Case Report

Adenoma of the Nasal Submucosal Glands in the BDF1 Mouse —One Case among 2000 Controls in 2-year Carcinogenicity Studies—

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Abstract: A case of submucosal gland adenoma developed in the nasal cavity of a male BDF1 mouse, 110 weeks of age, was presented. Histologically, a solitary nodule, 5 mm in diameter, showed an acinar structure resembling that of a serous gland. The present case was found in the posterior-most part of the nasal cavity, contrary to all previously reported, probably-induced, adenomas of the nasal cavity in mice, found in the anterior-most part of the nasal cavity. (J Toxicol Pathol 2003; 16: 179–181)

Key words: adenoma, nasal cavity, spontaneous tumor, BDF1 mouse

This is a case of adenoma occurring in the nasal cavity of a male mouse among a total of 1000 male and 1000 female BDF1 mice used as controls in two-year carcinogenicity studies carried out during the past 20 years from 1982 to 2002 at the Japan Bioassay Research Center. Because there appear to be no reports of a spontaneous adenoma that has probably arisen in the submucosal gland of the posterior-most part, of the nasal cavity (the ethmoid bone region) in mice, including those of the BDF1 strain, histologic characteristics of this case and its probable histogenesis are described.

Four-week-old BDF1 mice (1000 males and 1000 females; Charles River Japan, Kanagawa, Japan), were used as controls in our carcinogenicity studies. The animals were housed singly in stainless steel wire cages in an environment-controlled barrier system; the rooms were maintained at 24 ± 2°C and 55 ± 10% relative humidity, with a 12-hour fluorescent light/12 hour dark cycle. Water and a standard commercial diet (CRF-1, Oriental Yeast, Tokyo, Japan) were offered, and mice were allowed to feed ad libitum. Mice were euthanized with ethyl ether at 110–111 weeks of age, and a necropsy was performed. Routine necropsy studies were performed on all animals, including those found dead or moribund, during the course of each study.

Specimens of the maxillary nasal cavity from all experimental animals were fixed in 10% buffered formalin, decalcified in a solution of 5% formic acid and 5% formalin, and cut into tissue specimens at three levels—just behind the upper incisor teeth, on the incisive papilla, and just in front of the first upper molar tooth. These tissue specimens were dehydrated and defatted with alcohol and chloroform, respectively, and embedded in paraffin. The embedded specimens were cut at 5 µm and stained with hematoxylin and eosin stain (H&E), and periodic acid-Schiff reaction (PAS) after the deparaffinization procedure.

One male mouse, 110 weeks of age, used as a control in the inhalation carcinogenicity study, showed abnormal respiration a week before necropsy. A solitary nodule, 5 mm in diameter, was grossly seen unilaterally at the labial region of the upper molar teeth at the 3rd level of the nasal cavity occupying the cavity space and compressing the maxillary tissues (Fig. 1).

Histologically, an exophytic mass growing into the lumen of the nasal ethmoturbinal cavity caused pressure atrophy of adjacent structures. The mass was broad-based in its attachment to the mucosa, but without showing invasive infiltration around it. The tumor showed a circumscribed endophytic growth composed of epithelial cells with an acinar pattern resembling that of a serous gland. Acinar cells were cuboidal and had slightly basophilic cytoplasm and chromatin-rich round nuclei located on the basal side. Although a moderate irregularity of nuclear size was seen in
the cells, the mitotic rate was low (Fig. 2). Myoepithelial cells were not confirmed.

The surface of the tumor was mostly lined by a single layer of ciliated (Fig. 3A) or nonciliated (Fig. 3B) respiratory epithelium. There was no continuity between the surface epithelium and the tumor cells.

Around the acinar tissue, there was much mucous secretion that was stained pale red with hematoxylin and eosin and was PAS reaction positive. No inflammatory cell infiltration was found in the tumor mass or the surrounding tissue.

This tumor was diagnosed as an adenoma, probably developed from the submucosal glands of the nasal cavity, based on its characteristic acinar structure with mucous secretion. Although moderate cellular atypisms with nuclear-size pleomorphism and frequent desquamation of the tumor cells in abundant mucous mass were seen, this was distinguishable from adenocarcinoma, because of the absence of invasive growth into the surrounding tissues or absence of either marked cellular or structural atypisms of tumor cells.1–8

Although adenoma of the submucosal gland of the nasal cavity has mainly been found in chemical-treated rodents1–3,5, a spontaneous case appears to be rare. Consequently, the present case—the only one found in a total of 2000 control BDF1 mice—seems to be noteworthy. Recently, an adenoma seen in a p53 heterozygous male mouse was described5. Although reported adenomas were usually found in the anteriormost part of the nasal cavity4,5, the present case arose in the posteriormost part of the nasal cavity, at the 3rd level, probably from the submucosal glands of the olfactory mucosa. However, the origin of this tumor may be difficult to ascertain.

Both ciliated and nonciliated respiratory epithelium found at the surface of the present case seem to reveal metaplasia of the olfactory epithelium, regularly seen in the mucosa of the nasal cavity, at the 3rd level.

References

5. Herbert RA and Leininger JR. Nose, larynx, and trachea. In: Pathology of The Mouse, RR Maronpot (eds), Vienna:

