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### **Concurrent Transitional Meningioma and Ceruminous Gland Adenocarcinoma in a Scottish Wildcat Hybrid (*Felis silvestris*)**

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1 SHORT PAPER

2  
3 Concurrent Transitional Meningioma and Ceruminous Gland Adenocarcinoma in a Scottish  
4 wildcat hybrid (*Felis silvestris*)

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12  
13 Summary

14 The Scottish wildcat (*Felis silvestris*) is an iconic and endangered, sub-population of the  
15 European wildcat (*Felis silvestris silvestris*). As such, there is much research devoted to its'  
16 ecology, genetics and conservation but little published information on pathology and disease.  
17 The investigation and reporting of such information is vital to furthering our understanding of  
18 the effects of hybridisation, a factor which is crucial if we are to secure a future for the  
19 Scottish wildcat. This report describes the clinical presentation, gross post-mortem and  
20 histological findings, in an elderly Scottish wildcat hybrid with concurrent transitional  
21 meningioma and ceruminous gland adenocarcinoma. To the authors' knowledge there have  
22 been no previous reports of meningioma or ceruminous gland adenocarcinoma in the  
23 European wildcat (*Felis silvestris silvestris*) and there are only isolated reports of primary  
24 central nervous system neoplasia in other non-domestic felid species.

25 Keywords: Meningioma; Ceruminous gland adenocarcinoma; European wildcat; *Felis*  
26 *silvestris silvestris*.

27

28 The Scottish wildcat is an isolated sub-population of the European wildcat (*Felis silvestris*  
29 *silvestris*) and is also considered by some scientists to be a distinct sub-species (*Felis*  
30 *silvestris grampia*) (Miller, 1912; Beaumont et al., 2001; Kilshaw et al., 2010). The future of  
31 the European wildcat, and particularly the Scottish wildcat, is uncertain due to habitat loss,  
32 hunting and persecution throughout the 18<sup>th</sup> and 19<sup>th</sup> centuries (McOrist and Kitchener,  
33 1994), and more recently the effects of hybridisation, as a result of inter-breeding with  
34 domestic cats (*Felis silvestris catus*), (Daniels et al., 2001; Davis and Gray, 2010; Kilshaw et  
35 al., 2010), along with the potential transmission of common infectious diseases from  
36 domestic cats (McOrist et al., 1991). Now classified as endangered, they are legally protected  
37 under both UK and European legislation (Kilshaw et al., 2010). As such, the majority of  
38 published literature is focused on its ecology, genetics and conservation.

39 There have been a limited number of publications regarding pathology and disease of the  
40 European wildcat. Most publications are serological studies focusing on the prevalence of  
41 common feline viruses (McOrist et al., 1991; Watt et al., 1993; Daniels et al., 1999;  
42 Leutenegger et al., 1999; Millán and Rodriguez, 2009; Wasieri et al., 2009), although there  
43 are isolated reports dealing with other pathogens such as *Chlamydomphila* sp. (Millán and  
44 Rodriguez, 2009), *Toxoplasma gondii* (McOrist et al., 1991; Herrmann et al., 2013),  
45 lungworm (Falsone et al., 2014), hemoplasmas (Willi et al., 2007), and other endoparasites  
46 (Burt et al., 1980; Krone et al., 2008). Neoplasia has been rarely reported in the European  
47 wildcat; from 79 necropsy examinations reported in several articles (Jefferies, 1991; McOrist  
48 et al., 1991; Watt et al., 1993; Krone et al., 2008; Wasieri et al., 2009; Hermann et al., 2013;

49 Falsone et al., 2014), only one tumour (a pulmonary lymphoma) was found (Hermann et al.,  
50 2013).

51 This report describes the presentation, gross post-mortem, and histological findings in a  
52 Scottish wildcat hybrid with concurrent transitional meningioma and ceruminous gland  
53 adenocarcinoma. To the authors' knowledge, there have been no previous reports of  
54 meningioma or ceruminous gland adenocarcinoma in the European wildcat (*Felis silvestris*  
55 *silvestris*).

