Progress in Experimental Tumor Research
Publisher: S. Karger, Basel
Represent (Printed in Switzerland)

Prog exp Tumor Res., vol. 23, pp. 113-128 (Karger, Basel 1976)

Variably Differentiating Oral Neoplasms, Ranging from Epidermal Papilloma to Odontogenic Ameloblastoma, in Cunners (Tautogolabrus adspersus) Ostéichthyes; Perciformes: Labridae

J.C. HARWOOD, S.E. SHUMWAY and G.W. BANE
Registry of Tumors in Lower Animals, National Museum of Natural History, Smithsonian Institution, Washington, D.C.; Marine Science Laboratories, University College, North Wales, Menai Bridge, Anglesey; Marine Science Project, University of North Carolina, Wilmington, N.C.

Five hundred cunners, Tautogolabrus adspersus, an omnivorous coastal fish ranging from Newfoundland to Virginia, were collected with rod and reel from the Sakonnet River at Portsmouth, Rhode Island, for a survey of their biology and food habits [22]. Nine (1.8%) of the specimens had abnormal growths protruding from the mouth: Four of the nine growths were examined histologically and all four were found to be neoplasms. Subsequently, three more cunners with oral protrusions were collected from the same area and histologically examined: Two of the lesions were neoplastic and one was parasitic. The material from three seven cases has been accessioned into the permanent collection of the Registry of Tumors in Lower Animals (RTLA), The Smithsonian Institution, Washington, D.C.

Oral neoplasms have been recorded in 26 species of bony fish, usually manifested as papillomas and carcinomas of the lip epidermis and oral mucosa, as shown in table II. Neoplasms in close proximity to the mouth, but apparently arising from the skin of the upper or lower jaws, were excluded from the tabulation.

Normally, bony fish have conical, recurved, anklylosed teeth which fall out and are regenerated regularly. Normal tooth formation has not been studied in cunners, but in most respects tooth development in bony fish conforms to the generalized pattern for mammals. Initially in the formation of a fish tooth, a peg of oral epithelium, consisting of a basal layer (dental
<table>
<thead>
<tr>
<th>Species</th>
<th>Number</th>
<th>Diagnosis</th>
<th>First report</th>
<th>Selected other reports</th>
<th>STL A</th>
<th>Contributor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acanthogobius fluvianus</td>
<td></td>
<td>epidermal papilloma</td>
<td>[13]</td>
<td>[6, 7]</td>
<td>58</td>
<td>Ito</td>
</tr>
<tr>
<td>Alosa sapidus</td>
<td>1</td>
<td>epidermal papilloma</td>
<td>[18]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anguilla anguilla</td>
<td>3</td>
<td>epidermal papilloma</td>
<td>[25]</td>
<td>[3, 21]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anabas argenteus</td>
<td>several</td>
<td>epidermal papilloma</td>
<td>[12]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barbodes fluviatilis</td>
<td>1</td>
<td>papillary epithelium</td>
<td>[8]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barbodes vulturis</td>
<td>1</td>
<td>epidermoid carcinoma</td>
<td>[26]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceratobrama aurata</td>
<td></td>
<td>epidermal papilloma</td>
<td>[18]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cotropoma lutia</td>
<td>several</td>
<td>epidermal papilloma</td>
<td>[12]</td>
<td>[5, 6, 14, 27]</td>
<td>62</td>
<td>Harschbauger</td>
</tr>
<tr>
<td>Gobionichthys lineatus</td>
<td>masty</td>
<td>epidermal papilloma</td>
<td>[17]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ictalurus catas</td>
<td>1</td>
<td>papillary epithelium</td>
<td>[11]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ictalurus melas</td>
<td>1</td>
<td>neurofibroma</td>
<td>[5]</td>
<td>[5, 6]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ictalurus natalis</td>
<td>1</td>
<td>epidermal papilloma</td>
<td>[6]</td>
<td>682</td>
<td></td>
<td>Gains</td>
</tr>
<tr>
<td>Ictalurus natalis</td>
<td>1</td>
<td>epidermal papilloma</td>
<td>[6]</td>
<td>449</td>
<td></td>
<td>Combs</td>
</tr>
<tr>
<td>Ictalurus natalis</td>
<td>266</td>
<td>epidermal papilloma</td>
<td>[10, 20]</td>
<td>[5, 6]</td>
<td>288, 328</td>
<td>Combs</td>
</tr>
<tr>
<td>Macrognathus americana</td>
<td>1</td>
<td>epidermal papilloma</td>
<td>[6]</td>
<td>922</td>
<td></td>
<td>Wolfe</td>
</tr>
<tr>
<td>Malagocentrus electros</td>
<td>1</td>
<td>epithelidoma</td>
<td>[6]</td>
<td>760</td>
<td></td>
<td>Papena</td>
</tr>
<tr>
<td>Osmerus arienta</td>
<td>37</td>
<td>papillary epithelium</td>
<td>[2]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pteroglyphus scalaris</td>
<td>1</td>
<td>fibropapillomatous</td>
<td>[6]</td>
<td>972</td>
<td></td>
<td>Hink</td>
</tr>
<tr>
<td>Taeniostoma adspersus</td>
<td>2</td>
<td>epidermal papilloma</td>
<td>[6]</td>
<td>553</td>
<td></td>
<td>Shumway</td>
</tr>
<tr>
<td>Trachurus trachurus</td>
<td>2</td>
<td>papillary epithelium</td>
<td>[4]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(lamini) enclosing epithelium modified to form the stellate reticulum, grows into the underlying connective tissue. The terminal apex enlarges into a fungiform tooth bud and invaginates through a succession of stages (cap, bell and appositional) to form the enamel organ. Ameloblasts at the tip of the enamel organ induce connective tissue cells inside the "bell" to differentiate into an odontogenic pulp bounded by a layer of dentin-secreting odontoblasts (fig. 1). Finally, the crown of the new tooth erupts through the surface.
Table II Dental neoplasms in boys 6 yr.

