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Immunohistochemical Profile of 20 Feline Renal Cell Carcinomas

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Summary

Renal cell carcinoma (RCC) is uncommon in cats, but makes up the majority of epithelial neoplasms in the kidney. The immunohistochemical profile of 20 feline RCCs (13 tubular carcinomas, four tubulopapillary carcinomas, one papillary carcinoma and two anaplastic carcinomas) was evaluated. Primary antibodies used were specific for Pax8, KIT, CD10, cytokeratins and vimentin. A polymer-based immunoperoxidase procedure was used. Nineteen tumours (95%) expressed Pax8; 12 (60%), KIT; 15 (75%), CD10; 20 (100%), cytokeratins; and 19 (95%), vimentin. Nuclear Pax8 immunoreactivity was readily apparent, but variation in labelling intensity was present within a given section. KIT reactivity was diffuse, cytoplasmic and relatively homogeneous. CD10 immunoreactivity was predominantly membranous along the apical border of tubular epithelial cells and was less commonly cytoplasmic. CD10 immunoreactivity was less intense in areas with papillary differentiation and absent in solid areas. Cytoplasmic cytokeratin expression was strong in 18 tumours and weak in two; the papillary portion of one tumour had distinct submembranous expression. Vimentin immunoreactivity, which ranged from diffuse to focal, was difficult to evaluate due to strong stromal immunoreactivity and its patchy expression in phenotypically similar neoplastic cells. Fewer non-renal tumours were positive for Pax8 than for CD10. Considering overall sensitivity and specificity, Pax8 appears to be a valuable marker for distinguishing feline tumours arising in the kidney from other neoplasms.

Keywords: cat; immunohistochemistry; Pax8; renal carcinoma

Introduction

Primary renal tumours are uncommon in cats, accounting for less than 1% of all neoplasms reported in this species (Bonsembiante *et al.*, 2016). The majority of tumours diagnosed in the feline kidney are lymphomas (78%) or the result of metastasis (10%), with only 12% arising *de novo* in the kidney. Of the tumours that arise in the kidney, 77% are epithelial with the majority of them malignant (Meuten and Meuten, 2017). Feline renal cell carcinoma (RCC) is usually unilateral, but can be bilateral (Steinberg and Thomson, 1994). Other malignant epithelial neoplasms of the kidney are urothelial carcinoma and squamous cell carcinoma of the renal pelvis (Henry *et al.*, 1999; Gómez *et al.*, 2014). A variety of paraneoplastic syndromes are associated with renal neoplasms in small animals (Henry *et al.*, 1999; Johnson and Lenz, 2011; Meuten and Meuten, 2017).

Immunohistochemistry (IHC) can provide evidence for the cellular origin of epithelial neoplasms arising in the nephron and collecting duct. Pax8, CD10 and KIT (CD117) are commonly used for this purpose in characterizing human renal carcinomas (Truong and Shen, 2011; Netto and Epstein, 2014). The immunohistochemical profile of canine RCC has been examined by different groups (Kobayashi *et al.*, 2008; Gil da Costa *et al.*, 2011; Edmondson *et al.*,

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2015; Peat *et al.*, 2017). Markers used to characterize canine renal neoplasia include carcinoembryonic antigen, CD10, cytokeratin (CK), KIT, napsin A, Pax8, uromodulin and vimentin. Pax8 and uromodulin are the markers most widely expressed in canine RCC, followed by vimentin and KIT (Gil da Costa *et al.*, 2011; Edmondson *et al.*, 2015; Peat *et al.*, 2017). In contrast, the immunohistochemical profile of feline RCC is not well defined, with only one report examining a number of markers in four feline RCCs (Bonsembiante *et al.*, 2016). Those authors evaluated the expression of β-catenin, KIT, vascular endothelial growth factor (VEGF), CKs, vimentin, E-cadherin and CD10. All of the tumours expressed CKs and vimentin, but none were positive for KIT; β-catenin was expressed by three neoplasms and two tumours were positive for CD10 and VEGF.

