Cutaneous epitheliotropic lymphosarcoma in a captive white catfish (*Ameiurus catus* Linnaeus)

Ashlyn C. Heniff\(^1\) | Laura R. Chen\(^2\) | Emily F. Christiansen\(^1,3\) | Craig A. Harms\(^1,4\) | Jerry M. Law\(^2\) | Christian Legner\(^5\) | Keith E. Linder\(^2\)

\(^1\)Department of Clinical Sciences, College of Veterinary Medicine, North Carolina State University, Raleigh, North Carolina, USA
\(^2\)Department of Population Health and Pathobiology, College of Veterinary Medicine, North Carolina State University, Raleigh, North Carolina, USA
\(^3\)North Carolina Aquariums, Raleigh, North Carolina, USA
\(^4\)Center for Marine Science and Technology, North Carolina State University, Morehead City, North Carolina, USA
\(^5\)North Carolina Aquarium on Roanoke Island, Manteo, North Carolina, USA

Correspondence
Keith E. Linder, Department of Population Health and Pathobiology, College of Veterinary Medicine, North Carolina State University, 1060 William Moore Drive, Raleigh, NC 27607, USA.
Email: keith_linder@ncsu.edu

Present address
Christian Legner, Town of Duck Administration, Duck, North Carolina, USA

Funding information
Funding for this clinical report came from the North Carolina Aquariums and the state of North Carolina

Abstract
A wild caught white catfish (*Ameiurus catus* Linnaeus) developed multiple cutaneous masses. Cytology revealed neoplastic lymphocytes and microscopy confirmed dermal infiltration with epitheliotropism in the epidermis, oral mucosa, and cornea, without internal organ involvement. Transmission electron microscopy did not identify viral particles. Histopathology supported cutaneous epitheliotropic lymphosarcoma, a condition most commonly reported in mammals. This is the first reported case of cutaneous epitheliotropic lymphosarcoma in an ictalurid and one of the few published cases of this condition in any fish species.

KEYWORDS
*Ameiurus catus*, cutaneous epitheliotropic lymphosarcoma, neoplasia, white catfish

White catfish (*Ameiurus catus* Linnaeus) are native to streams and lakes in eastern North America and are important in both recreational fishing and aquaculture (Hardman & Page, 2003). Multiple pale cutaneous masses and abrasions along the dorsal fin were noted on a 500 g, adult female white catfish at the North Carolina Aquarium at Roanoke Island (Manteo, NC). Approximately, 9 months prior, the catfish was collected as a part of a large mixed group of fish obtained from two sampling locations within the Pasquotank River Basin: Scuppernong River (Columbia, NC) and Mashoes Wildlife Access within Alligator River National Wildlife Refuge (East Lake, NC). Within 1 week, the lesions had progressed and the catfish was moved from the exhibit to an off-exhibit holding system. Water
quality parameters were within normal limits with no known contaminants. Observation revealed erosions on the dorsal and pectoral fins, a deep ulceration at the base of the first dorsal fin spine, an ulceration on the left side ventral to the dorsal fin, and multifocal, soft, rubbery cutaneous masses spanning from the head to the dorsal fin (Figure 1a). The catfish was anesthetized with buffered tricaine methanesulphonate (MS-222) at 150 ppm for physical examination. Wet-mount preparations revealed one (incidental) turbellarian from skin scrape and no external parasites from gill biopsy. Pending evaluation of fine needle aspirate cytology, treatment with florfenicol 30% was started at 30 mg/kg intramuscularly daily for 10 days for possible systemic bacterial infection secondary to skin ulceration and salinity was increased to 0.4 ppt to aid in osmoregulation. Diff-Quik stained cytology of a cutaneous mass revealed pleomorphic, round neoplastic cells with dark basophilic cytoplasm, a high nuclear to cytoplasm ratio, and granular chromatin. With an absence of detectable bacteria, fungi, or neutrophils, the catfish was presumptively diagnosed with lymphosarcoma. Because of the severity and continued progression of the lesions and probable poor prognosis, the catfish was euthanized and necropsied approximately 4 weeks following the first observation of lesions. Euthanasia was performed via immersion overdose in buffered MS-222 to effect followed by severing of the spinal cord and pithing of the brain stem to ensure death prior to necropsy.

At post-mortem examination, the white catfish weighed 473 g and demonstrated clinically significant wasting (5% body weight loss over 3 weeks). The superficial abrasions noted at initial presentation had developed fibrosis. Multifocal, variably sized (<0.5 cm to 2 x 3 cm) cutaneous rubbery masses consistent with previous clinical findings extended from the dorsal rostrum to the dorsal fin and varied from tan to white. There was no evidence of systemic lymphosarcoma as all internal organs lacked gross abnormalities. Samples of cutaneous masses and organs were placed in 10% buffered formalin for routine histology processing. Samples of four cutaneous masses were immediately placed in buffered McDowell and Trump's fixative (4% formaldehyde and 1% glutaraldehyde) for routine transmission electron microscopy (TEM) processing to search for a potential underlying retrovirus aetiology.

Histopathology revealed nonencapsulated dermal masses composed of sheets of monotypic, enlarged neoplastic lymphoid cells in scant new connective tissue with prominent infiltration of the epidermis (epitheliotropism) and occasional formation of Pautrier's microaggregates (Figure 1b). Round nuclei were sometimes indented or had convoluted nuclear envelopes. Mild-to-moderate anisokaryosis and anisocytosis were observed, and zero-mitotic figures were counted per 10 microscope fields (2.37 mm²). Epitheliotropism was well established in the oral cavity and was also noted in the peripheral cornea where it extended from a skin mass. Neoplastic cells were also noted in the gill interstitium. Internal organs lacked significant microscopic findings, with no evidence of leukaemia. TEM revealed numerous enlarged, round, lymphoid neoplastic cells in the dermis and epidermis that had atypical morphology and contained moderate amounts of increased cytoplasm, nuclei with convoluted envelopes, highly cleaved nuclei, coarsely clumped heterochromatin, and enlarged nucleoli (Figure 1c). Small Golgi bodies, scant rough endoplasmic reticulum, and few oval and indented mitochondria were present, and mitochondria contained regular tubular cristae or sometimes cristolysis. Presumed degenerating mitochondria were electron dense and membrane bound (Arismenidi-Morillo, 2009). No viral particles were detected in numerous neoplastic cells reviewed in multiple ultrathin sections from different skin masses. Gross and

![Figure 1](https://example.com/fig1.png)
microscopic findings were consistent with cutaneous epitheliotropic lymphosarcoma. Immunohistochemistry for T lymphocytes was attempted to confirm the neoplastic cell type; however, no immunoreactivity of any lymphocytes in normal positive control fish tissues could be demonstrated with commercially available antibodies. Additionally, external fish immunopathologists were contacted and they confirmed the lack of commercially available immunohistochemical markers for fish lymphocytes. In this case, the ultrastructural morphology of the neoplastic cells is consistent with that of lymphocytes and helps to confirm lymphosarcoma.

This case identifies cutaneous epitheliotropic lymphosarcoma in a white catfish with no evidence of viral particles on TEM and no known exposure to carcinogenic chemicals. Neoplasia is not uncommon in fish; however, incidence and prevalence of particular neoplasms in different fish populations have rarely been quantified (Vergneau-Grosset et al., 2017). Reports of epitheliotropic lymphosarcoma in fish are very limited. A single presumed spontaneous case of cutaneous epitheliotropic lymphoma was reported in a wild-type zebrafish (Danio rerio Hamilton) used in a two-generation toxicity study, treated with tetrabromobisphenol A – a substance not known to be carcinogenic (Kuiper et al., 2009). An epizootic of an epitheliotropic lymphoblastic lymphoma of thymic origin presenting with neoplastic infiltration of the gills, integument of the opercular cavity, and integument around the nares and eyes was reported in a brood group of coho salmon (Oncorhynchus kisutch Walbaum) raised in a hatchery (Kieser et al., 1991). Infectious or chemical aetiology was suspected due to high disease prevalence within the group, but diagnostics performed failed to confirm either.

Although scarcely reported in fish, cutaneous epitheliotropic lymphoma has been reported in a variety of mammal species, most notably dogs and humans (Fontaine et al., 2009) and rarely in domestic cats (Fontaine et al., 2011). Single reports have been described in other mammals including a squirrel (Honnold et al., 2007), a coati mundi (Skorinsky et al., 2008), a baboon (Carías et al., 2019), an opossum (Higbie et al., 2015), and an alpaca (Hasbach & Stern, 2016). This uncommon condition is characterized by infiltration of neoplastic T lymphocytes with a specific tropism for the epidermis and adnexal structures. The Pautrier’s microaggregates (formerly microabscesses) in the epidermis of the white catfish and involvement of the oral cavity are typical of cutaneous epitheliotropic lymphoma in dogs and humans but extension to the cornea is usually not a feature (Fontaine et al., 2009). The aetiology of cutaneous epitheliotropic lymphoma remains unknown (Rook, 2019). Although, there are reports in dogs and humans speculating possible associations with viral infections and chronic dermatitis, causal relationships have not been proven (Fontaine et al., 2009).