56 A 16.5 year old, neutered male, Scottish wildcat hybrid from a zoological collection  
57 reportedly suffered from sporadic episodes of incoordination and mild lethargy over a four  
58 week period. Although this individual was deemed to be a hybrid (*Felis silvestris silvestris* x  
59 *Felis silvestris catus*), rather than a true wildcat, according to the records of the zoological  
60 institution, a sample of skeletal muscle was tested using a 35 Single Nucleotide

61 Polymorphism (SNP) marker test developed by the Royal Zoological Society of Scotland  
62 from a panel of markers published by Nussberger et al., (2013) in an attempt to confirm this  
63 and investigate the degree of hybridisation. Two extracts of DNA were conducted and three  
64 replicates of the assay were run but the assay failed to prove or disprove the hybrid status of  
65 this individual due to insufficient DNA quality, presumably due to sample degradation. The  
66 cat was transferred from a wildlife centre when it was 9 years old, and had since lived with a  
67 female Scottish wildcat in an outdoor enclosure. Prior medical history was unremarkable.

68 Husbandry and nutrition were considered appropriate for the species. Physical examination  
69 under general anaesthesia revealed loose skin, thought to be consistent with poor hydration or  
70 recent weight loss, a round bony proliferation on the right stifle joint and a hard mass behind  
71 the right ear. Body condition score was considered acceptable (4/9) with a weight of 4.5kg,  
72 teeth were in an excellent condition for an old cat and vital parameters (heart and respiratory  
73 rate, rectal temperature) were unremarkable. The cat initially appeared to recover well from

74 anaesthesia, but remained recumbent and died 2 hours later. The animal was subsequently  
75 submitted for post-mortem examination at the Royal (Dick) School of Veterinary Studies  
76 (The University of Edinburgh, Roslin, Midlothian, UK).

77 Post-mortem examination revealed the entrance to both external ear canals to be obscured by  
78 dark grey to blue black, well demarcated, multi-lobular, firm, occasionally cystic, exophytic,  
79 polypoid masses ranging from 1 to 5mm in diameter and a cream, well demarcated,  
80 60x30x20mm, multi-lobular, firm, subcutaneous mass at the base of the right ear which  
81 contained a dark red, central, well circumscribed, depressed area 3mm in diameter on cut  
82 section. The right pre-scapular lymph node was moderately enlarged and the brain contained  
83 a cream to yellow, well demarcated, multi-lobular, expansile and compressive mass,  
84 approximately 15mm in diameter, between the cerebral hemispheres in the region of the falx  
85 cerebri (Fig.1). Samples of all gross lesions along with representative samples from all tissues  
86 and internal organs were collected, fixed in 10% buffered formalin and routinely processed  
87 according to current histological methods. Sections 5µm thick were stained with  
88 haematoxylin and eosin.

89 Histopathological examination of the external ear canal masses (Fig.2) revealed a moderately  
90 acanthotic, stratified squamous keratinising epithelium elevated by numerous, multi-focal,  
91 dilated, cystic, glandular structures lined by a flattened to low cuboidal epithelium. Many  
92 cysts contained amorphous, tan to pale brown, granular material (cerumen) and low numbers  
93 of large foamy macrophages also contained this granular brown material. Within a mass from  
94 the right external ear canal, the superficial dermis was focally expanded by more dense  
95 proliferations of polygonal to cuboidal cells forming tubules, acini and fronds. Cells had  
96 variably well-defined cell borders, a moderate amount of eosinophilic, finely granular  
97 cytoplasm, open-faced, oval to round nuclei with 1-2 prominent nucleoli. Anisocytosis and  
98 anisokaryosis were mild with an average of 1 mitotic figure per high power field (x400). Foci

99 of necrosis expanded the centre of these cellular proliferations. Examination of the right ear  
100 base mass (Fig.3) was consistent with the pre-existing architecture of a lymph node, 80% of  
101 which was effaced by tubules and acini of cells, similar to those described in the mass from  
102 the right external ear canal, with evidence of lymphatic invasion. Similar cell proliferation  
103 was present in the right pre-scapular lymph node.

104 The histopathological appearance of the auricular lesions was consistent with a diagnosis of  
105 bilateral ceruminous gland dilatation and hyperplasia (feline ceruminous cystomatosis) with  
106 unilateral (right side) ceruminous gland adenocarcinoma and metastasis to cervical and pre-  
107 scapular lymph nodes.

108 Sections of cerebral cortex, lateral ventricle and meninges showed the leptomeninges of the  
109 cingulate sulcus to be expanded by a large, densely cellular, well demarcated, finely  
110 encapsulated, compressive, nodular mass (Fig.4). The mass consisted predominantly of  
111 lobules of loosely to densely packed cells forming concentric whorls, occasionally  
112 surrounding blood vessels or containing central areas of necrosis. Adjacent cells formed long,  
113 interlacing fascicles streaming around the whorls and were supported by a loosely arranged,  
114 eosinophilic, fibrillar stroma. Cells were fusiform to polygonal with indistinct cell borders  
115 and variable amounts of eosinophilic, wispy, fibrillar cytoplasm. Within the centre of  
116 concentric whorls, cells adopted a more epithelioid morphology. Nuclei were round to  
117 elongated with loosely packed, finely stippled chromatin and 1 to 2 nucleoli. Anisocytosis  
118 and anisokaryosis were moderate with occasional multi-nucleate forms. Mitoses were rare (1  
119 figure per 10 high power fields (x400)). Moderate numbers of neutrophils, occasional  
120 lymphocytes, plasma cells, pyknotic cells, small clusters of foamy macrophages and  
121 occasional acicular clear spaces (cholesterol clefts) were present within the mass. Both the  
122 grey matter and white matter tracts of the adjacent cerebral cortex contained mild diffuse  
123 vacuolation with mild perivascular clearing and spacing (oedema).

124 The histopathological findings of the cerebral mass were consistent with a diagnosis of  
125 transitional (mixed) meningioma containing features of both meningothelial (characterised by  
126 moderately cellular lobules of polygonal cells) and fibrous tumours (long interlacing fascicles  
127 of fusiform cells).

128 Also identified following post-mortem and histological examination were bilateral stifle joint  
129 osteoarthritis, nodular hyperplasia of both thyroid glands, mild hepatic lipidosis, mild, multi-  
130 focal, chronic cholangiohepatitis and mild, multi-focal, chronic interstitial nephritis with a  
131 focal, chronic, renal infarct.

132 Ceruminous gland adenocarcinomas are the most commonly diagnosed tumour of the  
133 external acoustic meatus in cats, accounting for up to 2% of all feline neoplasms (Njaa and  
134 Wilcock, 2012) and are more frequently diagnosed than adenomas in domestic cats (Moisan  
135 and Watson, 1996; London et al., 1996). They exhibit locally invasive behaviour (London et  
136 al., 1996) and metastasis to regional lymph nodes, lungs and viscera can occur in up to 50%  
137 of cases (Njaa and Wilcock, 2012). No evidence of pulmonary or visceral metastasis was  
138 found in this case.

139 Differentiation between ceruminous adenoma and adenocarcinoma can be challenging unless  
140 there is evidence of local invasion or metastatic disease, as in this case (Wilcock et al., 2002).

141 Meningiomas are the most common primary central nervous system (CNS) neoplasm of  
142 domestic cats (Koestner & Higgins, 2002; Troxel et al., 2003; Tomek et al., 2006; Motta et  
143 al., 2012) typically occurring in cats older than 9 years (Troxel et al., 2003; Tomek et al.,  
144 2006) with an increasing incidence with age. Domestic shorthaired cats seem to be  
145 predisposed but no significant sex predilection has been found (Troxel et al., 2003; Tomek et  
146 al., 2006). Transitional meningiomas, as reported here, and fibrous subtypes are most  
147 frequently encountered in domestic cats. Meningiomas are typically slow growing, with the  
148 exception of the uncommon anaplastic (malignant form), rarely metastatic and approximately

149 50% of cases do not exhibit any clinical signs. To the authors' knowledge this is the first  
150 report of meningioma in a European wildcat. There are only isolated additional reports in the  
151 literature of central nervous system neoplasia in non-domestic felids, such as meningioma in  
152 a Bengal tiger (*Panthera tigris tigris*) (Akin et al., 2013) and intracranial oligodendroglioma  
153 in a lion (*Panthera leo*) (Tucker et al., 2008).

