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DISEASE IN WILDLIFE OR EXOTIC SPECIES

Diffuse-type Gastric Mucinous and Signet Ring Cell Adenocarcinoma in a Captive California King Snake (*Lampropeltis getula californiae*)

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Summary

An adult female California king snake (*Lampropeltis getula californiae*) housed in Taipei Zoo was presented with a 2-week history of anorexia, fatigue and abdominal swelling. Exploratory laparotomy revealed a gastric mass with two circular perforations and multiple mottled white to beige protuberances along the mucosal surface. Histologically, the gastric mass showed an invasive, transmural growth of epithelial cells arranged in nests, lobules, acini and sheets in the mucosa and submucosa that progressively transformed into signet ring cells in the muscularis externa and subserosa. All of the neoplastic cells expressed pan-cytokeratin immunohistochemically. Based on the World Health Organization histological criteria, a diagnosis of diffuse-type gastric mucinous and signet ring cell adenocarcinoma was made.

Keywords: signet ring cell adenocarcinoma; snake; stomach

Spontaneously arising neoplasms in wild animals were thought to be uncommon; however, in captive snakes, the prevalence of neoplasia ranges from 12.4% to 23.1% due to improved husbandry resulting in prolonged life span (Ramsay *et al.*, 1996; Catao-Dias and Nichols, 1999). Structurally, the snake stomach is composed of proximal, middle (fundus) and distal (pylorus) parts, which are made up of variable thicknesses of mucosa, submucosa, tunica muscularis and serosa. The snake stomach is histologically and functionally similar to that of mammals (Dehlawi and Zaher, 1989; Khamas and Reeves, 2011). In previous retrospective studies, most gastric tumours in captive snakes were malignant and of mesenchymal origin (Catao-Dias and Nichols, 1999). Only few cases of gastric malignancies of epithelial origin were reported in snakes (Garner *et al.*, 2004). Gastric adenocarcinoma is rare in snakes, with only two case reports to date: one in a captive diamond python (*Morelia spilota spilota*) and another in a captive Florida indigo snake (*Drymarchon couperi*) (Martin *et al.*, 1994; Baron *et al.*, 2014). In the present report, histological and immunohistochemical characteristics of a rare gastric mucinous and signet ring cell adenocarcinoma in a California king snake (*Lampropeltis getula californiae*) are recorded. To our knowledge, this is the first case of a diffuse-type gastric mucinous and signet ring cell adenocarcinoma in a California king snake.

An adult female California king snake housed in Taipei Zoo was presented with a 2-week history of anorexia, fatigue and abdominal swelling. Exploratory laparotomy revealed a perforated caseous growth in the caudal stomach. Gastrectomy was performed. The excised gastric specimen had two circular perforations with a white, pasty and firm texture that had diameters of 0.5 cm and 1.5 cm, respectively. The gastric wall was diffusely and annularly widened and had multiple raised, mottled white to beige

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protuberances on its mucosal surface. During specimen processing, the snake died and was submitted for necropsy examination. The middle coelom, at a level caudal to the surgical region, had multiple round, soft to firm, yellow adipose nodules, which were approximately 0.5 cm in diameter. The gastrointestinal tract near the surgical region was affected by adhesions that were tan–green in colour. No other significant gross abnormalities or evidence of metastases were identified in the other organs. The gastric mass and the representative specimens were collected, fixed in 10% neutral buffered formalin and processed routinely.

Sections were stained by haematoxylin and eosin (HE) and were subjected to immunohistochemistry (IHC) with the following primary reagents: mouse anti-human monoclonal pan-cytokeratin (clone AE1/AE3, 1 in 100 dilution; Novocastra Laboratories Ltd, Newcastle, UK), cytokeratin 7 (CK7, clone OV-TL 12/30, 1 in 200 dilution; Novocastra), cytokeratin 20 (CK20, clone EPR1622Y, 1 in 200 dilution; Abcam, Cambridge, UK), HepPar-1 (clone OCH1E5, 1 in 100 dilution; Sigma–Aldrich, Steinheim, Germany), CDX-2 (clone EP25, 1 in 30 dilution; Novocastra), E-cadherin (clone 36B5, 1 in 250 dilution; Novocastra) and N-cadherin (clone IAR06, 1 in 100 dilution; Novocastra). Detection of binding was via use of the REAL Envision kit (Dako, Glostrup, Denmark) using 3,3′ diaminobenzidine as a chromogen. Internal and external controls consisted of tissues from this snake and mammalian tissues and negative controls were created by omitting the primary antibodies.

