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Spontaneous branchioblastoma in a koi carp

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Abstract. Gill neoplasia in fish is rare but has been reported in multiple elasmobranch and teleost species. Although more commonly a site of metastatic disease, primary neoplasms of the gill may occur, and both spontaneous and chemically induced tumors have been reported. Here we describe a spontaneous branchioblastoma in a koi carp (*Cyprinus rubrofuscus*) with no known history of chemical exposure. A soft-tissue mass on the inner surface of the dorsal opercular chamber appeared to originate from either a gill arch or a pseudobranch. Histologically, the mass was comprised of 3 well-differentiated cell types: blastemal cells, epithelial cells arranged in a lamellar fashion, and islands of cartilage resembling those present in gill filaments. To our knowledge, this is only the fourth case of spontaneous branchioblastoma recorded in koi.

Keywords: branchioblastoma; fish; koi; neoplasm.

The gills play a vital role in fish respiration, osmoregulation, and excretion of nitrogenous waste, facilitating the exchange of gases between the aquatic environment and the bloodstream. Macroscopically, the gills include 2 pseudobranches and 4 pairs of gill arches in teleosts, each arch possessing numerous filaments. The pseudobranch varies in size and prominence among species, yet appears to play an important role in immune response, pH balance, and cell proliferation and regeneration.[13]

The gill filaments—or primary lamellae—project into secondary lamellae, which increases the surface area for efficient oxygen uptake and carbon dioxide release.[17] Each gill filament is covered by a single epithelial cell layer, which contains specialized respiratory cells responsible for gas exchange, in addition to chloride cells, mononuclear inflammatory cells, eosinophilic granular cells, and mucous cells.[11,17,22] Gas exchange is facilitated by microvilli on the surface of epithelial cells—pavement cells—covering the vast majority of the lamellar surface.[11,17,22] A dense network of blood vessels is also described, supported by fish-specific pillar cells that prevent blood-filled capillaries from collapsing.[11,17]

Gill neoplasia is considered relatively rare in fish, with cases infrequently reported in both teleosts and elasmobranchs, although incidence is known to vary between different species and geographic locations.[1,3,4,8–10,16,19,20] Several types of tumors of the gills have been documented, including gill invasions by papillomas and adenomas, and secondary gill metastases in cases of adenocarcinomas and squamous cell carcinomas.[5,6,11,14,16,19] Thymic lymphoma with invasion of the gills was suspected in a gold crossback arowana (*Scleropages formosus*), eventually disrupting the gill anatomy.[8] In elasmobranchs, disseminated malignant lymphoma was histologically diagnosed in a bat ray (*Myliobatis californica*).[1] Primary neoplasia affecting the gills, although reported, remains scarce in the literature, limited to papillomas, squamous cell carcinomas, fibromas, chondromas, and branchioblastomas.[10]

Branchioblastomas consist of multiple cell types, including blastemal (or blast-type) cells with both mesenchymal and epithelial components, often resulting in the loss of normal gill architecture and function.[2] Understanding the intricate structure and function of the gill epithelium and lamellae is crucial for comprehending the impact of branchioblastoma on respiratory function in affected fish.

A privately owned, white longfin koi carp (*Cyprinus rubrofuscus*) of unknown age was presented for investigation of a fleshy growth within the dorsal opercular chamber. Because of its location, the mass was suspected to originate from the gill arch or pseudobranch, but thyroid proliferative lesions, such as goiter and hyperplasia, can often result in a fleshy mass protruding from the opercular cavity, and could not be ruled out. It is not known how long the mass had been growing, and the owner reported no history of chemical exposure. The fish had no clinical signs, and dyspnea was not reported. A healing superficial skin wound was present on the head of the fish, suspected secondary to minor self-trauma; no other clinical signs were reported or described by the submitting veterinarian. Unfortunately, post-operative information was not available, and long-lasting effects post intervention and survival time of the koi are unknown.

