Congenital aplasia and hypoplasia of the optic nerves are rarely seen in human beings and animals. Similar conditions occur infrequently in rats, but no detailed description of the condition has been given, except for the Bmn strain of rat. Bmn-wys rats are animal models of inherited retinal degeneration; aplasia or hypoplasia of the optic nerve occurs in association with microphthalmos in these rats. In Wistar rats of the CPB-WE strain, a high incidence of hydrophthalmus, accompanied by optic nerve aplasia and microphthalmia has been reported, but no histologic findings have been described in the ocular lesions.

We encountered two cases of unilateral optic nerve aplasia among 200 male and 200 female Slc: Wistar rats that were 6 weeks of age. Both cases were females. The animals were obtained from Shizuoka Laboratory Animal Center (Shizuoka, Japan) and maintained under barrier conditions in a room controlled at 23°C ± 2°C, 50% ± 20% relative humidity, and a 12-hour light-dark cycle. Standard commercial laboratory diet for rats (CRF-1, Charles River Japan Inc., Kanagawa, Japan) and chlorinated tap water were available ad libitum.

The affected animals showed no noticeable clinical signs. Ophthalmic examination revealed a fixed pupil in the left eye of one case (Case 1), and fundus examination by ophthalmoscopy disclosed a grayish brown fundus, absence of the optic disk and of the central retinal blood vessels in the left eyes in both cases. No abnormalities were observed in the right eyes of either animal.

The animals were subjected to a complete necropsy. In both animals, the left optic nerve was completely missing from the posterior pole of the eyeball to the optic chiasma. The right optic nerve appeared normal in size; the right optic tract was rudimentary and barely visible (Fig. 1). The left eyeball with no optic nerve was externally normal and similar in size to the normal right eyeball. No abnormalities other than those described above were observed. The eyeballs, optic nerves, and brains were fixed in 10% neutral buffered formalin. The tissues were embedded in paraffin, sectioned, and stained with hematoxylin and eosin (HE), luxol fast blue and HE, as well as by the Bodian and Holzer methods. Thickness of the retinas from the eyes with no optic nerve or with the normal optic nerve from both cases was measured at the central and peripheral regions with an eyepiece micrometer. The retinas from five, healthy, age-matched Slc: Wistar rats were also measured in an identical manner and served as controls.

Similar histologic abnormalities were observed in both animals, so they will be described together. The lesions observed were aplasia of the optic disk, retinal hypoplasia, rosette formations in the retina and hypoplasia of the ciliary body (Fig. 2). Case 1 revealed subretinal hemorrhage and nodular hyperplasia of the choroid, in which calcified foci were surrounded by thin connective tissue (Fig. 2). The inner portion of the retina, consisting of the inner limiting membrane and the layers of optic nerve fibers, ganglion cells, inner prexiform, inner nuclei, and outer prexiform, was more markedly hypoplastic than the outer portion, composed of the outer nuclear layer, outer limiting membrane, layer of rods and cones, and pigment layer. This resulted in a definite decrease in the ratio of the inner portion to the whole layer of the retina (Fig. 3, Table 1). The nuclei present in the ganglion cell layer were pyknotic and markedly reduced in number (Fig. 3). The nerve fiber layer was extremely attenuated and scarcely recognizable. The retinal blood vessels were slender and rarely seen. Sections through the posterior portion of the eyeball of Case 1 revealed collagenous bundles passing through the sclera, possibly representing the vestigial dural sheath. The surface of this area was covered by the retinal pigment epithelium, and neither the optic disk nor neural components of the optic nerve were detected. No such structures could be demonstrated in Case 2, despite an extensive search with serial sections. There were no abnormalities in other structures of the affected eyes.

As observed grossly, the right half of the optic chiasma and the right optic tract were markedly reduced in volume due to a reduced number of nerve fibers (Fig. 4); however, there were no degenerative or reactive changes in these areas.

True aplasia of the optic nerve in human beings has been defined as a complete absence of the optic nerve and disk, retinal ganglion cells, and retinal vasculature. In hypoplasia of the optic nerve, on the other hand, a small optic disk and the central retinal blood vessels were present, and the ganglion cell and nerve fiber layers were hypoplastic or absent. The findings in the present cases met neither definition, because the optic nerve and disk, as well as the central retinal blood vessels, were completely missing; but, the retinal ganglion cells were present, although they were sparsely populated and degenerative. Hence it appears that the present cases may be classified as atypical cases of congenital unilateral aplasia of the optic nerve.

The pathogenesis of aplasia of the optic nerve is controversial. It has been suggested that aplasia might result from developmental failure of the mesodermal elements that supply the connective tissue and hyaloid vessels and that hypoplasia might arise from developmental failure of the retinal ganglion cells. It appears unlikely that developmental failure of the mesodermal elements within the fetal fissure is the cause of aplasia of the optic nerve in the present cases; the affected eyes of our cases appeared normal in size, as reported in bilateral aplasia of the optic nerve in a cat and optic nerve hypoplasia in three Miniature Poodles. It has been well documented that the blood supply of the retina comes from the retinal artery, which supplies the inner layers of the retina, and from the choriocapillaries, which nourishes the pigment...
Fig. 1. Brain, ventral surface; Case 1. The left optic nerve is completely missing. The right optic tract is barely visible, compared to the normal-sized left optic tract. Bar = 1 mm.

Fig. 2. Eye; Case 1. Section shows hypoplasia and rosette formation of the retina and nodular hyperplasia of the choroid with calcified foci surrounded by thin connective tissue. HE.

