



Clinical presentation and outcome in cats with aural squamous cell carcinoma: a review of 25 cases (2010–2021)

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Abstract

Case series summary Ear canal neoplasia is uncommon in cats. Ceruminous gland adenocarcinoma is the most frequently reported malignant neoplasm of the feline ear canal, and squamous cell carcinoma (SCC) is the most common malignant neoplasm diagnosed in the feline middle ear. However, limited information exists on the outcome of cats diagnosed with SCC of the ear canal, middle or inner ear. Therefore, the objective of this study was to describe the outcome of cats diagnosed with SCC affecting these locations. Medical records were reviewed at multiple institutions to identify cats with a definitive diagnosis of SCC. Twenty-five cats were identified. Eleven cats were treated with surgery, eight with medical management, two with coarse fractionated radiation therapy, two with a combination of coarse fractionated radiation therapy and chemotherapy, one with a combination of surgery and coarse fractionated radiation therapy, one cat with systemic chemotherapy and one cat received no treatment following diagnosis. The median survival time of cats treated with surgery was 168 days vs 85 days ($P=0.28$) for those treated palliatively with either medical management, radiation therapy, chemotherapy, or a combination of radiation therapy and chemotherapy.

Relevance and novel information This case series documented that SCC of the ear canal, middle and/or internal ear is a locally aggressive tumor that carries an overall poor prognosis. The median survival time for cats treated with surgery was longer than that with any other modality, but this difference was not statistically significant.

Keywords: Ear canal; carcinoma; squamous cell; tumor

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Introduction

Ear canal tumors in cats are uncommon, representing 1–2% of all tumors.¹ Ceruminous gland adenocarcinoma is the most common malignant tumor of the feline ear canal, followed closely by squamous cell carcinoma (SCC).¹ SCC is the most common malignant tumor diagnosed in the feline middle ear.² While these two tumor types are the most frequently diagnosed feline aural tumors, there are limited reports evaluating outcomes.^{3,4}

Several negative prognostic indicators have been determined in cats with aural tumors, including neurologic deficits at presentation, histologic evidence of vascular invasion and a histologic diagnosis of SCC or carcinoma of undetermined origin vs adenocarcinoma.^{1,5} In a large retrospective study, 18 cats with ceruminous

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gland adenocarcinoma of the ear canal had a median survival time (MST) of 49 months vs an MST of 3.8 months for cats with SCC.¹ Reports of cats with SCC of the middle ear have been sparse, with only 14 cats described in the literature.^{1,6–10} All previously reported cases showed a poor long-term outcome despite treatment, with the lesion often displaying aggressive local behavior.^{1,6–10} It is widely accepted that surgery is the mainstay of treatment in cats with aural SCC without evidence of widespread metastatic disease, as it provides the best chance at local control.¹¹ However, few reports evaluate outcomes following surgery for cats with SCC.

Given the paucity of information regarding cats with SCC of the middle ear, inner ear or ear canal, the objective of this study was to describe the clinical presentation and outcome in cats affected by this tumor type.

Case series description

This was a multi-institutional retrospective case series where the medical records from four small animal referral hospitals (The Ohio State University, University of Pennsylvania, University of Georgia and Angell Animal Medical Center) were reviewed to identify cats with a definitive diagnosis of SCC of the middle ear, inner ear or ear canal over an 11-year period (1 January 2010 to 1 January 2021). Cats were included in the study if they had a cytological or histological diagnosis of SCC of the middle ear, inner ear or ear canal from sampling the primary mass or the locoregional lymph node. In addition, medical records were evaluated for information on physical examination findings at presentation, preoperative imaging, clinicopathological data, operative reports, radiation and/or chemotherapy treatment protocols, other in-hospital treatments received and follow-up. Cats were excluded from the study if the cytological or histopathological diagnosis was not SCC or if the location of SCC was not primarily within the middle ear, inner ear or ear canal.

The following data were obtained from the medical records of each cat: age, body weight, breed, sex and neuter status, date of presentation, comorbidities at the time of diagnosis and physical examination findings. Preoperative blood work results were evaluated, and abnormalities were reported. Preoperative diagnostic imaging (CT and thoracic radiographs) and preoperative cytology or histopathology results of the lesion and regional lymph nodes were also reviewed. Treatments pursued, including palliative medical management, radiation therapy (RT) protocols and/or chemotherapy regimens were recorded. Surgical procedures performed, as well as intraoperative complications, were recorded. Intraoperative complications were graded retrospectively by the institution according to the Classification of Intraoperative Complications (CLASSIC) system (0–IV).¹² Histopathology reports of primary and any metastatic lesions were reviewed. Immediate postoperative

complications, defined as complications that arose from recovery from anesthesia to discharge, were evaluated and graded according to the Accordion Severity Classification System (1–4).¹³ Short-term complications, defined as complications that occurred 2 weeks following surgery, as well as adjuvant treatments pursued, time to recurrence or metastases of SCC, date and cause of death were recorded. Information regarding the status of the cat was obtained from institutional medical records, primary veterinarian records or the cat's owner.

