



INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

STUDY OF TUMORS IN FISH AND ITS IMPORTANCE IN CANCER RESEARCH

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Abstract-

Although comparative oncologists two decades ago may have tended to be on the defensive when arguing that fish, which are water-dwelling, poikilothermic vertebrates of greatly diverse form, might be of interest to cancer investigators, justification of their use no longer seems necessary. As testified by the increasing number of publications on fish tumors appearing in international journals, various fish species have now become widely accepted as useful tools for cancer research with, in some cases, distinct advantages over models using rodents or avian species. In particular, the study of tumors in lower aquatic animals has recently gained considerable importance as a means of detecting injurious agents in the environment. Investigation of fish tumors is also integral part of the basic biological approach to understanding possible common mechanisms involved in cancer development at various phylogenetic levels. The finding that tumors can be readily induced at various sites in fish species by different chemical carcinogens or viruses was of central significance in this context. Also if such fish is eaten by humans what are the possibilities of effect of such fishes can be further studied.

Introduction-

Since the turn of the century there has been a massive accumulation of information affirming that neoplasms occur in non-mammalian species and that they often bear a striking resemblance to those arising in man. In searching for tumors in fish, efforts have been naturally directed to fish markets, public aquariums, private ponds and hatcheries, and early contributions have been comprehensively reviewed and discussed by (Schlumberger and Lucké, Wellings) and (Mawdesley-Thomas). However, a more systematic world-wide contribution is provided by the Registry of Tumors in Lower Animals (RTL A) at the Smithsonian Institution, started by (Clyde J. Dawe and John C. Harshbarger) in 1965. The registry specializes in neoplasms of subhomeothermic animals from all parts of the world and is responsible for documenting discovery, generating opinions on the nature and significance of lesions and preserving material for future use. The RTL A makes about 200 accessions per year and distributes activity reports to interested investigators. Over the past 20 years, tumors appearing in bony fish have been by far the most common (51%), with tumors in cartilaginous fish being in comparison rather rare (7%). Although the etiology is unknown for the most part, tumors were often found in clusters in the same species of family of bony fish and as will be mentioned below, some cases may be described to genetic factors, viruses and chemical contaminants in the water or food.

Characteristics of Fish Tumors-

1. Pathomorphology –

Regarding the comparability of neoplasms in fish with those in man and other mammals, similarities and differences in general biological and morphological features require discussion. The structures of some normal fish tissues are considerably different from those of mammals. For instance, the typical lobular structure of mammalian liver is not a feature of fish liver tissue, which consists of sheetlike arrangements of parenchymal cells with interlacing sinusoids and a few bile ducts. Histologically, however, tumors in fish do not generally differ markedly from equivalent mammalian tumors, and this enables the comparative oncologist to classify fish tumors on much the same bases as tumors in mammals. For example, various types of liver neoplasms develop which can be classified as trabecular hepatocellular carcinomas, poorly differentiated hepatocellular carcinomas, cholangiocellular carcinomas, etc. Although fish ovarian tumors are diverse and exhibit great variation, they are mainly composed of similar cells to those observed in human dysgerminomas, granulosa-theca cell tumors or embryonal carcinomas, suggesting a range of histogenetic origins. Further more seminomas in fish are composed of typical germ cells similar to those in human seminomas or embryonal carcinomas. However, it must be borne in mind, as already pointed out by (Dawe and Harshbarger) that diagnostic names are no substitute for a detailed knowledge of the individual biological features of a particular neoplasm in a particular species. Histologically, only a few fish neoplasms can be classified as renal adenocarcinomas equivalent to those developing in adult humans (Grawitz tumor). Other examples where fish neoplasms differ from those observed in man include the erythrophoromas or iridophoromas, peculiar pigment cell neoplasms which do not exist in mammals. Several descriptions of either spontaneous Or induced tumors of the swim bladder, which is the fish counterpart of mammalian lung, have appeared. However, the lesions were papilloma-like growths or sarcomas, histologically quite different from mammalian lung tumors. Epithelial neoplasms can also be induced in the gills, the functional equivalent of the mammalian lung. The examples above suggest that the types of neoplasms which develop in either fish or mammals purely reflect the range of normal cells possessed. Virtually all of the major organs and cell types have been observed to give rise to neoplasms in a wide range of fishes with the notable exception of brain tumors. There are as yet no reports of fish intracranial tumors which are histopathologically equivalent to brain tumors such as gliomas in man The fact that fish lack the well-developed neopallial cortex which constitutes the largest portion of the brain in higher mammals may be an important factor in this context. Phylogenetically, a thymus first appeared in jawless fish (lamprey and hagfish) and fish possess a more highly evolved antibody-forming capacity.

