ICR 系マウスの尾に認められた脊索腫様病変

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—NOTE—

Chordoma-Like Tumor in the Tail of a Mouse

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ABSTRACT. A chordoma-like tumor occurred in the coccygeal region of a 101-week-old female ICR mouse. The tumor cells were growing in sheets with a lobular pattern and showed cytoplasmic vacuolation in varing degrees. Markedly vacuolated cells closely resembled the physaliferous cells in human chordoma. Aggregates of cytoplasmic filaments or fibrillar materials in the large vacuoles were demonstrated by electron microscopy.—KEY WORDS: chordoma, mouse.

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Chordoma is a rare tumor originating from the notochordal remnants and mostly occurs in the cranial and sacrococcygeal regions in man [4]. The occurrence of the tumor is also rare in experimental animals. In the rat, two cases of chordomas [7, 10] have been reported since Reznik and Russfield [11] first described a chordoma in the lumbar region of a 112-week-old female F344 rat in 1981. However, no case has been described in the mouse. We encountered a chordoma-like tumor in the tail of a mouse used in a chronic toxicity study with a pesticide. The present report describes the details of the lesion.

The material was obtained from an SPF female ICR mouse purchased from CLEA Japan, Inc. at 4 weeks of age. The mouse was fed a test diet containing a pesticide for a period of 96 weeks (5 to 101 weeks of age). The animal showed focal swelling of the tail since 24 weeks of treatment. The lesion was about 5 mm in diameter when noticed at week 24 but not changed thereafter. At the termination of treatment, the animal was killed and the swollen region of the tail was removed and fixed in 10% neutral buffered formalin. The specimen was processed into paraffin sections, stained with hematoxylin and eosin, periodic acid-Schiff reaction (PAS) with or without predigestion with saliva, mucicarmine, alcian blue, and phosphotungustic acid hematoxylin (PTAH). One paraffin section was deparaffinized, fixed in 2% osmium solution, and processed for electron microscopic observation. In addition, the notochord of normal mouse embryos on days 15–19 of pregnancy and the nucleus pulposus of an untreated adult mouse at 80 weeks of age were also examined by light and/or electron microscopy for histological comparison.

Macroscopically, white cartilaginous tissue was observed on the sagittal and transverse sections of the swollen area. A piece of coccygeal vertebra was replaced by the tumorous tissue. Histologically, the lesion was composed of neoplastic cells with varying degrees of vacuolation and surrounded by dense fibrous tissue. The neoplastic cells were growing in sheets with a lobular pattern and each lobule was separated by thin septa of fibrous tissue. These cells showed a marked infiltration into the

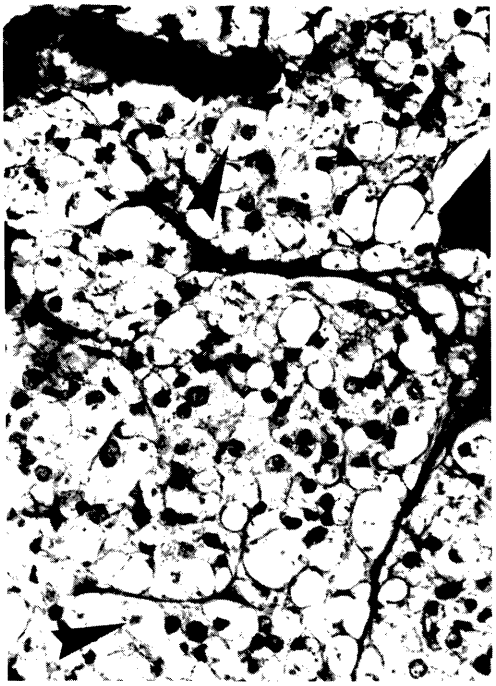

Fig. 1. Neoplastic cells containing vacuoles of various sizes. Some of these cells also have eosinophilic and PAS-positive bodies (arrow head) in their vacuoles. H-E. ×300.

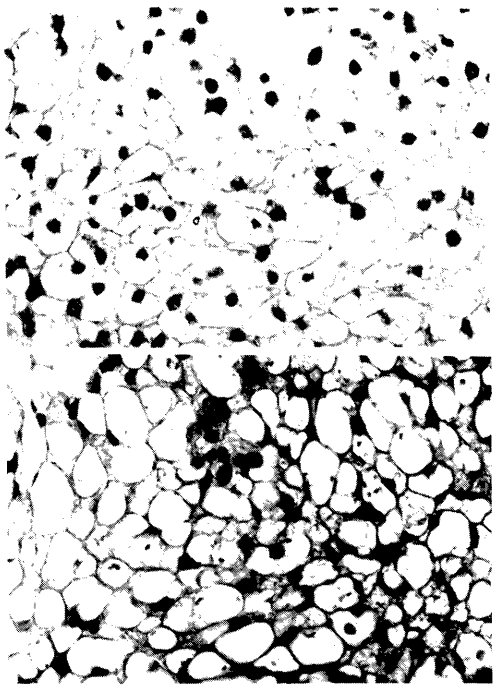

Fig. 2. Normal figures of notochord of a mouse embryo on day 17 of pregnancy (upper) and of nucleus pulposus of the tail of an adult mouse (lower). H-E. ×300.