Descriptive statistics were calculated for continuous variables, and Kaplan–Meier curves were generated to estimate MSTs. Cats were censored from survival analysis if they were alive at the time of last follow-up or the date of loss to follow-up. An event was considered a death due to any cause. A log-rank test was used to compare the survival distribution of cases that had surgery vs cases that did not. Time to recurrence was calculated as the number of days from the date of treatment to the date of recurrence.

After reviewing medical records, 25 cats met the inclusion criteria (summarized in Table 1). Median age at the time of presentation was 11 years (range 4–20). Median weight was 4.5 kg (range 2.6–7.0). The following breeds were represented: domestic shorthair ($n = 18$), domestic mediumhair ($n = 3$), domestic longhair ($n = 3$) and Ragdoll ($n = 1$). Ten cats were female and 15 were male. All cats were neutered. In total, 12/25 cats (48%) displayed neurologic signs at presentation. Neurologic abnormalities and aural examination findings are summarized in Table 1.

Complete blood count (CBC) and serum biochemistry were performed, and available for review in 23/25 cats (92%). Consistent CBC or biochemistry abnormalities were not recognized. CT of the skull was performed in 16/25 cats (64%). Mass locations included within the external ear canal ($n = 5$), extending from the external ear canal to the middle ear ($n = 4$), within the middle ear ($n = 3$), within the inner ear ($n = 2$), extending from the middle ear to the inner ear ($n = 1$) and extending from the external ear canal through the middle ear to the inner ear ($n = 1$). Bulla lysis was noted in three cats (cases 8, 12 and 14), lysis of the temporal bone was noted in three cats (cases 3, 6 and 7) and lysis of the zygomatic and frontal bones were noted in one cat (case 19). Extension into the calvarium and brain (cases 22, 23 and 24), temporomandibular region (case 23), and right parotid and mandibular salivary glands were also reported. Findings also included ipsilateral ($n = 7$) and contralateral otitis ($n = 3$), ipsilateral medial retropharyngeal lymphadenopathy ($n = 10$), ipsilateral mandibular lymphadenopathy ($n = 4$) and bilateral medial retropharyngeal lymphadenopathy ($n = 1$). Two cats had ipsilateral retropharyngeal lymphadenopathy reported, though medial vs lateral was not specified. Three-view thoracic

Table 1 A summary of demographics and diagnostic results at presentation of 25 cats with aural squamous cell carcinoma (SCC)

Case	Age	BW (kg)	Breed	Sex	Neurologic abnormalities at presentation	Additional pertinent physical examination findings	Bloodwork findings	Location of SCC lesion	CT findings	Thoracic radiograph findings	Preoperative cytology: aural lesion	Preoperative cytology: locoregional lymph node	Preoperative biopsy: aural lesion	Preoperative biopsy: locoregional lymph node
1	20y 2mo	6.3	DSH	MN	NR	Otitis externa, discomfort with aural examination	WNL	External ear canal and middle ear	Mass extending from external ear canal to middle ear, bilateral otitis externa and media	NP	NP	NP	NP	NP
2	7y 5mo	3.7	DSH	FS	Ipsilateral head tilt, ipsilateral vestibular disease	Otitis externa	WNL	Middle ear	NP	NP	NP	NP	NP	NP
3	6y 9mo	4.5	DLH	FS	Ipsilateral facial nerve deficits, ipsilateral head tilt	Discomfort with aural examination, suspected polyp in contralateral ear canal, decreased retropulsion, corneal ulceration	Hyperproteinemia	External ear canal and middle ear	Mass extending from external ear canal to middle ear, lysis of the temporal bone, polyp in contralateral ear canal, ipsilateral otitis externa and media, ipsilateral retropharyngeal lymphadenopathy, periodontal disease	Mild generalized cardiomegaly	NP	NP	NP	NP
4	10y	3.4	DSH	FS	NR	-	WNL	External ear canal	Right pinna neoplasm with vertical and horizontal ear canal involvement and suspected invasion into the right parotid and mandibular salivary glands, nodules on contralateral pinna	Normal thorax	NP	NP	SCC, official report not available	Metastatic carcinoma
5	11y 9mo	4.5	DSH	MN	NR	Otitis externa, palpable mass associated with ear canal	WNL	External ear canal	NP	NP	NP	Metastatic carcinoma	SCC, mitotic count: 27/10 40 x fields	NP

(Continued)

Table 1 (Continued)