2. Tumorigenesis -

Temperature seems to be an important factor in tumorigenesis in poikilothermic animals. For example renal tumors (Lucké tumors) in the leopard frog (*Rana pipiens*) are known to be sensitive to environmental temperature, with seasonal changes being described to temperature dependent viral activation. Although no such examples are known for fish neoplasia, chemical carcinogenesis studies have demonstrated that tumors appear later and their growth is retarded when the temperature is low. A number of reports have indicated that different species of fish differ greatly with regard to spontaneous tumor incidence or susceptibility to chemical carcinogens. For example, different varieties of salmonid fish show wide variation in their response to aflatoxins.²⁴ Two aspects may be of particular relevance to such inter-species variation. Firstly, the high susceptibilities of some species might be related to a high capacity for specific carcinogen metabolism and a correspondingly high rate of DNA modification. Comparative biochemical studies on the metabolism of carcinogens in various species give us clues for the solution of this problem in general. Secondly, species differences could be due to some genetic resistance or proneness to cancer unrelated to carcinogen activation. Several factors might be involved, including the DNA repair systems, which are thought to play an important role in the initial steps of neoplastic development.

3. Chemical Contaminants and Fish Tumors

The study of neoplasms in lower aquatic animals is useful for detecting injurious factors in the environment. The accumulating evidence demonstrates that wild fish taken from contaminated waters present with a variety of preneoplastic and neoplastic lesions. Prior to 1965, liver tumors were reported to be rare in feral fish. More recently, however, hepatomas (adenomas, hepatocarcinomas, cholangiocarcinomas) have been found at high incidence in English sole (*Pleuronectes vetulus*) and in winter flounder (*Pleuronectes americanus*) from Boston Harbor associated with increased levels of sediment contamination (including carcinogens). A similar range of lesions has been described in brown bullhead (*Ictalurus nebulosus*) living in rivers entering Lake Erie and white perch. These hepatic neoplasms or preneoplastic lesions have been observed in bottom-dwelling fish inhabiting areas where sediments are known to contain toxic and potentially carcinogenic chemicals. Thus, (Malins et al. found a strong association between hepatic lesions in English sole and polycyclic aromatic hydrocarbons (PAHs). Hendricks et

a). further demonstrated that the PAH carcinogen benzo[a]pyrene is capable of producing hepatic neoplasms in rainbow trout (*Salmo gairdneri*). Liver tumors were also induced by benzopyrene and 7,12-dimethylbenzanthracene in medaka by (Hawkins et al.) In general, the fact that bottom dwelling/ feeding fish species have the highest rates of neoplasia has therefore been interpreted as evidence that exposure to sediment-bound chemical carcinogens may play an essential role in tumor induction in these fishes. But also there are some cases of shallow water fishes like tilapia have also tumor ,hence the actual reason of tumor cannot be directly blame on chemical contaminants at bottom of sea.

4. Viral Etiology of Fish Tumors-

A role for viruses as etiological agents for fish neoplasms has been established in a few cases. For example the lymphosarcomas found in northern pike (*Esox lucius*), which are enzootic in North America, Ireland, and Sweden, are transplantable with evidence of cell-free transmission, suggesting the involvement of an infectious agent Furthermore, (Papas et al.) reported the presence of reverse transcriptase and C-type viruslike particles associated with these lymphosarcomas. Tumors were also inducible in salmon (*Onchorhynchus kisutch*) and the virus was successfully recovered from a tumor sample. (Sano et al.) also isolated a herpesvirus (yamame tumor virus, YTV) from a spontaneous tumor of the mandible of cultured yamame. Young fry inoculated with the virus developed similar tumors in the mandibular region and it was reported that salmon (*Onchorhynchus keta*) were also susceptible. However, at present it has not yet been confirmed whether OMV and YTV are identical or whether the tumors produced by these viruses are histopathologically the same.

Summary-

Fish occupy a distinct segment of the phylogenetic tree and constitute the largest and most diverse class of vertebrates. With over 20,000 species and enormous spectra in life style, size and longevity, fish serve as an ideal material source for the comparative study of cancer. This range allows extensive comparisons and should perhaps allow a more penetrating insight into basic principles than investigations limited to mammalian models.

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