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Pathology in Practice

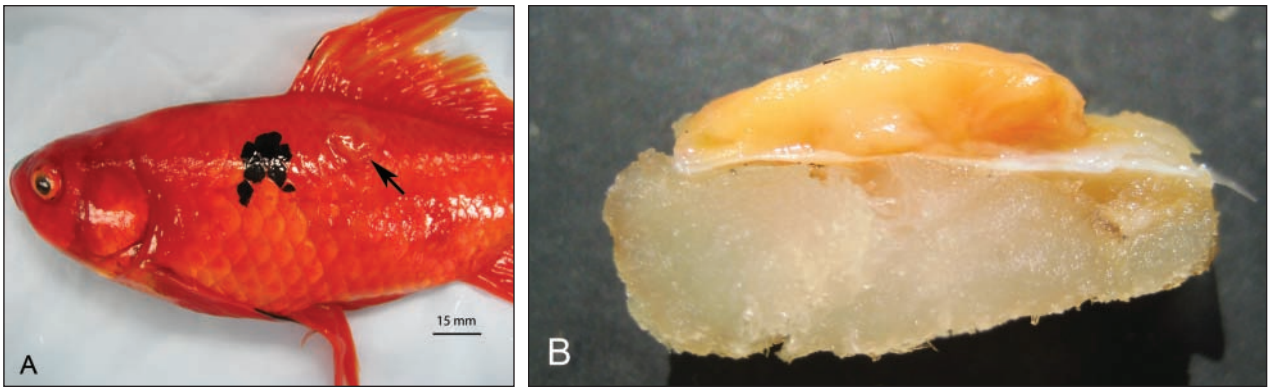

Figure 1—Photographs of a 14-mm-diameter mass in the skin of an otherwise normal approximately 8-year-old 115.2-g female Shubunkin goldfish from a privately owned ornamental goldfish pond. A—Gross appearance of mass ventral to the cranial end of the dorsal fin (arrow). B—Gross appearance of the cut surface of the mass after preservation in neutral-buffered 10% formalin.

History

A hobbyist reported a mass on an approximately 8-year-old Shubunkin goldfish from a 57,000-L ornamental goldfish and koi pond in Alabama. The mass was first noticed 5 months previously. It did not appear to be increasing in size over time. Of the other 80 to 100 fish present in the pond, none appeared to have the same type of mass. The owner requested that the cause of the mass be determined.

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Clinical and Gross Findings

Because the owner chose the option of a complete necropsy, the goldfish was transported back to the USDA Agricultural Research Service Aquatic Animal Health Research Unit. With the exception of the mass, the goldfish appeared clinically normal. It was euthanized by immersion in water containing tricaine methanesulfonate[a] (300 mg/L). Fish length excluding the caudal fin (ie, standard body length) was 15 cm, and body weight was 115.2 g (0.25 lb). Necropsy revealed that the fish was a gravid female. Other than the mass, the fish appeared grossly normal, both internally and externally. The skin mass was located on the left side approximately 1 cm below the cranial end of the dorsal fin. It was covered by scales with an uneven surface, well circumscribed, 14 mm in diameter, and slightly raised above the skin surface (**Figure 1**). On cut section, the mass was orange with a yellow center. It did not appear to penetrate the body wall but was loosely attached and was soft and friable when cut.

Formulate differential diagnosis from the history, clinical findings, and Figure 1—then turn page →

Microbiological and Histopathologic Findings

Following euthanasia, samples of the mass, gills, liver, stomach, heart, and cranial and caudal kidney were processed routinely and stained with H&E stain for histologic examination. An impression smear of a cut surface of the mass was stained with Gram stain for microscopic examination, which revealed no evidence of bacteria, fungi, or protozoa. Cultures on Mueller-Hinton agar and tryptic soy agar that had been streaked with a swab sample from the mass yielded no bacterial growth. By use of virus isolation techniques, samples of the mass were inoculated onto fish cell lines (eg, a koi fin cell line and an epithelioma papulosum cyprini cell line); cultures did not yield koi herpesvirus or spring viremia of carp virus. Samples of the mass were used for PCR assay[1] for koi herpesvirus (CyHV1-TKF/R1), and results were negative.