<table>
<thead>
<tr>
<th>Species</th>
<th>Number</th>
<th>Diagnosis</th>
<th>First report</th>
<th>Other reports</th>
<th>RTLA No.</th>
<th>Contributor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caprionum variiceps</td>
<td>1</td>
<td>ameloblastoma</td>
<td>[23]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Melanomaculatus</td>
<td>1</td>
<td>ameloblastoma</td>
<td>[24*]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microcyclus hypercercus</td>
<td>1</td>
<td>odontoma</td>
<td>[60]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthokeratoara</td>
<td>2</td>
<td>fibroameloblastoma</td>
<td>[19] [6]</td>
<td>348</td>
<td>Waker</td>
<td></td>
</tr>
<tr>
<td>Salivinus fontinalis</td>
<td>2</td>
<td>odontoma</td>
<td>[15]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trivagriostoma adspersus</td>
<td>4</td>
<td>ameloblastoma and ameloblastic</td>
<td>[6]</td>
<td>590-7, SiVakay</td>
<td></td>
<td>675, 921</td>
</tr>
<tr>
<td></td>
<td></td>
<td>odontoma</td>
<td></td>
<td></td>
<td>Bange</td>
<td></td>
</tr>
</tbody>
</table>

Case Reports

Case I (RTLA 553): The gross specimen was a 3-year-old adult of undetermined sex, 16.5 cm in total length. It had a firm, white growth attached to the left side of the palate. The growth extended outward, involving the dorsal lip, which was forced to curl upward (fig. 2). Dimensions of the growth were: lateral and longitudinal, 6 mm; vertical, 4 mm. Microscopically, the lesion was composed of pegs of dense squamous epithelium interspersed with well vasculatureed connective tissue papillae. One to several rows of columnar cells were marked the margins of the pegs and there was no evidence of invasion. The typical protruding epithelial cells were smaller, more basophilic, and exhibited more mitoses than cells of nearby normal skin, and in contrast to the normal skin, mitosis were not present. No differentiation toward dentin tissue was observed and the lesion was interpreted as an epidermal papilloma.

