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DISEASE IN WILDLIFE OR EXOTIC SPECIES

Spontaneously Arising Concurrent Ileocaecal Adenocarcinoma and Renal Pelvis Transitional Cell Carcinoma in a Rhesus Macaque (*Macaca mulatta*)

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Summary

A 25-year-old, female rhesus macaque (*Macaca mulatta*) presented with a history of weight loss despite a normal appetite and supportive care. The animal was humanely destroyed due to poor prognosis. Post-mortem examination revealed a focally extensive, firm, white annular constriction at the ileocaecal junction and an incidental finding of a pale white nodule approximately 0.8 cm in diameter in the left renal pelvis. Based on the microscopical findings, ileocaecal adenocarcinoma and renal pelvis transitional cell carcinoma (TCC) were diagnosed. The use of cytokeratin (CK)-7 and -20 and uroplakin III as potential renal TCC markers was evaluated. The neoplastic cells were labelled intensely with antibodies to uroplakin III, but not to CK-7 or -20. Spontaneous intestinal adenocarcinoma has been documented in the rhesus macaque, but concurrent renal pelvis TCC is highly unusual.

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The rhesus macaque (*Macaca mulatta*) is an excellent model species for the study of human ageing and disease (Roth *et al*., 2004). Rhesus macaques have a close genetic relationship to man with a similar ageing phenotype at roughly three times the rate of man. These animals also develop spontaneously arising tumours (Bodkin *et al*., 2003; Simmons and Mattison, 2011). The correlation between increasing age and increa sing incidence of neoplasia is well known in man. There are similar reports of an increased incidence of neoplasia in rhesus macaques >20 years of age (Uno, 1997; Uno *et al*., 1998). Rhesus macaques are consid ered good comparative oncology models for investiga tion of spontaneous neoplasia and age-related diseases (Simmons and Mattison, 2011). One of the most commonly reported age-related diseases in rhesus macaques is intestinal adenocarcinoma (Rodriguez *et al*., 2002). Rhesus macaques are also suggested to be an excellent candidate model for ovarian cancer chemoprevention (Brewer *et al*., 2001). Urogenital tumours (e.g. uterine leiomyomas) are the second most commonly reported tumours in rhesus macaques and are diagnosed as fibroids in over half of women over the age of 40 (Simmons and Mattison, 2011). In man, carcinoma of the ampulla of Vater accounts for only 0.2% of all intestinal tumours, similar to less commonly diagnosed tumours in rhesus macaques (Carter *et al*., 2008; Simmons and Mattison, 2011). In contrast, renal pelvis transitional cell carcinoma (TCC) has not been reported in this species. The present report describes the gross, microscopical and immunohisto chemical features of a case of concurrent renal pelvis TCC and ileocaecal adenocarcinoma in an aged rhesus macaque.

A 25-year-old, female rhesus macaque was presented to the Yerkes National Primate Research Center (YNPRC) Veterinary Service with a history of weight loss and continuing deterioration despite a normal appetite and supportive care. The animal

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had been born at the YNPRC and was enrolled in several research protocols during her life. These were all approved by the Institutional Animal Care and Use Committee of Emory University. The research protocols were designed to examine the role of female hormonal state and sexual activity in male social integration, in-utero transplantation of human cells into primates and to study the evolution of ageing and dementia in female primates. The animal was fed a standard diet of commercial primate chow (5037 Old World Primate Diet, PMI International, Brentwood, Missouri, USA) supplemented daily with fresh fruit and vegetables. Water was provided *ad libitum*. Room conditions included a 12:12 h light:dark cycle, temperature of 24.6–29°C and 10–15 air changes per hour. On physical examination, the animal was in thin body condition (condition score of 2/5) with a pendulous abdomen, severe kyphosis and decreased extensibility of stifles and hips. Cardiac auscultation revealed a grade V/VI systolic heart murmur. Thoracic radiographs showed right-sided lung atelectasis with a pulmonary fissure line between the right cranial and caudal lung lobes. An abdominal ultrasound examination was within normal limits. No significant findings were noted on haematological and serum biochemical screening. Due to the poor prognosis and old age, the animal was humanely destroyed and a complete necropsy examination was performed. Tissue samples were fixed in 10% neutral buffered formalin, processed routinely and embedded in paraffin wax. Sections (5 μm) were stained with haematoxylin and eosin (HE).