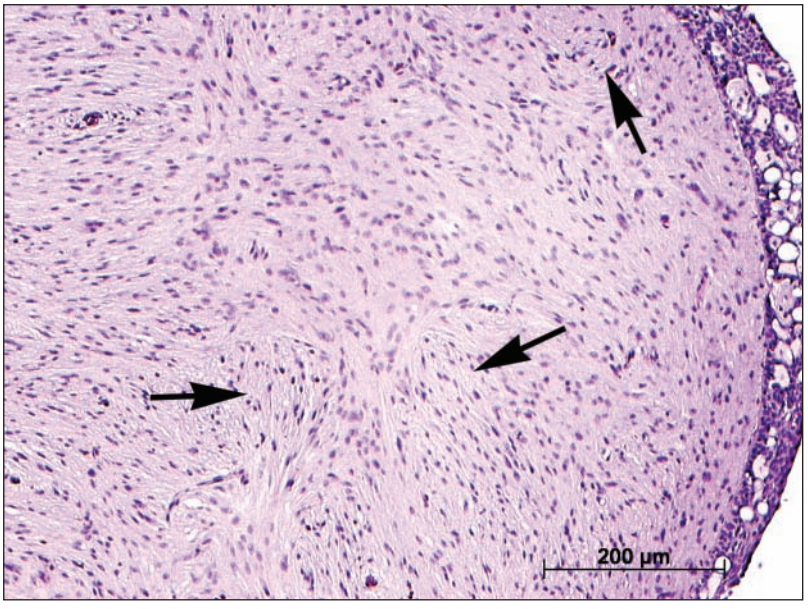

Figure 2—Photomicrograph of a section of the mass obtained from the fish in Figure 1. The tumor is oriented with the overlying epidermis to the right. Within the mass, there are periodic partial whorls and storiform bundles (arrows) of neoplastic cells, which are characteristic of an Antoni type A pattern. H&E stain; bar = 200 µm.

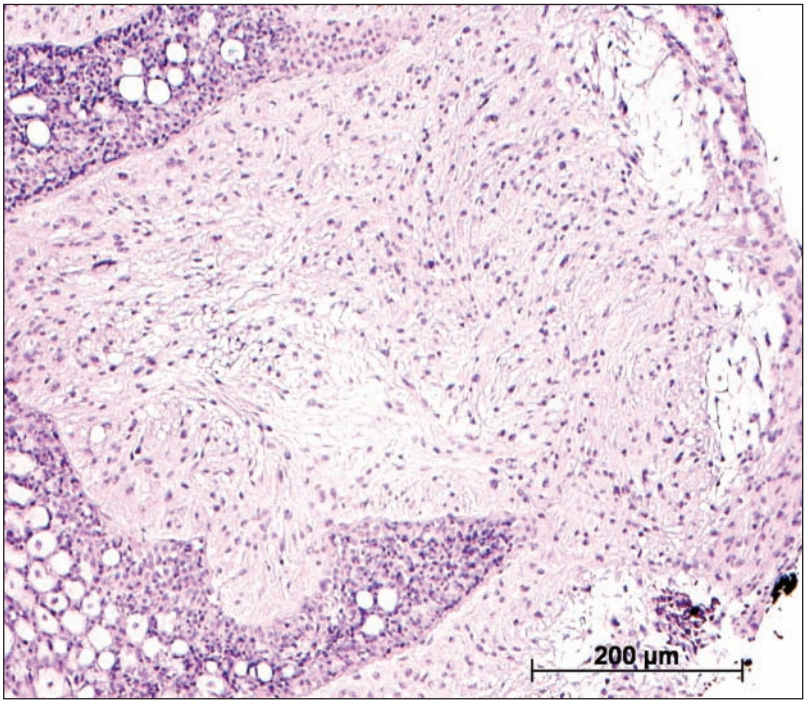

Figure 3—Photomicrograph of a section of the mass obtained from the fish in Figure 1. The mass also contained loose reticulated areas composed predominantly of stellate cells, which are characteristic of an Antoni type B pattern. Pegs of hyperplastic epidermis extend deep into the mass. H&E stain; bar = 200 µm.

Histologically, the gills, liver, stomach, heart, and cranial and caudal kidney were all considered normal. Microscopically, the neoplasm was covered with both hyperplastic and apparently normal epidermis, the former having papillary folds that were readily observed in some sectioned areas. Moderate numbers of mucous cells and alarm cells were present in hyperplastic epidermal regions. Within the mass, cell boundaries were indistinct, mitotic figures were uncommon, and the neoplastic tissue was poorly vascularized.

A key diagnostic feature of this neoplasm was the presence of Antoni type A and B tissue patterns, which are characteristic of nerve sheath tumor origin. Such patterns have been described previously in nerve sheath tumors (eg, schwannomas and neurofibromas) of other vertebrates.[2] In areas consistent with the Antoni type A pattern, the elongated, whorling, spindle-shaped neoplastic cells periodically formed storiform bundles (**Figure 2**) with subtle nuclear palisading. The tumor cells in these regions were separated by a finely fibrillar collagenous matrix. Conversely, in areas consistent with the Antoni B pattern, irregularly arranged stellate cells with rounded nuclei were embedded in an abundant myxoid matrix (**Figure 3**); such areas were less prominent than those with type A pattern.