154 The findings reported here pose the question for future studies to determine the incidence of  
155 common neoplasms of domestic felines in pure-bred wildcats and their hybrids. This may  
156 help to elucidate whether their occurrence may be an associated effect of hybridisation, or  
157 purely a reflection of the increasing age of individuals living in zoological collections in  
158 comparison to their free living relatives.

159

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165

166 Conflict of Interest Statement: The authors declare no conflict of interest.

167

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Legend for Figures:



Fig 1. Brain, showing the presence of a nodular mass between the cerebral hemispheres.

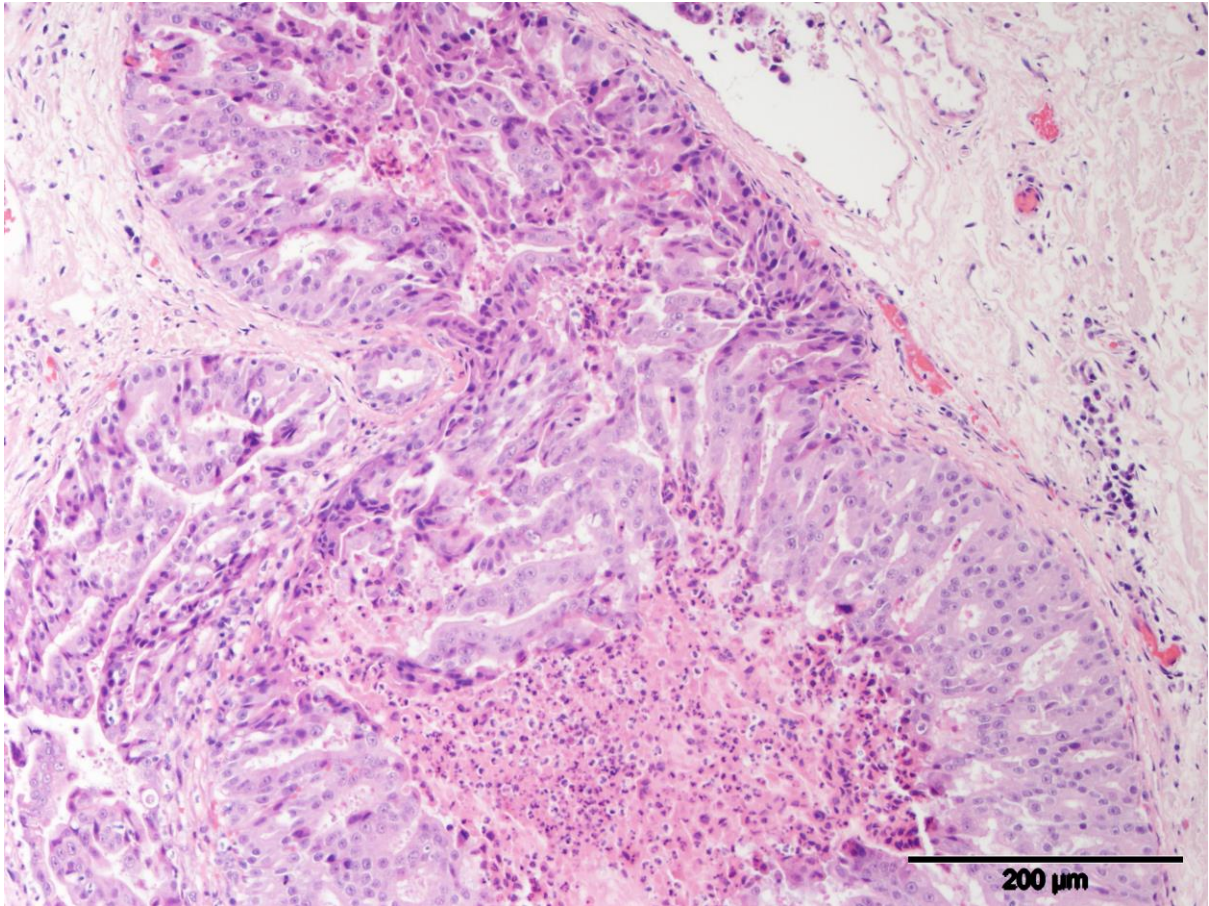


Fig 2. Section of tissue from the right external ear canal showing acinar arrangement of neoplastic epithelial cells with central necrosis. Epithelial cells are present within the lumen of the thin-walled vessel at the top of the image. HE.

