Diagnosis and surgical treatment of a malignant trichoepithelioma of the ear canal in a pet rabbit (Oryctolagus cuniculus)

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Case Description—A 10-year-old spayed female Holland Lop–mix pet rabbit (Oryctolagus cuniculus) was evaluated because of purulent-hemorrhagic discharge from the right ear canal and a suspected mass within that ear canal.

Clinical Findings—Results of contrast-enhanced CT, video otoscopy, and histologic examination of endoscopic tissue biopsy samples indicated severe otitis media and externa and a benign trichoepithelioma of the right ear canal.

Treatment and Outcome—Total ear canal ablation and lateral bulla osteotomy were performed. Histologic examination of a surgical biopsy sample of the mass indicated malignant trichoepithelioma. Tumor recurrence was detected 22 weeks after surgery. The rabbit was euthanized 33 weeks after surgery because of the large size of the recurrent tumor and declining quality of life. Necropsy findings indicated a malignant trichoepithelioma with local and lymphatic invasion into the right mandibular lymph node.

Clinical Relevance—This was the first report of the clinical diagnosis, surgical treatment, and outcome for a domestic rabbit with a diagnosis of a malignant trichoepithelioma of the ear canal and associated otitis media and externa. Neoplasia should be included as a differential diagnosis for pet rabbits with otitis externa and media. Although such tumors are typically benign, trichoepitheliomas in rabbits can be malignant. Computed tomography and histologic examination of tissue samples were useful diagnostic techniques, but histologic examination of an endoscopic biopsy sample did not allow identification of malignant characteristics of the trichoepithelioma. (J Am Vet Med Assoc 2014;245:227–231)

A 10-year-old spayed female Holland Lop–mix pet rabbit (Oryctolagus cuniculus), with a body weight of 2.7 kg (5.94 lb), was referred to the University of Wisconsin Veterinary Medical Teaching Hospital for evaluation of purulent-hemorrhagic discharge from the right ear canal and a suspected mass in that ear canal. Initial physical examination revealed that the right ear was inflamed and signs of pain were detected during palpation. A small amount of dried blood and purulent discharge was detected on the pinna and the opening of the right ear canal (Figure 1). The left ear appeared clinically normal with no discharge. Results of the remainder of the physical examination, plasma biochemical analyses, and CBC were unremarkable.¹ The patient was anesthetized, and contrast-enhanced CT of the head was performed. The rabbit was premedicated with butorphanol (0.25 mg/kg [0.11 mg/lb], IM) and midazolam (0.5 mg/kg [0.23 mg/lb], IM). Isoflurane was administered by mask for anesthetic induction and maintenance. Transverse plane CT images were obtained before and after IV administration of iodinated contrast medium² (2.2 mL of iohexol/kg [1 mL/lb]; 300 mg of iodine/mL). The CT findings were consistent with right chronic otitis media. In addition, there was an irregular polyloid (diameter, 1.5 cm) soft tissue mass containing local regions of heterogeneous mineralization and a contrast-enhancing rim extending laterally from the distal aspect of the right ear canal (Figure 2). Results of video otoscopy indicated accumulation of purulent material in the right ear canal and a broad-based poorly defined mass in the vertical portion of that ear canal. The mass obliterated the anatomic architecture of the right ear canal and occluded the vertical portion of that ear canal. Examination of an endoscopic tissue biopsy sample³ (submitted in neutral-buffered 10% formalin) revealed a benign trichoepithelioma characterized by epithelial aggregates with various degrees of infundibular, isthmus, and matrical differentiation (Figure 3). Results of bacterial culture indicated moderate mixed growth of gram-positive bacteria; all of these bacteria were susceptible to enrofloxacin. Before those results were available, treatment was started including enrofloxacin⁴ (10 mg/kg [4.55 mg/lb], PO, q 12 h), penicillin G procaine and penicillin G benzathine⁵ (50,000 U/kg [22,727 U/lb], SC, q 5 d [total number of doses administered = 6]), and meloxicam⁶ (0.3 mg/kg [0.14 mg/lb], PO, q 12 h). In addition, topical treat-

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mements included corticosteroid and antimicrobial otic drops\(^1\) (administered in the right ear, q 24 h, for 14 days).

The owners were counseled regarding surgical, medical, and palliative treatment options.

Five weeks after the initial evaluation, a total ear canal ablation and lateral bulla osteotomy were performed by use of described methods.\(^2,3\) The rabbit was premedicated with midazolam (1 mg/kg [0.45 mg/lb], SC) and oxymorphone\(^4\) (0.18 mg/kg [0.08 mg/lb], SC).

After anesthetic induction with isoflurane (administered with a face mask), the rabbit was intubated and anesthesia was maintained with isoflurane. Additional pain management treatments included a fentanyl\(^5\) constant rate infusion (15 \(\mu g/kg/h\) [6.82 \(\mu g/lb/h\]); administered throughout the procedure) and buprenorphine\(^6\) (30 \(\mu g/kg\) [13.64 \(\mu g/lb\]), IV; administered 30 minutes prior to the end of anesthesia and continued for 3 more doses, q 8 h). The tumor in the vertical portion of the external ear canal did not penetrate the osseous bulla (Figure 1). Moderate blood loss (estimated 2% of body weight) occurred during debridement of bone fragments from the bulla. Following lateral bulla osteotomy, amikacin-impregnated plaster of Paris antimicrobial beads\(^7\) and ceftiofur-impregnated polymethyl methacrylate beads\(^7\) were placed in the remaining portion of the tympanic bulla. The deep portion of the subcutaneous tissue was closed in a simple interrupted pattern,\(^8\) and the remaining subcutaneous tissue was closed in a simple continuous pattern.\(^9\) The skin was closed in a simple continuous pattern. After surgery, the patient received fresh whole blood (25 mL administered over 3 hours; 9 parts blood to 1 part acid-citrate-dextrose solution\(^9\)) that had been collected from a donor rabbit within 1 hour prior to administration. The patient recovered from anesthesia without complications.

Home care instructions were routine and included monitoring of the surgical site to detect complications and monitoring of appetite and fecal production. Administration of meloxicam (0.3 mg/kg, PO, q 24 h for 5 doses) and procaine penicillin G benzathine (50,000 U/kg [22,727 U/lb], SC, q 5 d for 2 doses) was continued. Further, a petroleum-based lubricant was applied to the right eye every 4 hours for 2 weeks because of temporary right facial nerve paresis that developed secondary to the total ear canal ablation and lateral bulla osteotomy.

Aerobic and anaerobic bacterial culture results for samples collected from the right tympanic bulla indicated no growth. Histologic examination of the surgical biopsy sample, which consisted of the resected mass in the vertical portion of the right ear canal and bone fragments from the tympanic bulla, indicated a well-demarcated unencapsulated lobular exophytic mass (Figure 2) expanding the dermis and invading but not breaching the aural cartilage (Figure 3). The histologic diagnosis was malignant trichoepithelioma (matrical carcinoma) with squamous differentiation and intralymphatic invasion. The endoscopic biopsy
sample that had been obtained before surgery was reexamined; results were consistent with the initial results (benign trichoepithelioma). The surgical biopsy sample contained similar benign areas superficially with irregular and malignant-appearing areas deep in the tissue that were not represented in the sample obtained before surgery. Histologic examination of the tympanic bulla bone fragment indicated osseous metaplasia and osteomyelitis with intraleisional bacteria.

The surgical site healed without complications, although the rabbit had mild facial asymmetry and signs of facial nerve damage for several days following surgery. Because the tumor was malignant and had not been completely removed, adjuvant radiation therapy and systemic administration of chemotherapeutic drugs were offered; these treatments were declined by the owner.

The rabbit was reevaluated 22 weeks after surgical treatment. Results of physical examination were unremarkable except for a movable subcutaneous mass (approx 3 x 3 x 2 cm) in the area just caudal to the right mandibular ramus. The surgical site had healed completely. Repeated pre- and postcontrast CT of the head and neck was performed after the rabbit was sedated (midazolam [0.5 mg/kg] and butorphanol [0.25 mg/kg], IM). Transverse plane CT images were obtained before and after IV administration of iodinated contrast medium (2.2 mL of iohexol/kg; 300 mg of iodine/mL). Results of CT indicated a large soft tissue mass in the right retromandibular region, static lysis of the right temporal bone, and new lysis of the bones of the right inner ear. Findings of cytologic examination of a fine-needle aspirate of the mass were consistent with an epithelial carcinoma with squamous differentiation. In addition, there was abundant necrotic cellular material and moderate inflammation characterized by a mixed population of heterophils and macrophages. Given the history of malignant trichoepithelioma, tumor recurrence was suspected. Results of aerobic bacterial culture of the mass indicated no growth. Treatment options discussed with the owners at that time included marginal surgical reexcision of the tumor and local lymph node, followed by palliative or curative-intent radiation therapy, chemotherapy, and treatment with a cyclooxygenase-2 inhibitor. The owner decided to treat the rabbit only with meloxicam (0.3 mg/kg, PO, q 12 h).

Thirty-three weeks after total ear canal ablation and lateral bulla osteotomy and 38 weeks after the initial evaluation, the rabbit was reevaluated because of increasing size of the right retromandibular region tumor and increased local self-excoriation. The rabbit’s appetite and body weight remained stable, but it had increasing difficulty drinking from a water bottle. Physical examination revealed the right mandibular mass had substantially enlarged and was fluctuant. Removal of a superficial crust resulted in discharge of hemorrhagic, malodorous fluid. The skin over the mass was partially discolored and necrotic. On the basis of a poor prognosis, the animal was euthanized and a complete necropsy performed. Multiple masses and enlarged lymph nodes (often with central necrosis) were identified in the region caudal to the right mandibular ramus and surgical site. Histologic findings confirmed a recurrent and metastatic malignant trichoepithelioma with rafts and islands of neoplastic epithelial cells in connective tissue, many lymphatics, and, rarely, small blood vessels in the region of the previously removed right ear canal and bulla. The local draining lymph nodes were...
almost completely effaced by large amounts of necrosis, with few islands of viable neoplastic cells.