Case	Age	BW (kg)	Breed	Sex	Neurologic abnormalities at presentation	Additional pertinent physical examination findings	Bloodwork findings	Location of SOC lesion	CT findings	Thoracic radiograph findings	Preoperative cytology: aural lesion	Preoperative cytology: locoregional lymph node	Preoperative biopsy: aural lesion	Preoperative biopsy: locoregional lymph node
6	16y	4.4	DSH	MN	Ipsilateral facial nerve deficits (mild ipsilateral tongue paralysis as well as paralysis of cranial nerves V, VII, XII), ipsilateral Horner's syndrome, ipsilateral head tilt, ipsilateral vestibular disease	Otitis externa, mass visualized on otoscopic examination, discomfort with aural examination	Anemia, hypernatremia	External ear canal and middle ear	Mass extending from external ear canal to middle ear, lysis of the temporal bone, ipsilateral retropharyngeal lymphadenopathy, periodontal disease, nasal planum mass	NP	NP	Metastatic carcinoma	NP	NP
7	11y 5mo	5.5	DSH	FS	Ipsilateral facial nerve deficits, ipsilateral Horner's syndrome, ipsilateral head tilt, ipsilateral vestibular disease	Otitis externa	Lymphopenia, hyperalbuminemia, hypercholesterolemia	Inner ear	Lysis of the temporal bone, ipsilateral medial retropharyngeal lymphadenopathy, periodontal disease	Broncho-interstitial pattern, esophageal and intestinal gas, bilateral humeral joint osteophytosis	NP	NP	NP	NP
8	14y 5mo	3.9	DSH	FS	Ipsilateral facial nerve deficits, ipsilateral Horner's syndrome, ipsilateral head tilt, ipsilateral vestibular disease	Otitis externa	WNL	Inner ear	Bulla lysis, ipsilateral medial retropharyngeal lymphadenopathy, periodontal disease	Loculated mediastinal and/or pleural effusion, nephroliths or dystrophic mineralization, poor serosal detail in cranioventral abdomen	NP	NP	SCC, mitotic count not reported	NP
9	13y 7mo	5.2	DSH	MN	NR	Otitis externa, mass visualized on otoscopic examination, discomfort with aural examination	Hyperproteinemia, hyperglobulinemia, elevated ALT	External ear canal	Mass within external ear canal, ipsilateral otitis externa, ipsilateral medial retropharyngeal lymphadenopathy, ipsilateral mandibular lymphadenopathy	Thoracic CT performed, nodular changes in right cranial and middle lung lobes	NP	NP	Focal areas of atypical epithelial cells	NP

(Continued)

Table 1 (Continued)

Case	Age	BW (kg)	Breed	Sex	Neurologic abnormalities at presentation	Additional pertinent physical examination findings	Bloodwork findings	Location of SCC lesion	CT findings	Thoracic radiograph findings	Preoperative cytology: aural lesion	Preoperative cytology: locoregional lymph node	Preoperative biopsy: aural lesion	Preoperative biopsy: locoregional lymph node
10	12y 7mo	7.4	Ragdoll	MN	NR	Otitis externa, mass visualized on otoscopic examination	Elevated ALT, elevated AST	External ear canal	Mass within external ear canal, ipsilateral otitis media, ipsilateral medial retropharyngeal lymphadenopathy, bilaterally enlarged thyroid glands, probable meningioma right parietal lobe	Normal thorax	NP	NP	SCC, mitotic count: 1–2/40 × fields	NP
11	14y 9mo	3.4	DSH	MN	NR	Otitis externa	Lymphopenia, hyperglycemia, azotemia, hypernatremia	Middle ear		NP	NP	NP	NP	NP
12	13y 2mo	2.8	DLH	MN	Ipsilateral Horner's syndrome, ipsilateral vestibular disease	Otitis externa, discomfort with aural examination	Hyperglycemia, hyperproteinemia, hyperglobulinemia	Middle ear	Mass within middle ear with bulla lysis, ipsilateral otitis media, contralateral otitis externa, ipsilateral medial retropharyngeal lymphadenopathy, incidental lateral ventricle asymmetry	Normal thorax	NP	NP	NP	NP
13	7y	4.7	DSH	FS	Ipsilateral Horner's syndrome	Otitis externa, palpable mass associated with ear canal, mild ocular and nasal discharge	WNL	Middle ear	Mass within middle ear with extensive disease characterized by osseous lysis and proliferation, bilateral medial retropharyngeal lymphadenopathy	Broncho-interstitial pattern, mild generalized cardiomegaly	NP	No evidence of metastatic disease	SCC, official report not available	NP
14	9y 1mo	5.2	DSH	MN	NR	Otitis externa	WNL	Middle ear	Mass within middle ear, bulla lysis, ipsilateral otitis externa and media, ipsilateral medial retropharyngeal lymphadenopathy	NP	NP	NP	NP	NP
15	14y	7	DSH	MN	NR	Excoriations around ear base	WNL	External ear canal	NP	Normal thorax	NP	Metastatic carcinoma	SCC, official report not available	NP

(Continued)

Table 1 (Continued)