Case II (RTLA 556): The gross specimen was a 3-year-old adult male approximately 8 cm in total length. It had a soft, white, slightly oval growth inside the mouth attached to the roof (fig. 3). Dimensions of the growth were: lateral, 4 mm; longitudinal, 3 mm; vertical, 2 mm. Microscopically, the growth contained medium-to-long pegs of squamous epithelium separated by connective tissue papillae and in some cases extended to the surface. The growth was underlain with collagenous connective tissue and bone. There was no distinct basal layer boundary visible in the surface epithelial pegs and connective tissue fibers intermingled with the deeper epithelial cells. A few pegs presented the spiky appearance of dental lamina. Columnar epithelial cells along the apical margin of some of these pegs had nuclei polarized away from the surface and had cytoplasmic plaques, ‘Tzone’ processes, separating them from the stroma (fig. 4). Both of these characteristics typify ameloblastoma. One structure comparable to an enamel organ was observed. The pegs extended deeply to the bone, suggesting local invasion. Due to the fact that ameloblastic
Fig. 1. Appositional stage of normal developing tooth in a bony fish. a = Ameloblasts; p = pulp; o = odontoblasts; d = dentin.

Fig. 2. Case 1: Epidermal papilloma in the open mouth.
**Fig. 3.** Case II: Early ameloblastoma in roof of mouth.

**Fig. 4.** Case II: Tomes' processes (arrow) at the edge of a dental lamina. ×370.
Fig. 5. Case III: Ameloblastoma in left lower jaw.
Fig. 6. Case III: Plexiform pattern. ×150.
differential was occurring in multiple areas, the growth was interpreted as showing ameloblastic change within a plaque of epithelial papillomatosus.

Case III (RTL A 555): The gross specimen was a 3-year-old, adult female, 12 cm in total length. It had a white, papillary growth 1 cm in diameter involving the left inside of the lower jaw and the lower left lip (fig. 5). Dimensions of the growth were: lateral, 7 mm; longitudinal, 10 mm; vertical, 5 mm. Microscopically, the growth was composed of long, double strands of ameloblastic epithelium in a branching arborial pattern embedded in a spongy, well-vascularized, fibrous stroma (fig. 6). Cells of the stellite reticulum were enclosed within the double cords of some of the strands. General change suggested that odontogenic tissue was beginning to differentiate in several localized areas, but most of the connective tissue had the normal spindle cell pattern. The lesion interpreted as an odontoma having a plasma form pattern.

Case IV (RTL A 551): The gross specimen was a 3-year-old, adult male, 11.5 cm in total length. It had a firm, white growth attached to the roof of the mouth causing the upper lip to curl upward (fig. 7). Dimensions of the growth were: lateral, 8 mm; longitudinal, 6 mm; vertical, 6 mm. Microscopically, the growth was characterized by long, flagellum-like pags of both epithelial and ameloblastic epithelium radiating 180 degrees from the point of attachment and interpenetrating with well vascularized fibrous papillae that extended to the surface (fig. 8). The ameloblastic cells were tall columnar cells with nuclei polarized away from the basement membrane. Some fibrous cells in close proximity to the ameloblasts had taken on the shortened basophilic appearance of odontogenic pulp cells (fig. 9). However, well differentiated odontoblasts were not present and dentin had not been produced. Some areas of the tumor exhibited a folicular pattern and a few of the follicles contained bone. The epithelial pags appeared locally invasive as they extended through the fibrous stroma to the maxillary bone. The growth was interpreted as an ameloblastic odontoma with both papillary and folicular patterns.