**Discussion**

Disorders of the external ear canal and middle ear are common in pet rabbits, and lop-eared rabbits in particular seem to be prone to this problem because of the anatomic characteristics of the external ear canal in such animals.\(^\text{4}\) Otitis externa is one of the most common dermatologic disorders in pet rabbits and is detected in 12% of rabbits with dermatologic disorders.\(^\text{3}\) Parasitic (e.g., *Psoroptes cuniculi*) and secondary bacterial and yeast infections are commonly associated with otitis externa, whereas otitis media is primarily due to bacterial infections.\(^\text{4,5}\) Neoplasia associated with the external ear canal or middle ear disease in rabbits has not been reported, to the authors’ knowledge, but there are 2 reports\(^\text{6,7}\) of rabbits with cutaneous neoplasms (malignant melanoma or sebaceous adenocarcinoma) originating from the pinna and extending into the external ear canal.\(^\text{1,3}\) Otitis externa or otitis media were not associated with neoplasms in those 2 rabbits. Nonviral skin tumors in rabbits are uncommon, but trichoblastomas are reported most frequently.\(^\text{8,9}\)

Benign trichoepitheliomas have been detected on the head, thorax, limb, perineum, and ischium of rabbits and are characterized as well demarcated and encapsulated.\(^\text{7,9}\) Malignant trichoepitheliomas have not been reported for rabbits, to the authors’ knowledge. In dogs, malignant trichoepithelioma is distinguished from benign trichoepithelioma on the basis of invasion into surrounding tissues, lymphatic involvement, and a high mitotic cell rate, resulting in diffuse metastatic disease to lymph nodes and lungs and a poor prognosis.\(^\text{9,11}\) The endoscopic biopsy sample for the rabbit of the present report had only benign characteristics. However, subsequent histologic examination of the surgically excised ear canal and neoplasm indicated malignant features including lymphatic invasion. Histologic examination of tissue samples obtained during necropsy indicated metastasis to the regional lymph nodes but not to the lungs. Therefore, results for endoscopic biopsy samples should be interpreted cautiously because the tissues collected may not be representative of an entire mass and malignant features might not be identified.

Little information is available regarding response to treatment for malignant trichoepitheliomas in any species. For the rabbit of the present report, local surgical resection with incomplete margins resulted in recurrence within 22 weeks and metastasis to the local lymph node within 33 weeks. Local treatment including wide surgical excision of the tumor is recommended. The use of palliative radiation therapy has been reported for a dog with a malignant trichoepithelioma, yielding a partial response\(^\text{12}\); however, diffuse metastasis was detected 18.6 months after the initial diagnosis in that dog, and it died 22.5 months after the initial diagnosis. Additional systemic treatments could be considered, but the optimal chemotherapeutic protocol has not been determined.

Otitis media can develop as an extension of otitis externa or because of ascending infection through the auditory tube.\(^\text{4}\) The rabbit of the present report had bacterial otitis media and externa concurrent with a malignant trichoepithelioma of the external ear canal. Considering that the contralateral ear was not affected, we suspected that the trichoepithelioma and the bacterial infection were directly associated, possibly because of impaired drainage from the obstructed ear canal. Ear canal ablation and bulla osteotomy are performed with increasing frequency for treatment of otitis media and externa in rabbits.\(^\text{2,13}\) Total or partial ear canal ablation may be performed, depending on the disease. In the rabbit of the present report, total ear canal ablation was performed because the trichoepithelioma was located in the vertical portion of the ear canal. The rabbit recovered from the procedure without complications, and meloxicam and buprenorphine seemed to be effective for control of pain after surgery. Temporary or permanent mild facial nerve damage may develop secondary to such surgical procedures. In the rabbit of the present report, facial nerve paresis was temporary and resolved within 2 weeks after the procedure.

The pet rabbit of the present report had a malignant trichoepithelioma of the external ear canal with associated severe bacterial otitis externa and otitis media. Computed tomography and histologic evaluation of tissue samples were useful for determination of a diagnosis, but malignant neoplasia was not identified during examination of an endoscopic biopsy sample. Total ear canal ablation, lateral bulla osteotomy, and medical treatments were effective for treatment of severe bacterial otitis externa and media, but incomplete tumor excision led to local recurrence and metastasis. Neoplasia should be included as a differential diagnosis for otitis externa and media in pet rabbits. Although such tumors are typically benign, trichoepitheliomas in rabbits can be malignant.

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**References**

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