Case	Age	BW (kg)	Breed	Sex	Neurologic abnormalities at presentation	Additional pertinent physical examination findings	Bloodwork findings	Location of SCC lesion	CT findings	Thoracic radiograph findings	Preoperative cytology: aural lesion	Preoperative cytology: locoregional lymph node	Preoperative biopsy: aural lesion	Preoperative biopsy: locoregional lymph node
16	11y	3.3	DMH	MN	NR	Palpable mass associated with ear canal	WNL	External ear canal	NP	NP	NP	Metastatic carcinoma	SCC, official report not available	NP
17	9y	3.9	DLH	FS	NR	Mass visualized on otoscopic examination, discomfort opening mouth	Not available for review	External ear canal	NP	NP	NP	NP	SCC, official report not available	NP
18	4y	4.2	DSH	MN	Ipsilateral facial nerve deficits, ipsilateral Horner's syndrome	Otitis externa	WNL	External ear canal and middle ear	Mass extending from external ear canal to middle ear, ipsilateral medial retropharyngeal lymphadenopathy, ipsilateral mandibular lymphadenopathy	Possible hiatal hernia or esophageal dilation	Carcinoma	NP	SCC, mitotic index: 30/5 400 × fields	NP
19	16y	6.1	DSH	MN	NR	Otitis externa, excoriations on pinna	WNL	External ear canal	Mass within external ear canal, lysis of the zygomatic and frontal bones, ipsilateral otitis media, contralateral otitis externa, ipsilateral medial retropharyngeal lymphadenopathy, bilateral nasal turbinate atrophy	Normal thorax	NP	NP	SCC, mitotic count: 0-1/10 40 × fields	NP
20	8y 1 mo	3.5	DSH	FS	Ipsilateral facial nerve deficits	Otitis externa, discomfort with aural examination, regional peripheral lymphadenopathy	Not available for review	Middle ear and inner ear	NP	Normal thorax	NP	No evidence of metastatic disease	SCC, mitotic count: 19/10 400 × fields	NP
21	5y	3.6	DSH	MN	Ipsilateral facial nerve deficits, ipsilateral head tilt	Mass visualized on otoscopic examination	Leukocytosis, mature neutrophilia	External ear canal	Mass within external ear canal, extension into calvarium and brain, ipsilateral mandibular lymphadenopathy	Aerophagia	NP	NP	SCC, mitotic count: 32/10 40 × fields	NP

(Continued)

Table 1 (Continued)

Case	Age	BW (kg)	Breed	Sex	Neurologic abnormalities at presentation	Additional pertinent physical examination findings	Bloodwork findings	Location of SOC lesion	CT findings	Thoracic radiograph findings	Preoperative cytology: aural lesion	Preoperative cytology: locoregional lymph node	Preoperative biopsy: aural lesion	Preoperative biopsy: locoregional lymph node
22	12 y	3	DMH	FS	Ipsilateral Horner's syndrome, ipsilateral head tilt, ipsilateral vestibular disease	Otitis externa, discomfort with aural examination, regional peripheral lymphadenopathy	WNL	Middle ear	NP	NP	NP	NP	SCC, mitotic count: 10/10 40 × fields	NP
23	8 y	5.8	DMH	MN	Ipsilateral facial nerve deficits, ipsilateral Horner's syndrome	Otitis externa, mass visualized on otoscopic examination	Elevated creatinine, total hypercalcemia, hyperproteinemia, hyperglobulinemia, hyperalbuminemia	Middle ear and inner ear	Mass extending from middle to inner ear, extensive disease with extension into calvarium, brain and temporomandibular region, ipsilateral medial retropharyngeal lymphadenopathy, periodontal disease	Mild generalized cardiomegaly	NP	NP	SCC, mitotic count: 67/10 40 × fields	NP
24	12 y 6 mo	4.4	DSH	FS	NR	Mass visualized on otoscopic examination, discomfort with aural examination	WNL	External ear canal, middle ear and inner ear	Right periaural soft tissue mass with right ear canal involvement, extension into calvarium and brain, ipsilateral medial retropharyngeal lymphadenopathy, ipsilateral mandibular lymphadenopathy, chronic right rhinitis and frontal sinusitis	Broncho-interstitial pattern with right middle and cranial lung lobe atelectasis, left scapular soft tissue dystrophic mineralization	NP	NP	SCC, mitotic count: 19/10 400 × fields	NP
25	7 y 3 mo	2.6	DSH	MN	Ipsilateral facial nerve deficits, ipsilateral head tilt, ipsilateral vestibular disease	Otitis externa	WNL	Middle ear	NP	Poor serosal detail in cranioventral abdomen, aerophagia	NP	NP	SCC, mitotic count: 23/10 40 × fields	NP

BW = body weight; y = years; mo = months; DSH = domestic shorthair; MN = male neutered; NR = not reported; WNL = within normal limits; NP = not performed; FS = female spayed; ALT = alanine aminotransferase; AST = aspartate aminotransferase; DLH = domestic longhair; DMH = domestic medium hair

radiography was performed in 16/25 cats (64%). There was no evidence of pulmonary metastasis on thoracic radiographs in any cat.