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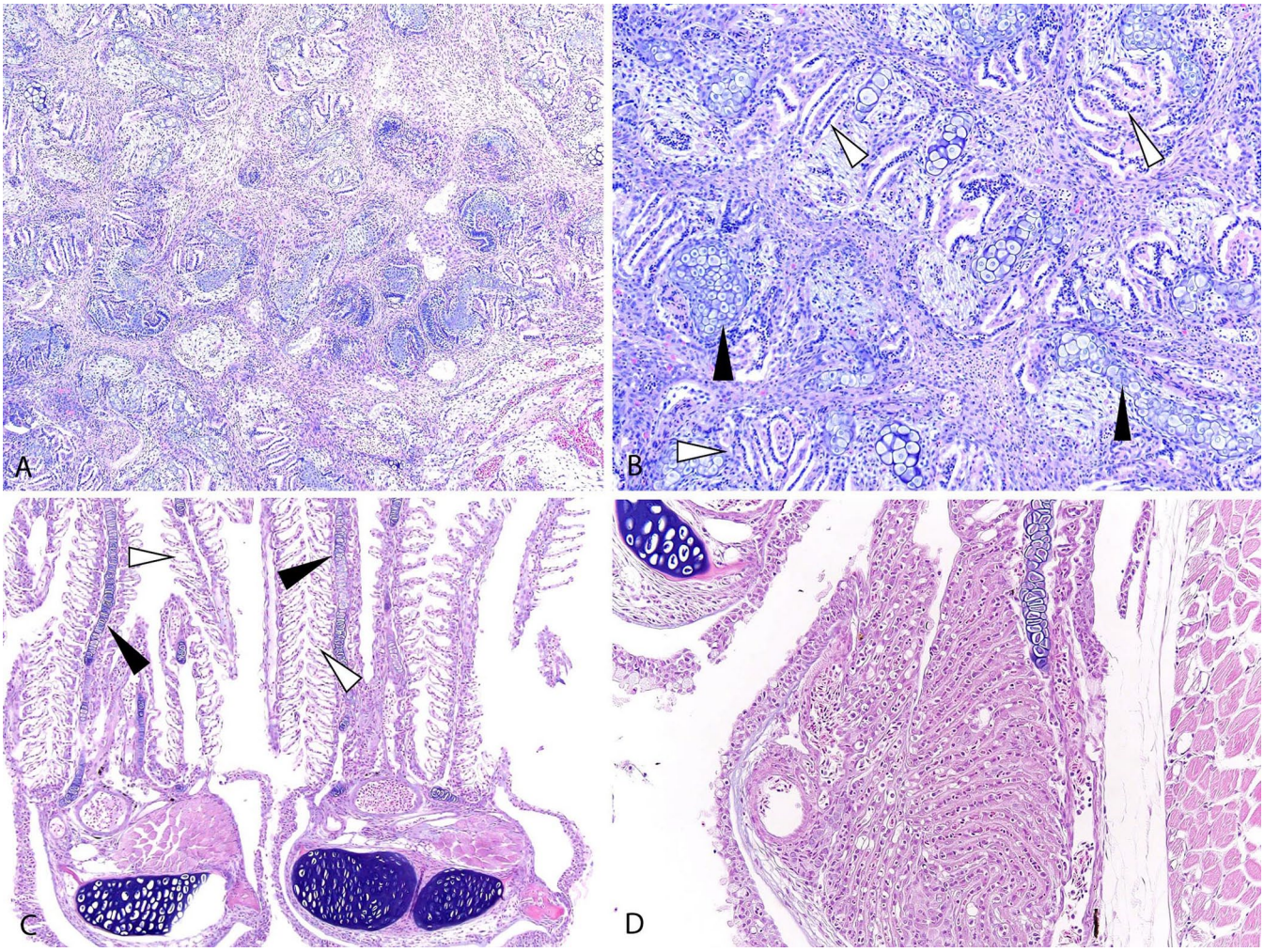

Figure 1. Histology of a branchioblastoma in a koi carp. **A, B.** Microscopic features including lamellar structures (black outlined arrowheads) and islands of cartilage (black arrowheads) consistent with a branchioblastoma. H&E. **C.** Histology of normal gill tissue including the presence of lamellae (black outlined arrowheads) that project from the gill filaments (black arrowheads). H&E. **D.** Histology of a normal pseudobranch. H&E.

Fish are prone to many causes of infectious diseases, and fungal or bacterial infections were considered primary differential diagnoses. Conversely, non-infectious causes such as spontaneous neoplastic changes remain rare but have been described in teleosts.[5,10,20] An incisional biopsy of the 13 × 7 × 6-mm mass was performed under anesthesia by the submitting veterinarian and submitted to the San Bernardino branch of the California Animal Health and Food Safety Laboratory System (CAHFS; University of California–Davis, Davis, CA, USA). The tissue specimen was fixed by immersion in 10% neutral-buffered formalin (pH 7.2) for ≥24 h. Samples were processed routinely to obtain 4-µm thick H&E-stained sections.

Histologic examination of the mass revealed an unencapsulated, expansile, densely cellular neoplasm with 3 distinct cell populations: polygonal-to-spindle basophilic blastemal cells, cuboidal-to-polygonal epithelial cells occasionally arranged in lamellar structures, and haphazardly arranged, well-differentiated islands of cartilage that resembled gill filaments (Fig. 1). Neoplastic cells had mild anisocytosis and anisokaryosis, a low mitotic count (2 mitoses/2.37 mm^2 area), and were supported by a moderate fibrovascular stroma (mitoses were noted in the blastemal or blast-type cells). Karyorrhectic debris and mixed mononuclear leukocytes, predominantly eosinophilic granulocytes and lymphocytes, were scattered throughout the mass. Histopathologic findings were consistent with a diagnosis of branchioblastoma.