Case V (RTL A 675): The gross specimen was an adult of undetermined sex, 12 cm in total length. It had a firm, yellowish-white growth arising in the maxillodental area which extended caudally into the oral chamber and cephalad through the mouth opening, causing the dental lip to curl upward (fig. 10). Dimensions of the growth were: lateral, 30 mm; longitudinal, 9 mm; vertical, 4 mm. Microscopically, the bulk of the growth was composed of large, irregularly-shaped, epithelial cords separated from each other by a thin, fibrous stroma (fig. 11). The cords had multiple finger-like infoldings, each with a median rib of connective tissue continuous with the stroma. The epithelial cells adjacent to this rib were ameloblastic in reactivity and those further away resembled stellite reticulum cells. The connective tissue rib had differentiated into odontogenic pulp tissue bordered by a single row of dentin-producing odontoblasts (fig. 12). A smaller area of the tumor, somewhat similar to case III, was composed of interdigitating double cords of ameloblastic epithelium interposed with a thin, highly vascularized, fibrous stroma. "Tomes' processes" were conspicuous on the outer layer of cells lining the cords, and stellite reticulum cells occupied the interior of the cord. Some odontogenic differentiation had occurred and one incomplete and malformed tooth was present (fig. 13). The growth was interpreted as an ameloblastic compound odontoma.

Case VI (RTL A 923): The gross specimen was a 3-year-old adult of undetermined sex, 7.5 cm in total length. It had a firm, creamy-white, slightly granular growth attached to the upper jaw and or (fig. 14). Dimensions of the growth were: lateral, longitudinal and vertical,
Fig. 7. Case IV: Ameloblastic odontoma attached to roof of mouth, deflected upper lip.

Fig. 8. Case IV: Histologic overview. ×24.
Fig. 9. Case IV: Odontogenic pulp (p) between dental lamina composed of ameloblasts (a) enrobing enamel rods (e). × 70X.

Fig. 10. Case V: Ameloblastic compound odontoma attached to fossa dental surface of mouth. Cut-away view.
Fig. 11. Case V: Irregular epithelial cysts separated by thin fibrous stroma. Finger-like ingrowths having ovals (arrows) of pulp-like connective tissue are continuous with the thin fibrous stroma. ×80.

Fig. 12. Case V: Higher magnification of a dental dentin from figure 11. p = pulp; o = odontoblasts; d = dentin; a = ameloblasts. ×140.
Fig. 13. Case V: Plexiform area to the left; Malformed denticle to the right (arrow).

Fig. 14. Case VI: Well differentiated compound odontoma deflecting upper lip.
Fig. 15. Case VI: Large fibrous component (f), patches of dentin (d), dental papillae (right arrow), and malformed denticle (left arrow). × 60.

Fig. 16. Case VI: Cleft in bone (b) cut by invading neoplasm. Two malformed teeth (arrows). × 60.
Fig. 17. Case VII: Parastic granuloma inside mouth.

Fig. 18. Case VII: Trematode metacercaria in a dense fibrous capsule. × 190.
3.4 mm. Microscopically, the tumor was composed of randomly distributed islands and papillae of various dental elements within a large, dense, fibrous stroma (fig. 15). The dental elements included areas of ameloblastic and odontogenic tissues. In several areas, apparently isolated odontoblasts produced patches of dentin. Five poorly formed replicas (denticles) of complete teeth were present at the level studied. Molars were easily found, but not identified. A large cleft had been produced in the mandibular bone by invading tumor cells (fig. 16). The tumor was interpreted as a well differentiated compound odontoma.

Case VII (RTLA 790): The gross specimen was an adult of undetermined sex, 13.5 cm in total length. It had a small, firm, white growth in the maxillotemporal area (fig. 17). Dimensions of the growth were: lateral and longitudinal, 3 mm; vertical, 2 mm. Microscopically, dense fibrous capsule containing trematode metacercariae distorted the overlying skin (fig. 18). The lesion was interpreted as a multifocal parasitic granuloma.