Preoperative cytology of the aural lesion was performed in one cat (case 18). Cytology was consistent with carcinoma and characterized by clusters of epithelial cells displaying cellular atypia. Preoperative cytology of regional lymph nodes was performed in six cats, four of which were consistent with metastatic carcinoma (cases 5, 6, 15 and 16). Preoperative histopathology was performed in 17/25 cats (68%). Findings were consistent with SCC in 16 cats. In the remaining one cat, histopathology revealed focal areas of atypical epithelial cells. Though a final diagnosis of carcinoma could not be made, it was later confirmed on postoperative histopathology. One cat (case 4) had a preoperative biopsy of the regional lymph node performed, and findings were consistent with metastatic carcinoma.

The treatments and outcomes of the 25 cats are summarized in Table 2. Following diagnosis, one cat (case 5) did not receive treatment. Eight cats were treated palliatively with medical management (cases 6, 17, 20, 21, 22, 23, 24 and 25) utilizing prednisolone (cases 6, 20, 22, 23 and 25), meloxicam (case 17) and/or buprenorphine (cases 17, 20, 21, 22, 23, 24 and 25). Other prescribed oral medications included maropitant, ondansetron, mirtazapine and gabapentin, as well as cefovecin and methylprednisolone subcutaneously.

Two cats (cases 8 and 15) were treated with coarse fractionated RT, one of which had cytologic evidence of lymph node metastasis and had regional lymph nodes irradiated in addition to the primary lesion (case 15). Case 8 developed hemifacial spasms following the sixth and final dose of RT suspected to be due to RT-induced facial neuritis. Otherwise, no acute or late complications were reported. Case 8 was treated concurrently with oral prednisolone.

One cat was treated with systemic chemotherapy alone (case 16). The cat was treated with 11 doses of toceranib over 30 days q48h. However, inconsistent dosing intervals occurred due to inappetence, and toceranib therapy was discontinued once progression was noted.

Two cats (cases 18 and 19) were treated with a combination of coarse fractionated RT and systemic chemotherapy, one of which had cytologic evidence of lymph node metastasis and had regional lymph nodes irradiated in addition to the primary lesion (case 18). Case 19 only received one fraction (8 Gy) due to development of an abscess in the region. Otherwise, no acute or late complications were reported. Case 18 was treated with toceranib for 105 days before progressive disease was detected. At that time, the cat was treated with carboplatin then doxorubicin, owing to further progression of the disease. Case 19 was treated with toceranib for four doses before the

medication was discontinued, owing to development of a facial abscess.

Surgery was performed in 11 cats, one of which had cytologic evidence of lymph node metastasis (case 4). A total ear canal ablation and bulla osteotomy (TECA-BO) was performed in 10 cats. A ventral bulla osteotomy (VBO) was performed on one cat (case 2). Procedures performed in addition to the TECA-BO included ipsilateral pinnectomy, ipsilateral canthoplasty, contralateral ear base mass removal and contralateral pinnectomy (case 4), as well as ipsilateral pinnectomy (case 10). Mean anesthesia time was 205 mins (range 114–333) with a mean surgery time of 94 mins (range 45–176). Three cats experienced intraoperative complications, including intermittent hypotension (cases 1, 2 and 3) treated successfully with dopamine and hetastarch, mild hemorrhage (case 3) controlled with electrosurgery and tachycardia (case 3). The complications reported for cases 1 and 2 were classified as grade 0 and the complications noted for case 3 were classified as grade I according to the CLASSIC system.¹²

Samples of the primary lesion were submitted for histopathology following surgery in all cats, confirming a diagnosis of SCC for all cats. The mitotic count ranged from 1 to 42 per 10 high power fields, with a mean of 19. One cat had evidence of metastasis to the mandibular lymph node (case 4). Other findings included ulcerative dermatitis of the contralateral pinna (case 4), histologically unremarkable parotid and mandibular salivary glands (4) and a mast cell tumor of the skin of the ear pinna (case 1). Histopathologic margins were complete in three cases (cases 1, 9 and 10), microscopically incomplete in four cases (cases 3, 4, 7 and 12) and grossly incomplete in three cases (cases 2, 13 and 14). Margins were not reported in one case (case 11).

Four cats were discharged the same day as surgery, eight were discharged 24 h postoperatively and two were discharged 48 h postoperatively. The reported immediate postoperative and short-term complications are summarized in Table 2. All complications were categorized as grade 1 (minor complications) according to the Accordion Severity Classification System.¹³ Only complications that were new findings postoperatively were considered.