Branchioblastomas are neoplastic proliferations of primitive, blast-like cells with the ability to differentiate into epithelial and mesenchymal cells.[10] Similar to other tumors of embryologic origin, including teratomas or nephroblastomas,

they include multiple cell types and structures. Histologically, these tumors typically have benign biologic behavior; however, given their location, significant disruption of gill function may occur.[10]

Branchioblastoma has been reported only sporadically in fish, and our review of the literature through Google, PubMed, Scopus, and Web of Science using the search terms "branchioblastoma" and "spontaneous gill neoplasia" revealed only 3 cases in koi carp.[10,21] Spontaneous branchioblastoma was first believed to be reported in a koi carp in 1995, characterized by irregularly shaped masses on the gill arches.[21] Histologically, the tumors originated from both the gill and pseudobranch filaments, and comprised irregular cartilage islands and poorly recognizable gill tissue.[21] Two further cases of spontaneously occurring branchioblastomas in koi carp have since been described.[10] In both cases, the neoplastic masses had the same 3 cell types described above, although the epithelial cells were arranged in lamellae structurally resembling normal branchial architecture.[10] Additionally, the islands of cartilage cells were found to be densely vascularized without infiltration of surrounding tissues.[10] In one fish, the neoplasm originated from the branchial arch, and in the other from the pseudobranch.[10] Spontaneous branchioblastomas have also been reported in a rainbow trout (*Oncorhynchus mykiss*) and a brown trout (*Salmo trutta*).[12]

In addition to spontaneous occurrences, exposure to certain irritants and toxins has been implicated in the development of branchioblastomas in fish. Toxicants and irritants can induce structural changes in fish gills; for example, histologic lesions consistent with severe inflammation, hyperplasia, and necrosis of gill tissue have been described in cutthroat trout (*Salmo clarki*) exposed chronically to the insecticide endrin.[6] Structural changes in gill tissues can subsequently result in neoplastic transformation.[11] Branchial neoplasms have been induced in medaka fish (*Oryzias latipes*) using N-methyl-N′-nitro-N-nitrosoguanidine (MNNG), a potent carcinogen.[2,20] Branchioblastomas have also been induced by MNNG in sun bass (*Morone saxatilis* × *Morone chrysops*), in which neoplastic cells extended into the lumen of the branchial blood vessels, likely leading to hematogenous spread in these animals.[10,18]

The presence of branchioblastomas in fish, whether spontaneous or induced by irritants/toxins, can significantly impact normal gill function.[5,10] Tumors may disrupt the delicate structure of the gills, impairing gas exchange and osmoregulation. This disruption can lead to respiratory and metabolic disturbances, compromising the overall health and survival of the affected fish.[10] Effects include reduced growth rates, decreased feed conversion efficiency, and increased susceptibility to secondary infections.[15] In aquaculture operations in regions where water pollutants are abundant, the increased risk of neoplasia (including branchioblastomas) in response to toxicants could contribute to decreased productivity, lower survival rates, and ultimately financial losses for fish farmers.[15]

Branchioblastomas can also highlight the presence of toxic chemicals in water sources, which may pose a risk if fish are sold for human consumption.[2,3,7,11] In turn, such potential health risks can negatively impact consumer confidence in the aquaculture industry, risking significant economic losses.[15] The prevalence and histopathology of branchioblastomas in Indian oil sardines (*Sardinella longiceps*) was studied extensively because of the commercial importance and economic value of this fish species in India.[15] These tumors had detrimental effects on fish health, which was correlated directly to losses in overall production.[15] The economic impact of this type of neoplasm in fish demonstrates the importance of disease surveillance, early detection, and effective management strategies to minimize its occurrence and mitigate the associated economic losses in the aquaculture sector.[15] Reducing the use of toxic irritants, such as environmental pollutants and carcinogens, is key to reducing fish exposure and therefore disease prevalence.

Care should be taken before breeding animals with a history of branchioblastoma and should be thoroughly evaluated as the genetic component of the disease is not well understood. In fact, genetic predisposition is possible in the development of certain neoplastic changes in fish, including branchioblastomas.[10]

Although koi carp may be highly valuable and their esthetic appearance is of high priority in show animals, the economic impact of branchioblastomas in this species is currently of low significance as cases appear to be sporadic and rare. However, these tumors can have important welfare implications for individual fish; although the fish in our case had no apparent respiratory disease, branchioblastomas have the potential to impair normal gill function. In addition, despite their histologically benign nature, branchioblastomas are often locally expansive and surgically difficult to remove and may therefore be associated with a poor long-term prognosis.

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