While reports of epitheliotropic lymphosarcoma in fish are very limited, there are many descriptions of other haematopoietic neoplasms in fish species. Many haematopoietic neoplasms that have been reported in fish are associated with retroviral or chemical aetiologies, rather than spontaneous origin. Retroviral-induced esocid lymphosarcomas in muskellunge (Esox masquinongy Mitchell) and northern pike (Esox lucius Linnaeus) manifest as non-epitheliotropic cutaneous round cell tumours. Immunohistochemistry and ultrastructural analysis have not yet determined a T lymphocytic or histiocyctic origin (Coffee et al., 2013). In Chinook salmon (Oncorhynchus tschawytscha Walbaum), the tentatively named Salmon Leukaemia Virus causes plasmacytoid leukaemia, resulting in accumulations of neoplastic round cells in visceral organs, including the liver, spleen, pancreas, kidney, pericardium, and retrobulbar tissue (Coffee et al., 2013). In channel catfish (Ictalurus punctatus Rafinesque), two cases of visceral lymphosarcoma were reported following exposure to N-methyl-N’-nitro-N-nitrosoguanidine, a known potent carcinogen (Chen et al., 1996). Lymphoma was reported in a black bullhead (Ameiurus melas Rafinesque) collected as part of a survey procedure in the Allouez Bay, Lake Superior, Wisconsin (Blazer & Schrank, 1995). Neoplastic cells were detected in liver, spleen, kidney, and gill tissues on histologic examination. Chemical aetiology was proposed based on collection location, but this was not confirmed.

Although many haematopoietic neoplasms in fish have been associated with retroviral or chemical aetiology, there are also numerous reports of haematopoietic tumours speculated to be of spontaneous origin. A single case of presumed spontaneous lymphosarcoma within the family Ictaluridae was reported in a channel catfish (I. punctatus) from a commercial production operation in Mississippi, with neoplastic cells noted in liver, intestine, gill, and kidney tissues on histologic examination (Bowser et al., 1985). In a broodstock population of Japanese medaka (Oryzias latipes Temminck & Schlegel) lymphomas were reported as the most common spontaneously occurring tumour in deceased or moribund fish (Okihiro & Hinton, 1989). Single cases of presumed spontaneous lymphosarcomas have also been reported in an African tilapia ( Sarotherodon spilurus spilurus Günther) (Haller & Roberts, 1980), an Astyanax sp. (Nigrelli, 1947), and a rainbow trout (Oncorhynchus mykiss gaindneri Richardson) (Bernstein, 1984).

The case of cutaneous epitheliotropic lymphosarcoma in a white catfish described in this report was presumed to be of spontaneous origin given that there was no known exposure to potential viral or chemical aetiologies such as those described above. This is further supported by the fact that no other fish in the exhibit tank developed observable neoplasia over the 9 years from the introduction of the catfish to the present. However, viral or chemical aetiologies could not be ruled out as the fish was wild caught. This report adds to the limited body of literature surrounding the prevalence and presentation of cutaneous epitheliotropic lymphosarcoma in fishes.

ACKNOWLEDGEMENT
The authors thank Sandra Horton and the North Carolina State University College of Veterinary Medicine histopathology laboratory for sample preparation, Heather Broadhurst for technical assistance in case management, and husbandry staff at the North Carolina Aquarium on Roanoke Island.

CONFLICT OF INTEREST
The authors have no conflicts of interest to report.
DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID
Ashlyn C. Heniff https://orcid.org/0000-0003-4569-0896
Craig A. Harms https://orcid.org/0000-0002-1262-9274
Keith E. Linder https://orcid.org/0000-0002-2970-2992