coccygeal vertebral bone, resulting in atrophy and deformation of its architecture, and also invaded into the surrounding connective tissue. The matrix of the lesion was scanty and negatively stained with PAS method, alcian blue, or mucicarmine. The matrix was also vacant on the specimen stained with PTAH in contrast with darkly brown interlobular septa. Metastasis was not observed.

The cytoplasm of the neoplastic cells was occupied by single large or multiple vacuoles with varying sizes and appeared to be much porous (Fig. 1). The neoplastic cells had nuclei which were largely round and located in the central part of the cytoplasm. The nuclei were occasionally flattened in the peripheral area of the cytoplasm by compression of large vacuoles and the cells showed an appearance of signet-ring cells. The vacuolated appearance of these cells resembled that of embryonal notochordal cells or nucleus pulposus cells of the mouse (Fig. 2) as well as highly vacuolated cells being known as physaliferous cells in human chordoma. Most of the vacuoles in the neoplastic cells were not stained with PAS, alcian blue, or mucicarmine, although they occasionally contained eosinophilic bodies which were positive for PAS reaction and resistant to saliva digestion.

Besides sheet-like proliferation, the neoplastic cells occasionally showed a trabecular or nodular proliferation giving a profile of epithelial-like arrangement (Fig. 3). These cells were polygonal or round in shape, and they had finely granular or agranular and faintly eosinophilic cytoplasm. PAS positivity of fine granules in the cytoplasm was diminished by predigestion with saliva. Some cells also contained small

Fig. 3. Less vacuolated area of the lesion composed of round or polygonal cells in epithelial-like arrangement. H-E. ×300.

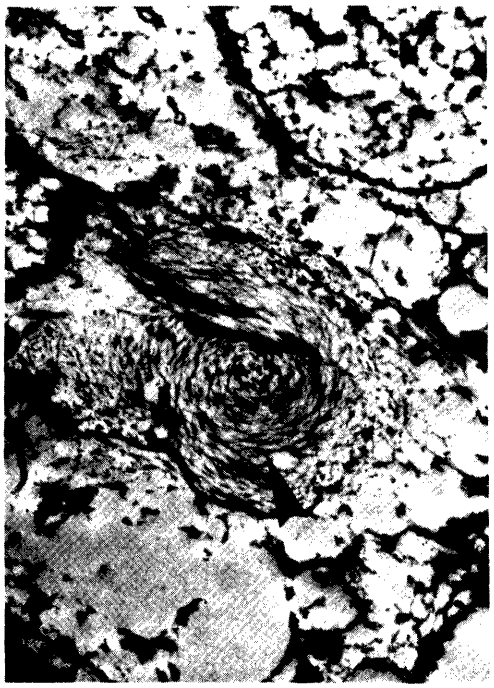

Fig. 4. Aggregates of cytoplasmic filaments (arrow head) in the polygonal cells. ×5,400.

intracytoplasmic vacuoles.

Electron microscopy revealed small aggregates of whirled cytoplasmic filaments in the polygonal neoplastic cells which showed a lower degree of vacuolation (Fig. 4). Markedly vacuolated cells had fibrillar materials in some of large vacuoles (Fig. 5). Notochordal cells of a mouse embryo sampled on day 15 of pregnancy also had fine fibrils in the cytoplasm (Fig. 6), though the fibrils of these cells were finer than those observed in the neoplastic cells. The notochordal cells also contained glycogen granules and dilated mitochondria. However, only limited information was available on the ultrastructural feature of the neoplastic cells, because electron microscopic examination of these cells were conducted using paraffin sections.