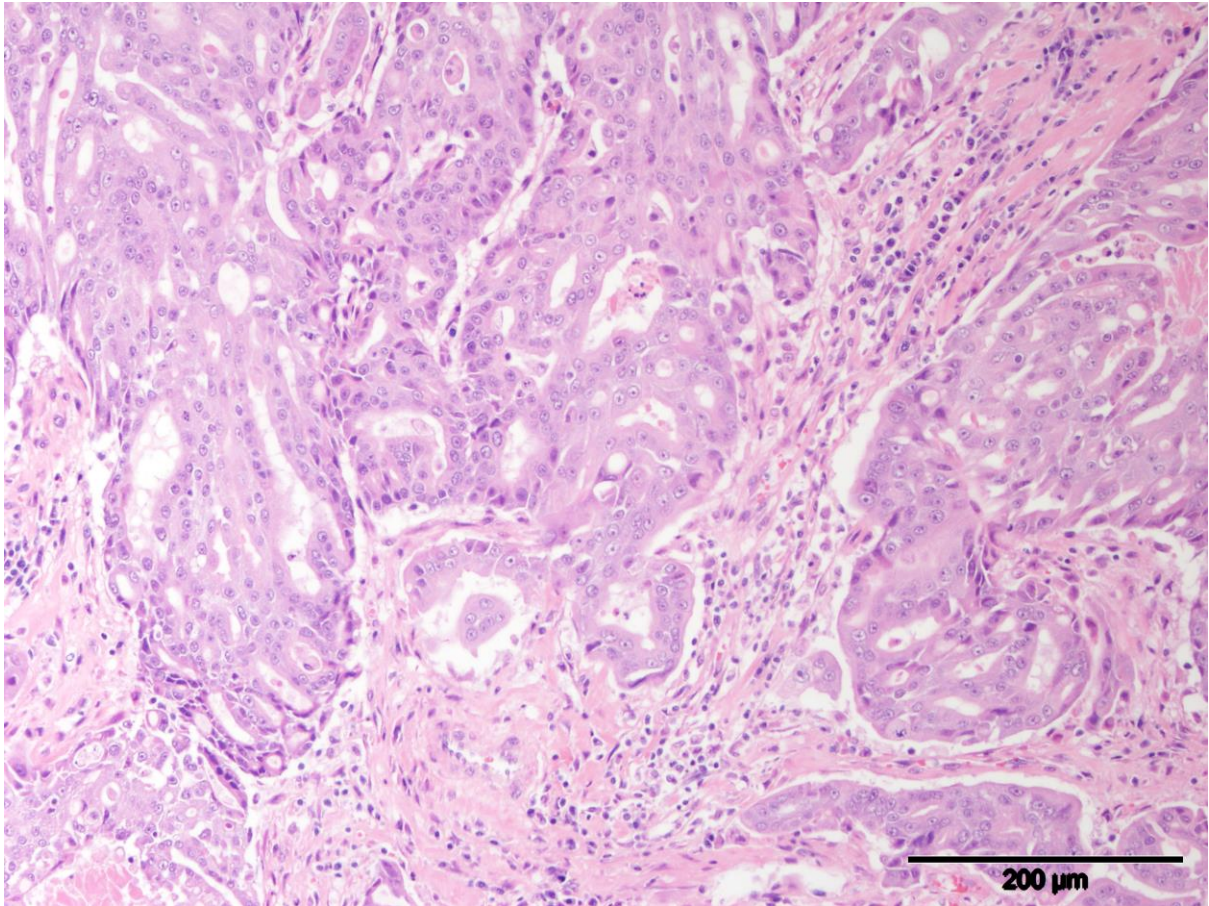


Fig 3. Section of the right cervical lymph node showing replacement of normal architecture by metastatic neoplastic epithelia forming acinar structures. HE.