In the current study, we examined the immunohistochemical profile of 20 feline RCCs using antibodies specific for Pax8, KIT, CD10, pan-CK and vimentin, and compared results with those published in cats, dogs and man. For comparative purposes, we examined the expression of Pax8 and CD10 in a variety of other feline neoplasms.

Materials and Methods

Case Selection and Histopathological Analysis

A search of the Purdue University Animal Disease Diagnostic Laboratory and Colorado State University Veterinary Diagnostic Laboratory formalin-fixed, paraffin wax-embedded tissue archive for cases between 2004 and 2016 was performed. Twenty cases of feline renal epithelial lesions were selected based on the quality of samples available for IHC. All tumours were reviewed and reclassified independently by the authors using the growth pattern (e.g. solid, papillary, tubular or cystic) (Gil da Costa *et al.*, 2011; Meuten and Meuten, 2017). When two different microscopical patterns were present in the same tumour in a similar percentage, both patterns were included in the tumour classification (Table 1).

To evaluate the cross-reactivity of Pax8 and CD10 antibodies, normal feline tissues including adrenal gland, bone marrow, eye, gallbladder, heart, kidney, large and small intestine, liver, lung, lymph node, mammary gland, nasal mucosa, ovary, pancreas, thyroid, parathyroid gland, salivary gland, skin, spleen,

Table 1
Summary of immunohistochemical studies of feline renal neoplasms

Diagnosis	*Pax8*		*KIT*		*CD10*		*CKs*		*Vimentin*	
	*Reactivity**	*Intensity†*	*Reactivity*	*Intensity*	*Reactivity*	*Intensity*	*Reactivity*	*Intensity*	*Reactivity*	*Intensity*
Solid (anaplastic) carcinoma	–	NA	3+	3+	–	NA	1+	3+	3+	3+
Solid (anaplastic) carcinoma	3+	3+	3+	2+	–	NA	3+	3+	2+	3+
Papillary carcinoma	3+	3+	3+	3+	1+	3+	3+	3+	3+	3+
Tubular carcinoma	1+	2+	–	NA	–	NA	3+	3+	1+	3+
Tubular carcinoma	3+	3+	3+	3+	–	NA	3+	3+	2+	3+
Tubular carcinoma	3+	3+	–	NA	2+	3+	3+	3+	1+	3+
Tubular carcinoma	3+	3+	–	NA	1+	3+	3+	3+	2+	3+
Tubular carcinoma	2+	3+	–	NA	2+	3+	3+	3+	3+	3+
Tubular carcinoma	2+	2+	–	NA	3+	3+	3+	3+	2+	3+
Tubular carcinoma	2+	2+	3+	1+	3+	3+	3+	3+	3+	3+
Tubular carcinoma	3+	3+	–	NA	3+	3+	3+	3+	3+	3+
Tubular carcinoma	3+	3+	–	NA	–	NA	1+	3+	3+	3+
Tubular carcinoma	3+	3+	3+	2+	3+	3+	3+	3+	2+	3+
Tubular carcinoma	3+	3+	3+	2+	2+	2+	3+	3+	1+	2+
Tubular carcinoma	3+	3+	3+	3+	3+	3+	3+	3+	3+	3+
Tubular carcinoma	2+	2+	3+	2+	1+	3+	3+	3+	–	NA
Tubulopapillary carcinoma	3+	3+	3+	1+	2+	3+	3+	3+	1+	3+
Tubulopapillary carcinoma	3+	3+	–	NA	2+	3+	3+	3+	2+	3+
Tubulopapillary carcinoma	3+	3+	3+	3+	3+	3+	3+	3+	3+	3+
Tubulopapillary carcinoma	3+	3+	3+	2+	1+	3+	2+	3+	1+	3+

NA, not applicable.
*Reactivity (% of positive cells): –, <5%; 1+, 6–15%; 2+, 16–50%; 3+, 51–100%.
†Intensity of reaction was subjectively scored as 1+ (weak), 2+ (moderate) or 3+ (intense).