Four cats received postoperative treatment. One cat received adjuvant RT following surgery (case 13). Only one dose (6.5 Gy) was administered, as progressive disease was noted at the time of the second treatment. One cat was treated supportively with prednisolone and maropitant (case 3). Other reported pertinent treatments included chlorambucil for concurrent small cell splenic and hepatic lymphoma (case 9) and *yunnan baiyao* for left-sided epistaxis noted 186 days postoperatively (case 10). In total, 6/25 cats (24%) were suspected to have local recurrence based on clinical signs at a mean of 78 days following treatment (range 32–146), two of which had

Table 2 A summary of treatments and outcomes of 25 cats with aural squamous cell carcinoma (SCC)

Case	Treatment	Postoperative biopsy aural lesion	Immediate postoperative complications	Complications 2 weeks postoperatively	Time to recurrence (days)	Overall survival (days)
1	TECA-BO	SCC, mitotic count: 24/10 40 ×	Swelling of surgical site absent palpebral	NR	102	173
2	VBO	SCC, mitotic count: 42/10 40 ×	Ipsilateral Horner's syndrome	NR	111	168
3	TECA-BO: postoperative prednisolone and maropitant (dose and frequency not available)	SCC, mitotic count: 18/10 40 ×	Swelling of surgical site	Absent ipsilateral palpebral	–	65
4	TECA-BO, ipsilateral pinnectomy, ipsilateral canthoplasty, contralateral ear base mass, contralateral pinnectomy	SCC, mitotic count: 17/10 40 ×	Absent ipsilateral palpebral	Absent ipsilateral palpebral	–	9*
5	No treatment pursued	–	–	–	–	85
6	Medical management: prednisolone (1.1 mg/kg PO q24h)	–	–	–	–	38
7	TECA-BO	SCC, mitotic count not reported	NR	Ipsilateral Horner's syndrome, ipsilateral vestibular disease, ipsilateral facial nerve paralysis	146	67
8	Coarse fractionated RT. Protocol: 6 Gy once weekly for a total of 6 weeks (total dose of 36 Gy), treated concurrently with prednisolone (1.3 mg/kg PO [frequency not available])	–	–	–	–	129
9	TECA-BO: postoperative chlorambucil (dose and frequency not available)	SCC, mitotic count not reported	Ipsilateral facial nerve paralysis	Ipsilateral facial nerve paralysis	–	236
10	TECA-BO, ipsilateral pinnectomy, postoperative <i>yunnan baiyao</i> (dose and frequency not available)	SCC, mitotic count: 20–30/10 40 ×	Ipsilateral facial nerve paralysis	Ipsilateral facial nerve paralysis	36	247
11	TECA-BO	SCC, mitotic count not reported	Ipsilateral facial nerve paralysis	NR	–	262
12	TECA-BO	SCC, mitotic count 1/10 40 ×	Ipsilateral facial nerve paralysis	Ipsilateral head tilt, ipsilateral facial nerve paralysis, swelling of surgical site, nasal discharge	–	41
13	TECA-BO, postoperative RT. Protocol: two parallel-opposed fields of radiation from dorsal and ventral using a total dose of 6.5 Gy	SCC, mitotic count: 10/10 40 ×	Ipsilateral facial nerve paralysis	Ipsilateral vestibular disease, ipsilateral Horner's syndrome, persistent otitis, nasal discharge	42	103
14	TECA-BO	SCC, mitotic count not reported	Ipsilateral facial nerve paralysis	Ipsilateral facial nerve paralysis, discomfort opening mouth	32	51

(Continued)

Table 2 (Continued)

Case	Treatment	Postoperative biopsy aural lesion	Immediate postoperative complications	Complications 2 weeks postoperatively	Time to recurrence (days)	Overall survival (days)
15	Coarse fractionated RT. Protocol: 8Gy once weekly for a total of 4 weeks (total dose of 32Gy)	—	—	—	—	141
16	Systemic chemotherapy: toceranib (3.1 mg/kg PO q48h)	—	—	—	—	36
17	Medical management: meloxicam (0.5 mg/kg PO q48h) + buprenorphine (0.02 mg/kg TM q12h-q8h)	—	—	—	—	8*
18	Combination of coarse fractionated RT and systemic chemotherapy. Protocol: 8Gy once weekly for a total of 4 weeks (total dose of 32Gy) toceranib (2.5 mg/kg PO q48h); carboplatin (3.9 mg IV once); doxorubicin (0.94 mg/kg IV once)	—	—	—	—	165
19	Combination of coarse fractionated RT and systemic chemotherapy. Protocol: 8Gy once weekly for a total of 4 weeks (total dose of 32Gy) toceranib (2.5 mg/kg PO q48h)	—	—	—	—	43*
20	Medical management: prednisolone (0.86 mg/kg PO q12h) + buprenorphine (0.01 mg/kg TM q12h-q8h)	—	—	—	—	43
21	Medical management: buprenorphine (0.05 mg/kg TM q12h)	—	—	—	—	1085
22	Medical management: prednisolone (0.82 mg/kg PO q12h) + buprenorphine (dose not available) + maropitant (1.3 mg/kg PO q24h)	—	—	—	—	47
23	Medical management: prednisolone (1.0 mg/kg PO q24h) + buprenorphine (0.01 mg/kg TM q12h-q8h) + gabapentin (dose not available) + ondansetron (dose not available)	—	—	—	—	1*
24	Medical management: buprenorphine (0.02 mg/kg TM q12h-q8h)	—	—	—	—	9
25	Medical management: prednisolone (1.0 mg/kg PO q12h for 3 days then 0.5 mg/kg PO q24h for 4 days) + buprenorphine (0.02 mg/kg TM q12h) + mirtazapine (1.5 mg/kg PO q24h) + cefovecin (9.4 mg/kg SC once) + methylprednisolone (15.7 mg/kg SC once)	—	—	—	—	10