Microscopically, the gastric mass showed invasive and transmural growth of neoplastic mucinous cells that were arranged in nests, lobules, acini or sheets in the mucosa and submucosa and progressively transformed into single cells, small clusters and mixed patterns in the muscularis externa and subserosa (Fig. 1). The neoplastic cells were generally separated by desmoplastic fibrous stroma and prominently intermingled with a light, pale mucinous background. The neoplastic cells were more pleomorphic and loss of cell polarity was noted in the muscular and subserosal layers (Fig. 1). They had distinct borders and contained light basophilic and clear cytoplasm that frequently peripheralized the nuclei in certain areas, resembling 'signet ring' cells. The nuclei showed marked atypia, with shapes from round, flat, angular to crescent-shaped and had prominent marginated chromatin and one to two distinct nucleoli. The mitotic activity was high, with approximately 1–2 mitoses per high-power field (×400). Mucin in the neoplastic cells and the surrounding cellular stroma was

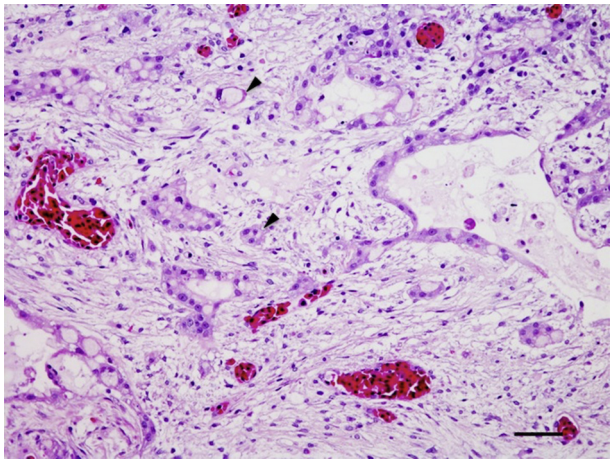

Fig. 1. Subserosal neoplastic cells form mucin-filled, cystic–acinar structures or are individualized (arrowheads). The latter cells have large amounts of cytoplasm that peripheralize the nuclei, resembling 'signet ring' cells. HE. Bar, 50 μm.

stained by alcian blue (Fig. 2). Multifocally, there were varying degrees of ulceration, deposits of necrotic hypereosinophilic debris and accumulation of intralesional colonies of grey and basophilic coccobacilli. Blood vessels in all examined organs were filled with intraluminal admixtures of erythrocytes, inflammatory cells, amphophilic and basophilic fibrin clots and colonies of coccobacilli.

Based on the microscopical features, a diagnosis of gastric mucinous and signet ring cell adenocarcinoma was made. Immunohistochemical expression of CK7, CK20, CDX-2 and HepPar-1 confirms neoplastic cells as being of gastric epithelial origin in man (Wong and Chu, 2012). In the present case, the

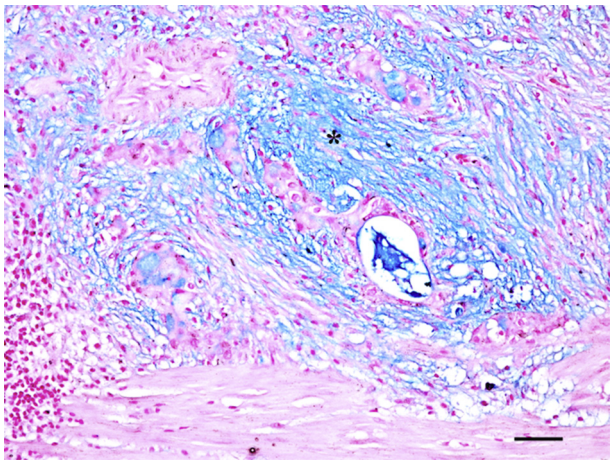

Fig. 2. Mucinous stroma (asterisk) surrounding the neoplasm is stained by alcian blue. Bar, 50 μm.