Fig. 3. Eyes, retina comparison; Case 1. Note the eye with no optic nerve (Fig. 3a) and the eye with the normal optic nerve (Fig. 3b). There is a marked reduction in thickness of the retina, particularly its inner portion in Fig. 3a. HE.

Fig. 4. Brain, frontal section; Case 1. The right optic tract is much smaller than the left optic tract due to a markedly reduced number of nerve fibers. Luxol fast blue-HE.

Table 1. Retinal thickness of Slc: Wistar rats.

<table>
<thead>
<tr>
<th>Case Number</th>
<th>Condition of Eyes</th>
<th>Thickness (μm)</th>
<th>Inner Portion*</th>
<th>Inner Portion: Whole Layer Ratio (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Whole Layer</td>
<td>Inner Portion</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CR† PR‡</td>
<td>CR PR</td>
<td>CR PR</td>
</tr>
<tr>
<td>1</td>
<td>No optic nerve</td>
<td>160.0 117.5</td>
<td>62.5 50.0</td>
<td>39 43</td>
</tr>
<tr>
<td></td>
<td>Normal optic nerve</td>
<td>262.5 192.5</td>
<td>150.0 105.0</td>
<td>57 55</td>
</tr>
<tr>
<td>2</td>
<td>No optic nerve</td>
<td>162.5 132.5</td>
<td>52.5 52.5</td>
<td>32 40</td>
</tr>
<tr>
<td></td>
<td>Normal optic nerve</td>
<td>227.5 175.0</td>
<td>122.5 87.5</td>
<td>54 50</td>
</tr>
<tr>
<td>Control§</td>
<td>Normal optic nerve</td>
<td>240.0 144.0</td>
<td>149.0 92.0</td>
<td>62 64</td>
</tr>
</tbody>
</table>

* Inner portion includes the inner limiting membrane and the layers of nerve fibers, ganglion cells, inner plexiform, inner nuclei, and outer plexiform of the retina.
† CR = central region of the retina.
‡ PR = peripheral region of the retina.
§ Values represent the average from five 6-week-old Slc: Wistar rats with normal eyes.

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epithelium, the layer of rods and cones, and the outer nuclear layer. In the present cases, the central retinal blood vessels were absent, and other retinal blood vessels were slender and rarely seen in histologic sections. These findings suggest that failure in differentiation or loss of the retinal ganglion cells and nerve fibers may be due to failure in the retinal vascularization with subsequent degeneration. It thus seems that as a result of failure in development of the ganglion cells, almost all nerve fibers may have failed to develop and reach the optic disk.

Retinal atrophy has frequently been observed in rats in association with aging and changes in lighting.\(^1\) In these cases, the outer layer of the retina particularly photoreceptor cells, became atrophic, whereas the ganglion cell and nerve fiber layers were absent or hypoplastic in cases of congenital aplasia or hypoplasia of the optic nerve.\(^1,2\) Our cases coincided with these observations, although the primary cause of these ocular defects remains unknown.

In our rats, the right half of the optic chiasma and the right optic tract appeared highly hypoplastic and rudimentary. These parts were interpreted as being composed exclusively of nerve fibers deriving from the right optic nerve, because of complete absence of the left optic nerve. This is based on the fact that the optic chiasma and tract of rats are composed of nerve fibers coming from the ipsilateral and contralateral optic nerves. This interpretation seems to be supported by the observation that neither degenerative nor inflammatory changes could be detected in any of the hypoplastic areas we examined.

Acknowledgements

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Cytologic, Histologic, and Ultrastructural Characteristics of a Canine Myxoid Liposarcoma

J. B. Messick and M. J. Radin

Lipomas, the most common mesenchymal tumor of dogs, are located in subcutaneous tissues and grow slowly by expansion.\(^4\) A separate group of adipose neoplasms, infiltrative lipomas, are composed of well-differentiated adipocytes that aggressively invade surrounding tissues but do not tend to metastasize.\(^4\) In contrast to their benign counterparts, liposarcomas are uncommon in dogs, arising de novo and not from pre-existing lipomas or infiltrative lipomas. The favored sites for a liposarcoma in human beings are the deeper soft tissues, including gluteal region, the thigh, lower extremity, and retroperitoneum. In the dog, there is a predilection for subcutis and deeper soft tissue involvement, yet the thoracic and abdominal cavities are also frequent sites of liposarcoma.\(^8\)

Liposarcomas vary greatly in their histologic pattern, and, in human beings, different subtypes are associated with different biological behavior. The myxoid liposarcoma is the most common subtype and has low metastatic potential. Other subtypes include pleomorphic, round-cell, and sclerosing liposarcoma. Round-cell and pleomorphic subtypes have a more malignant behavior and greater metastatic potential than other types of liposarcomas.\(^3\) The diagnosis of myxoid liposarcoma is based primarily on histologic criteria of mucinous areas within the tumor. Unlike the myxoma or myxosarcoma, in the myxoid liposarcoma mature and immature adipocytes are admixed with stellate- to spindle-shaped cells. An anastomosing vascular pattern is also characteristic.\(^10\) This paper records cytologic, histologic, and ultrastructural char-

References
8 Van Eden CG, Mullink JWMA: Internal hydrocephalus, optic nerve aplasia, and microphthalmia in CPB-WE (Wezob) and Cpb: WU (Wistar) rats. Lab Anim 20:257–265, 1986

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