*Lost to follow up

TECA-BO = total ear canal ablation and bulla osteotomy; NR = not reported; VBO = ventral bulla osteotomy; RT = radiation therapy; TM = transmucosally

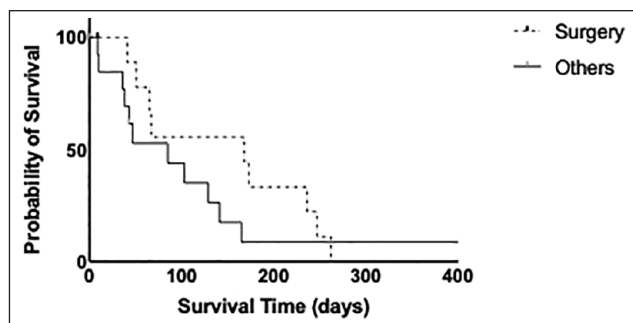


Figure 1 Kaplan–Meier survival curve for cats with surgically treated aural squamous cell carcinoma vs those treated palliatively. Cats were censored from the survival analysis if they were alive at the time of analysis or lost to follow-up

complete margins (cases 1 and 10) and four of which had incomplete margins on histopathology following surgery (case 2, 7, 13 and 14). Confirmation was obtained in one cat via recheck CT scan (case 13).

The MST for cats treated by surgery alone was 168 days vs 85 days for those treated palliatively with either medical management, RT, chemotherapy, or a combination of RT and chemotherapy, though no statistically significant difference was detected between the groups ($P = 0.28$; Figure 1). The survival times for cats treated with medical management, RT alone, chemotherapy alone, or a combination of RT and chemotherapy are summarized in Table 2. In total, four cats (cases 4, 17, 19 and 23) were lost to follow-up with a follow-up of 23 days, 8 days, 43 days and 11 days following initial presentation, respectively. Therefore, survival time represents the time elapsed from presentation to date of last follow-up.

Discussion

Tumors of the ear canal are rarely seen in cats, though they can develop from any of the structures associated with the ear canal, including squamous epithelium¹⁴ with SCC representing the second most common feline aural tumor.¹ This case series documented that SCC of the ear canal, middle and/or internal ear is a locally aggressive tumor that carries an overall poor prognosis.

Cats presented at a median age of 11 years at the time of presentation in the current study, with no sex predilection noted. Common clinical findings included ipsilateral head tilt, ipsilateral Horner's syndrome, ipsilateral vestibular disease, evidence of otitis externa and palpable discomfort. These demographic and examination findings are comparable to other reports.^{1,8,10,15,16} In the present study, 12/25 cats (48%) displayed neurologic signs at presentation. This varies from previous reports, where only approximately 25% of cats with benign polyps or malignant neoplasia presented with neurologic signs.¹¹ A possible explanation for this could be that all cases in the present study were affected by SCC, which is a

locally invasive tumor that can easily invade surrounding structures such as the middle and inner ear resulting in increased presentation of neurologic signs.

It has been reported that 25% of malignant aural tumors in cats will have bulla involvement. Thus, CT or skull radiography is recommended as part of the diagnostic work-up.¹⁵ In the present study, 5/16 cats (31%) had lesions localized to the external ear canal alone, 9/16 cats (56%) had middle ear involvement and 2/16 cats (13%) had lesions localized to the inner ear alone based on CT findings. This finding is consistent with a recent report in which SCC was the most common malignant tumor diagnosed in the feline middle ear.² This is not unexpected as squamous epithelium lines the auditory canal, tympanic cavity and tympanic membranes. However, squamous epithelium also lines the ear canal and the membranous labyrinth, which explains the reported external ear canal and inner ear involvement in this study. Common CT changes associated with neoplasia in the present study were the presence of a soft tissue mass effect with frequent invasion into adjacent tissues, bulla thickening, osteolysis and fluid accumulation. While previous reports largely utilized skull radiographs for imaging diagnosis, similar findings of space-occupying lesions and proliferative and lytic changes to the bulla have been reported.^{6,8–10,14,16,17} This is consistent with previous reports describing the locally aggressive nature of SCC.^{1,6,15} Pulmonary metastasis at the time of presentation was not detected in any cat in the current study. This is comparable to other studies evaluating feline aural tumors.^{1,16} Regional lymph node metastasis was detected in 5/7 (71%) total cats in which cytology or histopathology of the local lymph node(s) was performed. This contrasts with another report in which 5/56 total cats (9%) had regional lymph node metastasis.¹ However, in the previous study, all types of aural tumors were included. Therefore, the variability noted could be due to the more aggressive nature of SCC vs other tumor types. Furthermore, owing to the retrospective nature of the study, not all cats had lymph node aspirates as part of the diagnostic work-up as this was not standardized. Similarly, in the current study, only 7/25 total cats (28%) had lymph node sampling performed. Sampling was likely performed in those in which metastasis was suspected based on clinical and imaging findings. Subsequent metastasis was not detected in any cat in our study. Other studies have reported metastasis as a frequent sequela in cats with aural tumors.^{14,18} This inconsistency could be due to most cats being euthanized shortly after local recurrence was diagnosed in the present study.

