mesentery and serosal surface of multiple
abdominal organs showed multiple disseminated large
and small (diameter range: 0.2-1cm), white nodules
(Figure 1). One large (18x8x10cm), white, firm mass
was attached to the first gastric compartment (C1) and
expanded up to the abdominal aorta. The three gastric
compartments contained food and there were no spe-
cific changes visible on the mucosal surface. The liver
was enlarged and showed multifocal white soft nod-
ules (average diameter 2cm) within the parenchyma.

Histopathology and immunohistochemistry

Samples of the primary mass on C1 and thoracic
and peritoneal nodules as well as liver and lung were
fixed in 4%-neutral buffered formalin solution, rou-
tinely processed and embedded in paraffin. Five-µm-
thick sections were mounted and stained with hema-
toxylin and eosin for histological examination.

Histopathologic evaluation of the mass of C1 re-

Figure 1. Gross aspect of the mesentry and serosal surface of the intestine with multiple large and small metastatic nodules.
vealed a non-encapsulated and densely cellular neoplasm consisting of nests, anastomosing cords and islands of neoplastic cells, which were separated by a moderate amount of fibrovascular stroma with multifocal small numbers of lymphocytes (Figure 2). Neoplastic cells were polygonal with abundant eosinophilic to amphophilic cytoplasm. The nuclei of neoplastic cells were variably sized, sometimes large, oval to irregular, hyperchromatic to vesicular. They often contained a prominent single nucleolus. Many nests and islands of neoplastic cells show areas of necrosis characterized by karyorrhexis, karyolysis and pyknotic cell debris admixed with small numbers of neutrophils. Some neoplastic cells were undergoing disorderly individual cell keratinization (dyskeratosis). Multifocally, neoplastic cells surrounded variably-sized accumulations of concentric, lamellated eosinophilic material (keratin pearls). There were 2-5 mitoses per high power field with frequent bizarre mitotic figures. Anisokaryosis and anisocytosis were prominent. Multiple lymphatic vessels were dilated with intraluminal clusters of neoplastic cells attached to the lymphatic wall (tumor emboli).

Samples of the liver and mesenteric nodules showed a neoplastic process with similar histopathological characteristics as described for the primary mass.

Histopathologic examination of the lung showed multiple subpleural aggregates of cholesterol crystals surrounded by a rim of macrophages and multinucleated giant cells (cholesterol granulomas). No neoplastic lesions were present in the lung or on the pleura.

Immunohistochemical stains were performed on samples of the primary mass, liver and mesenterial metastases. In all tissue samples, neoplastic cells were positive for cytokeratin (monoclonal mouse anti-human Cytokeratin clone AE1/AE3, M3515, Agilent, Santa Clara, Unites States) and negative for vimentin (monoclonal mouse anti-Vimentin clone Vim 3B4, M7020, Agilent, Santa Clara, United States). Claudin staining (polyclonal rabbit anti-Claudin 1, 18-7362, Zymed Laboratories, South San Fransisco, United States) was strongly positive.

DISCUSSION

Gastric squamous cell carcinomas generally present as exophytic vegetative ulcerated masses bulging into the lumen of the stomach (Munday et al., 2017). The behavior of the SCC in this alpaca was unusual because the tumor did not present as a mucosal nodular exophytic growth but expanded into the peritoneal cavity without causing any changes on the mucosal surface. A similar case without mucosal lesions has been reported in a man with a primary squamous cell carcinoma of the stomach presenting as a huge retroperitoneal tumor adjacent to the anterior wall of the abdominal aorta and invasive to the dorsal wall of the stomach (Wu et al., 2016). In that case however, there was no evidence of metastatic disease.