The most striking feature of the present lesion is the highly vacuolated cells which resembled not only the embryonal notochordal and nucleus pulposus cells but also the physaliferous cells in human chordoma. The pathological diagnosis of human chordoma depends on the recognition of characteristic physaliferous cells. The negative PTAH staining reaction of the tumor [3] and the lack of cellular doublets or tetrads in lacunae indicate that this tumor is not of cartilaginous origin which is sometimes confused with chordoma. Scattered aggregations of cytoplasmic filaments may provide another evidence which supports the notochordal origin of the tumor, because fibrillogenesis is a conspicuous feature of the notochordal cells of mice [5, 12] and clusters of cytoplasmic filaments are occasionally reported in chordomas in human [1, 9] or rats [10]. Leeson and Leeson [6] described that larger vacuoles in notochordal cells of rabbit embryos contained PAS-positive materials being saliva-resistant. The eosinophilic, PAS-positive, and saliva-resistant bodies in some of large vacuoles in

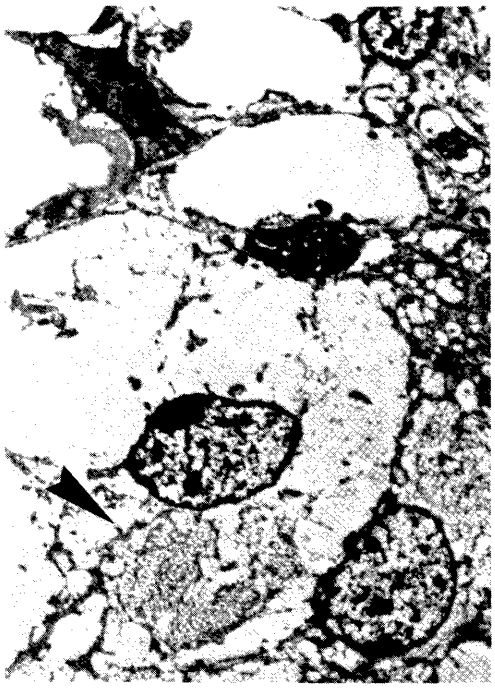

Fig. 5. A highly vacuolated cell containing fibrillar materials (arrow head). ×3,200.

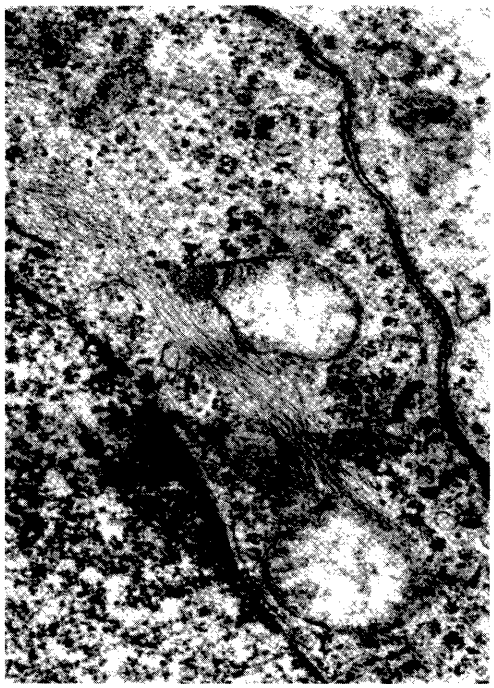

Fig. 6. A normal notochordal cell of a mouse embryo on day 15 of pregnancy which contains fine fibrils, glycogen granules, and dilated mitochondria. × 28,000.

the present study is consistent with their observation. Considerable amounts of PAS-positive and diastase-resistant cytoplasmic granules were also observed in the normal mouse notochord [8]. These PAS-positive granules or materials in the notochordal cells are considered to be corresponding to the cytoplasmic filaments observed in the electron microscopic examination. The eosinophilic bodies in the present case might be, therefore, also regarded to be compatible with the fibrillar materials on electron microscopy.

Other morphological characteristics such as lobular or epithelial-like arrangement of the tumor cells, PAS-positive granules (probably glycogen granules) in the cytoplasm, and destructive and invasive growth to the surrounding tissue, were all in accordance with those of the chordoma in human or rats. However, mucinous matrix, one of the most characteristic features of the chordoma, was not observed in the present lesion. But the amount of the matrix was variable among the previous cases of chordomas and several human cases were reported to be scanty of mucinous matrix [2]. It is, therefore, suggested that the present case would be of a type of chordoma.

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要　　約

ICR 系マウスの尾に認められた脊索腫様病変（短報）：榎本秋子・吉田明由[1)]・原田孝則・真板敬三[1)]・白須泰彦[1)]（残留農薬研究所水海道研究所，[1)]残留農薬研究所）——101週齢の ICR 系雌マウスの尾に脊索腫様病変を認めた。腫瘍組織は大小の空胞を有する細胞の分葉状増殖より成り，ヒトの脊索腫における担空胞細胞に類似した細胞も散見された。電子顕微鏡的には細胞質内あるいは空胞内に微細線維または線維状物質を認めた。