Surgery was the most common treatment for cats in the current study (11/25; 44%). Aggressive surgical management to include TECA and lateral bulla osteotomy is the reported treatment of choice for malignant aural tumors in cats, to achieve local control.^{11,15} One cat in the

present study had a VBO performed. While disease was localized to the middle ear, recurrence was noted 112 days following surgery, it is unclear if a TECA-BO may have resulted in a different outcome. As complications and recurrence after surgical treatment are not uncommon, RT can be utilized either alone or as adjuvant therapy.¹⁴ In the present study, 2/25 cats (8%) received RT therapy alone and one cat received RT following surgery. While chemotherapy has shown minimal efficacy as a single agent or as an adjuvant with either surgery or radiation for feline SCC, it has been used in cases that failed to respond to conventional treatment or for inoperable tumors.¹⁹ In the present study, one cat (3%) received chemotherapy alone and two cats (7%) received a combination of RT and chemotherapy.

Although surgery resulted in a longer MST than in cats treated palliatively with either medical management, RT, chemotherapy, or a combination of RT and chemotherapy, no statistically significant difference was found. The lack of significance could be due to low case numbers and type 2 statistical error. It is important to note that, given the retrospective nature of this study, the surgical cases may have been those with less advanced disease, resulting in a bias toward a better prognosis. Increased surgical dose has been correlated with increased survival time in cats and dogs with ceruminous gland adenocarcinoma.^{4,20} Owing to the invasive nature of most of these tumors, complete resection is often difficult. Similarly, the primary treatment for aural tumors in human patients is surgery, and if complete excision is not possible, postoperative RT is often recommended. In a study evaluating the results of RT for cancer of the middle ear (27/29 SCC and 2/29 unspecified), approximately 50% of humans with malignant tumors of the middle ear canal were cured when RT followed surgery.²¹ In another study, which examined the use of RT for ceruminous gland carcinomas in six cats and five dogs following incomplete surgical excision, it was found that 6/11 (55%) had a 1-year progression-free survival with a mean progression-free survival time of 39.5 months, concluding that RT was effective in some patients and should be considered as a treatment modality.³ Unfortunately, RT following surgery was used in one cat in the present study; therefore, conclusions as to the effectiveness of RT as an adjuvant to surgery cannot be reached. Similarly, very few cats received chemotherapy alone or in combination with RT; therefore, conclusions about the efficacy of these treatment modalities also cannot be reached.

A large study evaluating neoplasms of the external ear canal reported a MST of 11.7 months for cats with malignant aural neoplasia,¹ whereas previous studies have found middle ear neoplasia to be associated with poorer prognosis, with recurrence or progression of disease resulting in euthanasia occurring within 4 days to

3 months postoperatively.^{9,10,16} In the present study, 6/25 total cats (24%) had suspected recurrence occurring 32–146 days following the initial diagnosis, with no evidence of distant metastasis detected. As some cats were receiving no treatment or palliative care, routine evaluations for metastasis may not have been performed, which may have underestimated the true occurrence of metastatic disease. However, the MST of 168 days for cats treated with surgery and 85 days for cats treated palliatively supports the overall poor prognosis associated with a diagnosis of SCC of the middle ear, inner ear or ear canal.

This case series had low case numbers due to the uncommon nature of this disease. Case accrual was increased by a multi-institutional collaboration, but there are some associated limitations, including a greater number of patients with incomplete follow-up. While the medical records of all cats included information on signalment and physical examination findings, data on diagnostic imaging results, biological behavior, treatments pursued, time to recurrence, survival time and the rate of development of metastasis was more limited. The lack of necropsies performed could have also resulted in an underestimation of distant metastasis that occurred following initial diagnosis and treatment.

Conclusions

In this case series of cats with SCC of the ear canal (middle and internal), neurologic signs were common at presentation. Surgery was the most used treatment modality for disease control. The MST following medical treatment was shorter than that of surgery, though this was not statistically significant.

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Ethical approval This work involved the use of non-experimental (owned or unowned) animals. Established internationally recognized high standards ('best practice') of veterinary clinical care for the individual patient were always followed and/or this work involved the use of cadavers. Ethical approval from a committee was therefore not specifically required for publication in *JFMS*. Although not required, where ethical approval was still obtained, it is stated in the manuscript.

Informed consent Informed consent (verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (experimental or non-experimental animals, including cadavers) for all procedure(s) undertaken (prospective or retrospective studies). No animals or people are

identifiable within this publication, and therefore additional informed consent for publication was not required.

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