Post-mortem examination revealed a 3.5 × 1.75 × 2.5 cm focally extensive, firm, pale white mass forming a circumferential constriction at the ileocaecal junction. The renal pelvis of the left kidney contained a single pale white nodule, approximately 0.8 cm in diameter extending into the renal medulla (Fig. 1). Other findings included multifocal fibrous adhesions between the cranial and caudal lung lobes extending to the pleura and the diaphragm. The lung lobes frequently contained pinpoint black areas (pneumoconiosis) and the caudal lung lobes were multifocally atelectatic. The mitral valves had moderate endocardiosis. There was multifocal loss of articular cartilage on the right and left femoral condyles. The patella of the left knee joint was fixed by adherent fibrous connective tissue and severe kyphosis was confirmed. No other major gross findings, including of the urinary bladder or ureter, were noticed.

Microscopically, the nodule in the left renal pelvis was a densely cellular, unencapsulated tumour composed of neoplastic transitional epithelial cells forming papillary fronds, cords and trabeculae infiltrating the medulla and supported by fine fibrovascular stroma (Fig. 2). Neoplastic cells were polygonal with distinct cell borders and contained moderate amounts of eosinophilic granular cytoplasm. Nuclei were round to oval with finely stippled chromatin and a single, prominent, centrally located magenta nucleolus. Anisocytosis and anisokaryosis were mild. Mitoses were 2 per 10 high-power fields (×400) of view. There were many areas of squamous metaplasia within the tumour (Fig. 3). Multifocally, neoplastic cells had large cytoplasmic vacuoles with eccentric nuclei ('signet ring' cells) containing small amounts of homogeneous material or cellular debris, which stained positively with periodic acid–Schiff (PAS) stain (Fig. 3). The renal interstitium was

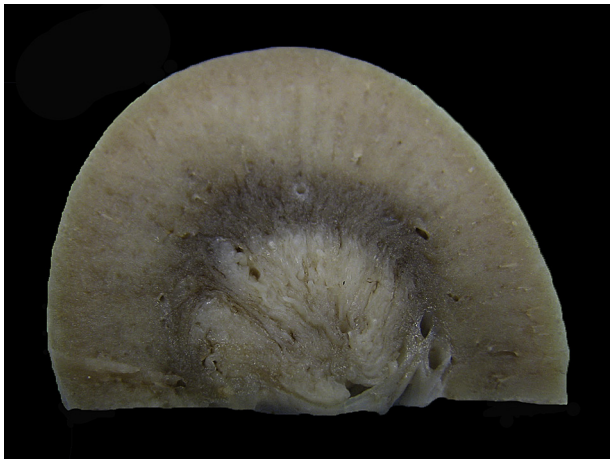

Fig. 1. An 0.8 cm diameter, pale white nodule in the renal pelvis of the left kidney extending into the medulla.

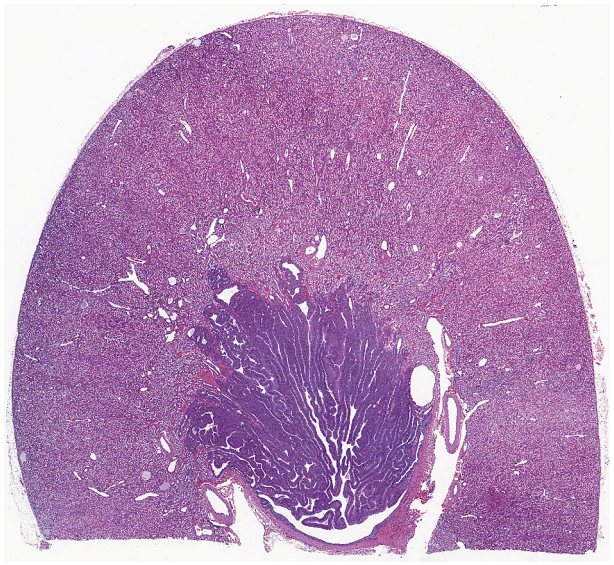

Fig. 2. The renal pelvis nodule is composed of neoplastic transitional epithelial cells forming papillary fronds, cords and trabeculae infiltrating the medulla. HE. ×5.

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