An Intracranial Epidermal Cyst in a Sprague-Dawley Rat

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(Received 1 October 1993/Accepted 10 January 1994)

ABSTRACT. An intracranial epidermal cyst was found incidentally in a 10-week-old female Sprague-Dawley rat. The cyst was located in the leptomeninx of the longitudinal cerebral fissure, ventral to the corpus callosum and dorsal to the third ventricle. It was approximately 0.7 mm in diameter, lined by stratified squamous epithelium and filled with concentric layers of desquamated keratin. The wall consisted of 2–4 layers of cells. Ultrastructurally, the sequence of epidermal differentiation was not normal in that the basal cell layer and was absent in certain areas. The adjacent brain tissues were slightly compressed but not otherwise damaged by the cyst.—**KEY WORDS:** brain, epidermal cyst, rat.

J. Vet. Med. Sci. 56(3): 577–579, 1994

Epidermal cysts are regarded as a congenital abnormality or a sort of hamartoma resulting from the inclusion of epiblastic elements in areas from which they are normally absent [20]. The cysts are considered to be relatively common, spontaneous lesions in the spinal cord of rats and mice with no preference to occur in any strain [7, 12, 14]. The intracranial cyst occurs extremely rarely and is described briefly in several text books without useful references [4, 21]. This report describes an intracranial epidermal cyst found incidentally in a 10-week-old female Slc: SD rat, that was used as an untreated control in a subacute toxicity study. All of 140 rats used in the study were housed ten per cage in metal cages in a barrier system room at a temperature of $24 \pm 2^\circ\text{C}$ and with relative humidity of 50–60%. A commercial feed (CE-2, Japan CLEA) and tap water were provided *ad libitum*.

At necropsy, selected tissues including the brain were fixed in 10% neutral buffered formalin and processed routinely for histopathology. Coronal section slices were taken through the infundibulum of the cerebrum and through the fissure prima of the cerebellum and brain stem. Paraffin sections were stained with hematoxylin and eosin (H-E), Phosphotungstic acid-hematoxylin and Klüver-Barrera. Ultrathin sections were prepared from a selected portion in a deparaffinized section, double-stained with uranyl acetate and lead citrate and examined with an electron microscope.

Neither neurological signs nor gross abnormalities were seen in the present case. The cyst was round, approximately 0.7 mm in diameter and detected microscopically in the midline ventral to the corpus callosum and dorsal to the third ventricle at the leptomeninx of the longitudinal cerebral fissure (Fig. 1). It was lined by stratified squamous epithelium and filled with concentric layers of desquamated keratin. The wall consisted of 2–4 layers of flattened cells with elongated nuclei. Unlike in the normal epithelial cells, the long axis of these nuclei was parallel to the wall of the cyst. The inner layer-constituting cells contained keratohyaline granules (Fig. 2a). The cells of the outer layers appeared to be connected by spinous processes or intercellular bridges. Mitotic figures were rarely seen in the outer layers (Fig. 2b). The adjacent brain tissues were slightly compressed by the cyst. The granule cell layer of the dentate gyrus, which is normally arranged in a trough-shaped structure, was branched at

Fig. 1. Epidermal cyst located in the midline dorsal to the third ventricle, showing concentric layers of keratin in the lumen. The adjacent brain tissues are slightly compressed and the granule cell layer of the dentate gyrus branches at the hilus in two directions along the cyst. H-E stain. $\times 40$.

Fig. 2. Higher magnification of Fig. 1 showing the cyst lined by stratified squamous epithelium. The inner layers contain keratohyaline granules (2a, $\times 400$). A mitotic figure (arrow) is seen in the outer layer (2b, $\times 800$). H-E stain.

the hilus in two directions along the cyst but was not otherwise damaged by the cyst. There was no inflammatory reaction or gliosis with special stains.

Electron microscopically, the cyst was surrounded by basal lamina bordering the outer lining cells, either the basal or prickly cells of the squamous epithelium, which contained bundles of tonofilaments in the cytoplasm and had highly folded cell margins which interdigitated with those of neighboring cells (Fig. 3). Desmosomes were frequently found between membranes of adjacent cells. In some areas, the prickly cells were directly in contact with the basal lamina without any intervening basal cells, as observed in spinal epidermoid cysts in the mouse [12]. This finding suggests that the process of epidermal differentiation may be altered in this kind of lesions. In the inner lining cells, an irregular electron-dense substance, probably corresponding to keratohyaline granules, also appeared. Thus, the cyst was composed of simple stratified squamous epithelial elements and was classified as an epidermal cyst, differing from epidermoid and dermoid cysts which contain other skin appendages, such as hair follicles and sebaceous glands [11]. The WHO classification of tumors of the central nervous system (1979) lists epidermoid cysts under the category of "other malformative tumors and tumor-like lesions" [9].

The central nervous system develops from the specialized ectoderm (neuroectoderm) which lies dorsal to the notochord throughout the axis of the embryo. Invagination of this neuroectoderm forms the neural groove and

lateral processes referred to as neural folds. The neural folds fuse to form the neural tube from which the ventricular system and central canal develop. At the time of closure of the neural tube, the neuroectoderm separates from the remaining ectoderm to form two distinct layers. The layer of nonneural ectoderm gives rise to structures such as the epidermis [2]. It has been generally accepted that epidermoid cysts develop from embryonic cell inclusions that result from faulty fetal differentiation. In humans, midline lesions may be a product of inaccurate neural groove closure between the 3rd and 5th weeks of intrauterine life, with more laterally placed lesions probably arising at a later stage of development during formation of the secondary cerebral vesicles [20]. In this case, as the cyst is located in the midline, the occurrence of this epithelium is probably related to a faulty separation of the neural tube from the ectoderm at about the seven-somite stage (8.25 days postcoitum) when the closure of the neural tube starts in rodents [10]. It is not known whether genetic influences or intrauterine diseases contribute to the development defects [14].

The neurological signs produced by the cysts can generally be explained by their site and growth patterns. Epidermoid growth rates have been estimated to be linear and to approximate that of normal skin [1]. Neither clinically neurologic dysfunction nor adjacent brain tissue injury was observed in the present case, reflecting a slow growth of the lesion. Lack of neurological signs may be also due partly to the adaptability of the central nervous system to gradual compression, which has frequently been noted in humans [19, 22]. Regardless of the site of origin, in humans, intracranial epidermoids are almost always cytologically benign, although there have been a few reports of the development of squamous carcinomas within them [3, 6, 16].

Intracranial epidermal cysts in human pathology account for only 1% of all intracranial tumors [20], and the intraspinal epidermoid tumors occur less frequently than the intracranial cases [18]. Although tumors of the central nervous system are not common in rats, various tumor types have been described [5, 8, 13, 15, 17]. No epidermal or dermoid cyst was recognized in their studies. The first observation of epidermal cysts in rats was reported by Levine [14], and only spinal cysts and no intracranial cysts were found in 47 out of 1,909 CDF rats as incidental findings during complete examination of the nervous system in experimental work on allergic encephalitis. The present case is the first case of an epidermal cyst occurring in the intracranial region in rats.

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Fig. 3. An electron micrograph of the cyst wall. The prickly cell (PC), which has marked foldings of the cell membrane, is directly in contact with basal lamina. Desmosomes (arrows) and tonofilaments (arrowheads) are also seen. Bar = 2 μ m.

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