REFERENCES
Arismendi-Morillo, G. (2009). Electron microscopy morphology of the mitochondrial network in human cancer. The International Journal of Biochemistry & Cell Biology, 41(10), 2062-2068. https://doi.org/10.1016/j.biocel.2009.02.002
Bernstein, J. W. (1984). Leukaemic lymphosarcoma in a hatchery-reared rainbow trout, Salmo gairdneri Richardson. Journal of Fish Diseases, 7(1), 83–86. https://doi.org/10.1111/j.1365-2761.1984.tb00909.x
Blazer, V. S., & Schrank, C. S. (1995). Malignant lymphoma in black bullhead from Alouez Bay, Superior, Wisconsin, USA. Diseases of Aquatic Organisms, 23, 229–234. https://doi.org/10.3354/dao023229
Bowser, P. R., McCoy, C. P., & MacMillan, J. R. (1985). A lymphoproliferative disorder in a channel catfish, Ictalurus punctatus (Rafinesque). Journal of Fish Diseases, 8, 465–469. https://doi.org/10.1111/j.1365-2761.1985.tb01280.x
Carias, E., DeLorenzo, M., Owston, M., Gonzalez, O., Kumar, S., & Dick, E. J. Jr (2019). Cutaneous epitheliotropic lymphoma in a baboon (Papio spp.): A case report and a brief literature review. Journal of Medical Primatology, 48(3), 192–196. https://doi.org/10.1111/jmp.12410
Chen, H. C., Pan, I. J., Tu, W. J., Lin, W. H., Hong, C. C., & Britelli, M. R. (1996). Neoplastic response in Japanese medaka and channel catfish exposed to N-methyl-N’-nitro-N-nitosoguanidine. Toxicologic Pathology, 24(6), 696–776. https://doi.org/10.1177/019262339602400604
Coffee, L. L., Casey, J. W., & Bowser, P. R. (2013). Pathology of tumors in fish associated with retroviruses: A review. Veterinary Pathology, 50(3), 390–403. https://doi.org/10.1093/vp/50.3.390
Fontaine, J., Bovens, C., Bettenay, S., & Mueller, R. S. (2009). Canine cutaneous epitheliotropic T-cell lymphoma: A review. Veterinary and Comparative Oncology, 7(1), 1–14. https://doi.org/10.1111/j.1476-5829.2008.00176.x
Fontaine, J., Heimann, M., & Day, M. J. (2011). Cutaneous epitheliotropic T-cell lymphoma in the cat: A review of the literature and five new cases. Veterinary Dermatology, 22(5), 454–461. https://doi.org/10.1111/j.1365-3164.2011.00972.x
Haller, R. D., & Roberts, R. J. (1980). Dual neoplasia in a specimen of Sarotherodon spilurus spilurus (Günther) (= Tilapia spilurus). Journal of Fish Diseases, 3(1), 63–66. https://doi.org/10.1111/j.1365-2761.1980.tb00185.x
Hardman, M., & Page, L. M. (2003). 2003 Phylogenetic relationships among bullhead catfishes of the genus Ameiurus (Siluriformes: Ictaluridae). Copeia, 1, 20–33.
Hasbach, A. E., & Stern, A. W. (2016). Pagetoid reticulosis (epitheliotropic cutaneous T-cell lymphoma) in an adult alpaca (Vicugna pacos). Journal of Veterinary Diagnostic Investigation, 28(4), 469–472. https://doi.org/10.1177/1040638716645833
Higbie, C. T., Carpenter, J. W., Choudhary, S., DeBey, B., Bagladi-Swanson, M., & Eshar, D. (2015). Cutaneous epitheliotropic T-cell lymphoma with metastases in a Virginia opossum (Didelphis virginiana). Journal of Zoo and Wildlife Medicine, 46(2), 409–413. https://doi.org/10.1638/2014-0201R1.1
Honold, S. P., Arun, I., Saturday, G., & McLeod, C. (2007). Epitheliotropic lymphoma in a squirrel (Sciurus sp.). Journal of Zoo and Wildlife Medicine, 38(3), 479–482. https://doi.org/10.1638/06-055.1
Kieser, D., Kent, M. L., Groff, J. M., Mclean, W. E., & Bagshaw, J. (1991). An epizootic of an epitheliotropic lymphoblastic lymphoma in Coho salmon Oncorhynchus kisutch. Diseases of Aquatic Organisms, 11(1), 1–8.
Kuiper, R. V., Kimpfli, S., & Grinwis, G. C. (2009). Case report: Epitheliotropic lymphoma in a zebrafish (Danio rerio). Tijdschrift Voor Diergeneeskunde, 134(24), 1018–1020.
Nigrelli, R. F. (1947). Spontaneous neoplasms in fishes: Lymphosarcoma in Astyanax and Exon. Zoologica; Scientific Contributions of the New York Zoological Society, 32(9–12), 101–108.
Okihiro, M. S., & Hinton, D. E. (1989). Lymphoma in the japanese medaka (Oryzias latipes). Diseases of Aquatic Organisms, 7, 79–87. https://doi.org/10.3354/dao007079
Rook, K. A. (2019). Canine and feline cutaneous epitheliotropic lymphoma and cutaneous lymphocytosis. Veterinary Clinics of North America: Small Animal Practice, 49(1), 67–81. https://doi.org/10.1016/j.cvsm.2018.08.007
Skorinsky, I., Papadogiannakis, E., Horowitz, I., & Anug, A. M. (2008). Epitheliotropic cutaneous lymphoma (mycosis fungoides) in a coat. Journal of Small Animal Practice, 49(4), 204–207. https://doi.org/10.1111/j.1748-5827.2007.00472.x
Vergneau-Grosset, C., Nadeau, M. E., & Groff, J. M. (2017). Fish oncology: Diseases, diagnostics, and therapeutics. Veterinary Clinics of North America: Exotic Animal Practice, 20(1), 21–56. https://doi.org/10.1016/j.cvex.2016.07.002

How to cite this article: Heniff, A. C., Chen, L. R., Christiansen, E. F., Harms, C. A., Law, J. M., Legner, C., & Linder, K. E. (2022). Cutaneous epitheliotropic lymphosarcoma in a captive white catfish (Ameiurus catus Linnaeus). Journal of Fish Diseases, 45, 971–974. https://doi.org/10.1111/jfd.13625