In human medicine, there are several hypotheses regarding the origin of SCC. According to one hypothesis, a metaplastic squamous focus is the origin; in another hypothesis, it has been suggested that SCC develops from an adenocarcinoma. Also growth of squamous cell tumors from undifferentiated stem cells mediated by unknown stimuli has been suggested (González-Sánchez et al., 2017). González-Sánchez et al. (2017) favor the theory that the SCC originates from foci of heterotopic squamous epithelium of the stomach submucosa or other layers. In human medicine, four histopathologic criteria for the diagnosis of squamous cell carcinoma have been described (Boswell and Helwig, 1965). These criteria of which at least one should be present to diagnose squamous cell carcinoma are 1. keratinized cells masses forming keratin pearls, 2. mosaic cell arrangement, 3. intercellular bridges and 4. high concentration of sulphhydryl and/or disulphide groups. However, the pathogenesis and etiology of SCC in the glandular stomach of human patients remain unclear (González-Sánchez et al., 2017).

The stomach is the most frequent location for gastrointestinal neoplasia with SCC reported most commonly in horses (Munday et al., 2017). Gastric SCC in horses develops in the proximal epithelial-lined portion of the stomach, and most commonly metastasizes transcoelomic after invading through the gastric serosa. There are also reports of lymphatic and hematogenous spread (Tennant et al., 1982; Taylor et al., 2009). Forestomach squamous cell carcinoma in ruminants is rare. In cattle, gastric SCC is often associated with esophageal papilloma caused by bovine papillomavirus 4 (BPV-4) and is specifically geographically spread (Kenya and North England) (Plowright, 1955; Bertone et al., 1985), being more common in certain regions of Scotland, England and Kenya (Sartin et al., 2017).

Figure 2. Photomicrograph (hematoxylin eosin) of the primary tumor composed of nests and islands of neoplastic cells, separated by a moderate amount of fibrovascular stroma with multifocal small numbers of lymphocytes. Some nests of neoplastic cells present individual cell keratinization (arrows).
1997). A mutagenic interaction between bovine papillomavirus and bracken fern ptaquiloside carcinogen can play a role in the development of gastric SCC in the rumen (Bertone et al., 1985). In a study by Sartin et al. (1997) on three llamas with gastric SCC, an environmental influence has been suggested because all three animals originated from the Southern United States. In some areas, where the genetic pool is rather narrow, genetic predisposition may be a factor to take into account (Sartin et al., 1997).

Although there are many similarities between the diseases of camels and cattle, one should be cautious of extrapolating from ruminants to camels (Esteban et al., 1988). Considering the differences in prevalence and type of neoplasia in llamas and alpacas, it is even questionable whether llamas and alpacas should be grouped and reported together. Neoplasia, such as lymphosarcoma, gastric SCC and adenocarcinoma are occasionally seen in these animals. However, due to their increasing popularity, pet status and related longevity, alpacas are more frequently presented to veterinary practices, which may increase the diagnosis of these neoplastic entities.

The clinical signs of anorexia, weight loss and lethargy present in the alpaca in the present case were similar to those reported in llamas and horses (Cornick, 1988; Sartin, 1997; Taylor et al., 2009). Routine blood analysis, gastroscopy, abdominocentesis and transabdominal ultrasonode have been described as useful techniques for the diagnosis of gastric neoplasia in horses (Taylor et al., 2009). These diagnostic techniques are being implemented in well-equipped camelid practices and could be useful for the diagnosis of gastric neoplasms in camels. Neutrophilia similar to that seen in horses with SCC has been reported in a llama (Cornick, 1988; Taylor et al., 2009). Given the location of the SCC in this case, the neoplastic mass would probably have been missed on gastroscopy. Nevertheless, abdominocentesis, transabdominal ultrasound and blood analysis could have aided in diagnosing the SCC in this case.

Further research on the pathological conditions, predisposing factors and genetic predisposition is necessary to gain more thorough knowledge of the specific diseases and their diagnosis in these species.

LITERATURE


Tennent B., Keirn D. R., White K. K., Bentinck-Smith J., King J.M. (1982). Six cases of squamous cell carcinoma...


---

**Uit het verleden**


Luc Devriese