Discussion

This report describes the largest collection of odontogenic neoplasms known from a particular species of fish or from a single geographic location. Each case shows a limited range of morphologic variation and, as a group, the six cases illustrate a spectrum of differentiation in oral neoplasms, ranging from no differentiation of tooth tissues to differentiation of all tooth elements, as follows: case I - no recognizable tooth elements; case II - early ameloblastic differentiation; case III - characteristic ameloblastic and very early odontogenic differentiation; case IV - ameloblasts and significant odontogenic pulp; case V - ameloblasts and odontoblasts with dentin production; case VI - all tooth elements, including numerous incomplete and malformed teeth.

The cause of these tumors is unknown, but a combination of factors is probably involved. Cunners feed on the bottom where one would expect chemical and viral carcinogens to accumulate. Their diet is mostly composed of abrasive types of food such as barnacles and clams, which could injure the mouth area and allow intimate contact with carcinogenic agents that might be present. Data from other fish tumor studies also indicate that abrasion can be a factor [9, 14]. The point of the hypothesized abrasion would be the site for tumor development, which would explain why the growth just described occurred on either jaw and arose from both lips and oral mucosa.

Trematode parasites, similar to the ones causing the pseudotumor in case VII, were seen in slides from the jaws in two of the specimens with neoplasms. In addition, randomly distributed intergumentary black spots, presumed to be the well known black spot disease of trematode etiology, were
seen in several of the cases. However, the presence of these parasites is considered incidental to the neoplasms.

The fact that cunners seem to be quite sensitive to some agent(s) that can induce tumors suggests that these fish may be useful in developing a model for studying neoplasms of dental origin.

References

2. Breitlacker, T.: Zur Kenntnis der Epidermoidschwellungen von Käthluren. Histologi- 
   logische Veränderungen des Inzimums und der Mundschleimhaut beim Schild- 
3. Denis, B. F.: Atlantic sea and calthiflower disease; in Homburger Tumors in aquatic 
   animals, Prog. exp. Tumor Res., vol. 20, pp. 94-100 (Karger, Basel 1976).
4. Führkr, J.: Über Hautgeschwülste bei Fischen nebst Bemerkungen über die Pocken- 
   krankheit der Karpfen. Z. Krebsforsch. 5: 163-179 (1900).
5. Hasebrügger, J. C.: Work of the Registry of Tumors in Lower Animals with 
   emphasis on fish neoplasms; in Womkleay-Thomas Diseases of Fsh. Symh. of The 
7. Ito, Y.; Komura, I., and Miyake, T.: Histopathological and virological investiga-
   tions of papillomas in sole and goby in coastal waters of Japan; in Homburger 
   Tumors in aquatic animals, Prog. exp. Tumor Res., vol. 20, pp. 86-93 (Karger, 
   (1900).
   Adenomatous polyps in the urogenital tract of breyer's salmonids and other types of 
   fishes; in Homburger Tumors in aquatic animals, Prog. exp. Tumor Res., vol. 20, 
10. Lucke, B. and Hasebrügger, J.: Transplantable epithelomas of the lip and mouth 
    of catfish. J. Pathol. Transplantation to superior chamber of eye and into cornea. 
    J. exp. Med. 74/5: 397-488 (1941).
    (1952).
    (1952).
    lineatum (white croaker): Tumoral considerations; in Homburger Tumors in 


Dr. J.C. HAMBROOKER, Director, Registry of Tumors in Lower Animals, Museum of Natural History, The Smithsonian Institution, Washington, DC 20560 (USA)
21 Schwanz-Fitzner, I.: Further studies of cell virus (Berlin) isolated from the blood of trout (Salmo fario) with skin papillomas; in Homburg. T. Tumors in aquatic animals, Prog. exp. Tumor Res., vol. 30, pp. 101-107 (Karger, Basel 1976).

Dr. J.C. Harshberger, Director, Registry of Tumors in Lower Animals, Museum of Natural History, The Smithsonian Institution, Washington, DC 20560 (USA)