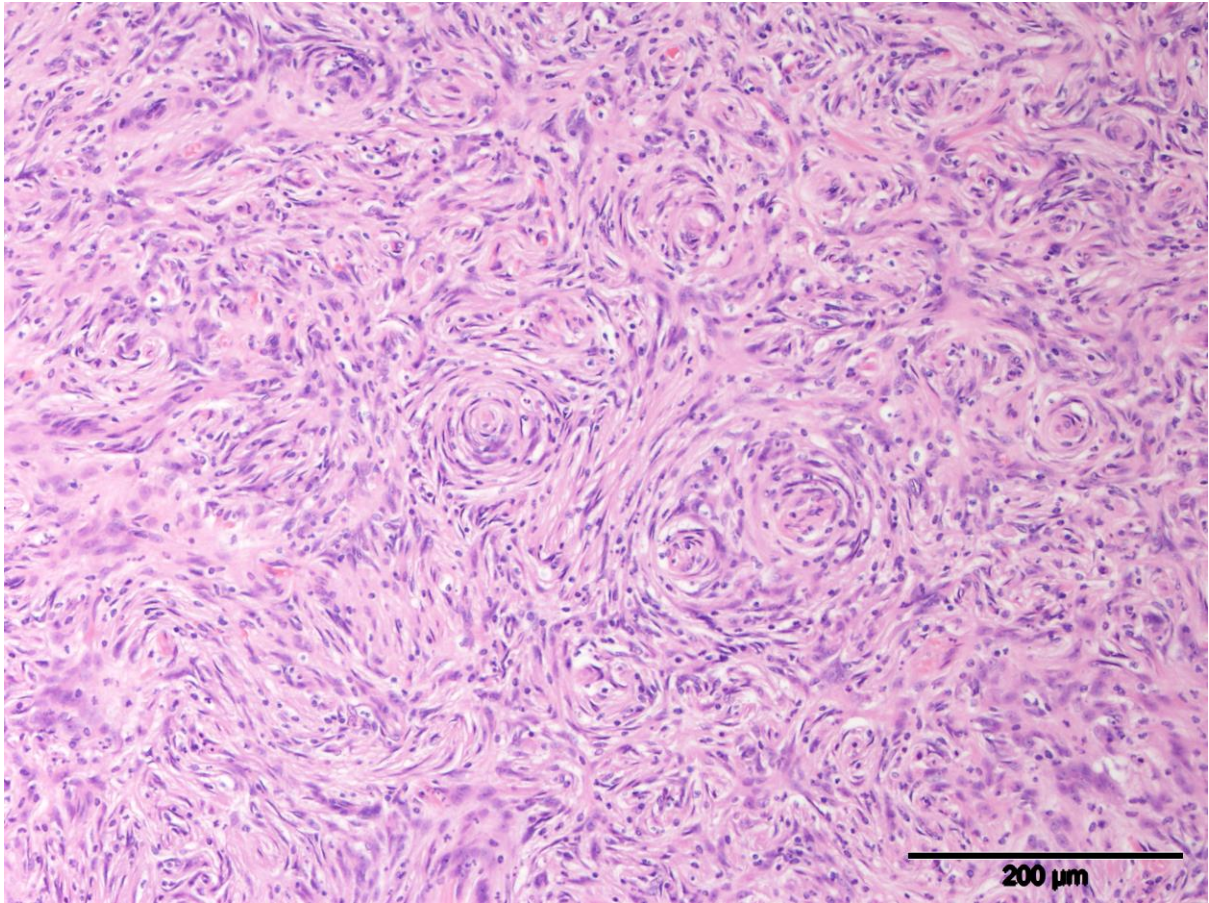


Fig 4. Section from the brain mass showing whorls and bundles of neoplastic spindle cells consistent with the transitional form of meningioma. HE.