Morphologic Diagnosis

Benign peripheral nerve sheath tumor (PNST).

Comments

Peripheral nerve sheath tumors are neoplasms that originate from neural crest cells and generally develop along the subcutaneous nerves.[3] In fish and other vertebrates, benign PNSTs have been classified as schwannomas or neurofibromas, which can be difficult to distinguish from one another in standard histologic sections. Both

tumor types usually appear as masses on the head, skin, or fins.[4] The chief cellular component of neurofibromas and schwannomas is the Schwann cell, which is a variety of glial cell that provides myelin insulation to axons in the peripheral nervous system of jawed vertebrates. Diagnostically, PNSTs need to be distinguished from pigment cell tumors (eg, erythrophoromas, xanthophoromas, melanomas, and guanophoromas) that also originate from neural crest cells, in addition to neoplasms derived from collagen-producing cells (ie, fibromas and fibrosarcomas).[5–7] Although the histologic patterns known as Antoni type A and B are highly suggestive of schwannoma,[2] these patterns can also be found in pigment cell tumors; however, the absence of cytoplasmic pigment granules, as in the fish of this report, is more compatible with a PNST diagnosis. The immunohistochemical markers S-100 and calretinin have also been used to differentiate schwannomas from other neoplasms in fish.[4,8]

Schwannomas have been detected in many fish species, including goldfish, several species of snapper, coho salmon, the bicolor damselfish, and rainbow smelt. Schwannomas are usually benign, except in damselfish and zebrafish, but they can also be locally invasive and progressive.[4,9] Because multiple fish have been affected in some populations, a viral cause of fish PNSTs has been proposed. However, the bicolor damselfish is the only species for which a virus-like agent has been associated with a type of PNST (neurofibroma).[10]

Peripheral nerve sheath tumors can be removed, either by excision or cryosurgery. However, hemorrhage is more likely with excision than with cryosurgery; recurrence is more likely after excision than after cryosurgery because freezing allows for more complete removal of tumor cells.[11,12]

a. MS-222, Argent Chemical Laboratories Inc, Redmond, Wash.

References

1. Hanson LA, Rudis MR, Vasquez-Lee M, et al. A broadly applicable method to characterize large DNA viruses and adenoviruses based on the DNA polymerase gene. *Virol J* 2006;3:28.
2. Wippold FJ II, Lubner M, Perrin RJ, et al. Neuropathology for the neuroradiologist: Antoni A and Antoni B tissue patterns. *AJNR Am J Neuroradiol* 2007;28:1633–1638.
3. Schlumberger HG. Nerve sheath tumors in an isolated goldfish population. *Cancer Res* 1952;12:890–899.
4. Marino F, Germana A, Panebianco A. A case of schwannoma in farmed seabream *Sparus aurata*. *Dis Aquat Org* 2008;82:249–252.
5. Duncan TE, Harkin JC. Electron microscopic studies of goldfish tumors previously termed neurofibromas and schwannomas. *Am J Pathol* 1969;55:191–202.
6. Clyde VL, Schultze AE, Donnell R. What is your diagnosis? Body wall mass from a goldfish. *Vet Clin Pathol* 1995;24:28–29.
7. Harshbarger JC. Neoplasia and developmental anomalies. In: Wildgoose WH, ed. *BSAVA manual of ornamental fish*. 2nd ed. Quedgeley, Gloucester, England: British Small Animal Veterinary Association, 2001;219–224.
8. Marino F, Germana A, Bambir S, et al. Calretinin and S-100 expression in goldfish schwannoma. *J Fish Dis* 2007;30:251–253.
9. Zhang GJ, Hoersch S, Amsterdam A, et al. Highly aneuploid zebrafish malignant peripheral nerve sheath tumors have genetic alterations similar to human cancers. *Proc Nat Acad Sci U S A* 2010;107:16940–16945.
10. Schmale MC, Gibbs PDL, Campbell CE. A virus-like agent associated with neurofibromatosis in damselfish. *Dis Aquat Org* 2002;49:107-115.
11. Johnson DH, Lane SL. Cryosurgery versus excision for removal of peripheral nerve sheath tumors in goldfish. *Exot DVM* 2007;9:14–16.
12. Miller SM. Surgical excision of a Schwannoma in a buffalo sculpin. *Exot DVM* 2000;2:41–43.