Histologic Characteristics of Normal Perivascular Spaces along the Optic Tract: New Pathogenetic Mechanism for Edema in Tumors in the Pituitary Region

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BACKGROUND AND PURPOSE: Perivascular (PV) spaces are known to distend and cause edema along the optic tract (OT) in pituitary-region tumors. Interstitial fluid may be retained in PV spaces when tumors block their drainage outlets to subarachnoid spaces. However, these spaces and their outlets have not been anatomically elucidated. Our purpose was to evaluate how often large PV spaces are present along the OT and demonstrate their superficial communication points to adjacent subarachnoid spaces.

METHODS: We examined serial histologic sections of 10 hemispheric blocks obtained from cadavers without cerebral abnormality.

RESULTS: Large PV spaces, 0.5–1.5 mm in maximum height, were always present along the middle portion of the OT. Perforation points of the largest spaces were noted at the medial sulcus of the OT in seven hemispheres and through the OT in three.

CONCLUSION: Large PV spaces are present along the middle portion of the OT. Their communication point to adjacent subarachnoid spaces was histologically demonstrated. The locations and variations of the outlet of large PV spaces explain the clinical features of edemas; these findings anatomically support the hypothesis that blockage of the outlets to subarachnoid spaces may play a role in distending the PV spaces and in causing edema in pituitary-region tumors. Only MR imaging has revealed this change; further pathologic investigations are awaited.
drainage outlets to the subarachnoid space. However, PV spaces along the OT and their outlets to the adjacent subarachnoid space have not been anatomically elucidated. This study was designed to provide background data about the formation mechanism of the edema along the OTs. Our purpose was to define the large PV spaces along the OT and to demonstrate the superficial perforation points of the vessels in these spaces (ie, communication routes between the subarachnoid space and the PV spaces along the OT).

Methods

Ten hemispheres were obtained from five cadaveric brains from 72–86-year-old men and women who died from non-neurologic causes. The specimens were fixed in 60% ethanol solution for 4–6 months. In this study, the OT was anatomically defined as the optic pathway located between coronal sections, including the pituitary stalk and the anterior border of the lateral geniculate body (11, 12). After the whole length of the OT was exposed, the OT was divided and cut into three equal portions: anterior, middle, and posterior (Fig 2). Each portion was coronally cut into a 3–3.5-mm-long tissue block, which was embedded in paraffin. Sections 4 μm thick were stained by using hematoxylin-eosin and myelin staining. The sections were viewed by using low-power light microscopy at up to ×50 magnification.

On the basis of previous reports, the PV spaces were pathologically defined as spaces lined by a pial layer, including vessels, and surrounded by the brain parenchyma without ischemic or necrotic components (1–5). In addition, histologic similarities were compared between large PV spaces along the OT and around the anterior commissure where they had pathologically proved PV spaces.

Results

In all 10 hemispheres, several large and small PV spaces were always visible along the middle and posterior portions of the OT (Figs 3A, 4B–D, and 5B–F). Only a few were seen along the anterior portion of the OT. The largest space in each specimen was always present along the middle portion of the OT on the section including the mammillary body and the anterior portion of the cerebral peduncle (Figs 2, 4D, and 5F). It was horizontally long and narrow (Fig 4C) or oval (Fig 5F). The space was 0.5–1.5 mm in maximum height (Figs 3A, 4A and D, and 5A and F) and adjacent to or within the upper part of the OT (Figs 4C and 5F).

Large spaces along the OT included vessels and were lined with a pial layer (Fig 3A). The spaces...
along the OT and those around the anterior commissure had the same histologic features, as described in the previous reports (1–5) (Fig 3B). Therefore, the spaces along the OT were considered PV spaces (Figs 4 and 5).

The vessel passed the perforation point medial to the OT (the sulcus between the OT and tuber cinereum) in seven of 10 hemispheric blocks (Figs 2 and 4) and through the OT in the remaining three (Figs 2 and 5) before reaching the large PV space on the OT. Therefore, there were two variations in the communication point between the PV space along the OT and the adjacent subarachnoid space.
Although our sample size was small, our histologic studies of 10 specimens showed the consistent presence of large PV spaces along the middle and posterior portions of the OT. The largest space in each specimen was present along the middle portion on the coronal section including mammillary body and anterior midbrain. The spaces possess histologic features compatible with those of spaces previously reported. Photographs from human anatomic atlases demonstrate similarly thin and small spaces in the same location on coronal brain sections but without correlation to their anatomic or clinical importance (13, 14). We believe that these large PV spaces along the OT are always present.

The present histologic studies also revealed that the outlets of the PV spaces along the OT to the adjacent subarachnoid space are present at two sites: medial to and through the OT.

The present anatomic findings of possible drainage outlets of interstitial fluid from PV spaces along the OT may explain clinical features of the edema along the OT in pituitary region tumors (Fig 6). First, the location of the outlets to the subarachnoid space in the middle portion of the OT may explain why the edema is common in tumors in which the main mass is located behind the optic chiasm; examples of these include craniopharyngiomas, lymphomas, and germnomas (8). Tumors in the pituitary region commonly extend behind the optic chiasm and involve the posterior lobe system and the floor of the third ventricle (6, 8, 15). Second, the change is occasionally and remarkably unilateral and deviated to the side of tumoral extension (8) (Fig 1). This explanation is feasible because the outlets to the subarachnoid space are not on the midline; they are present bilaterally and off the midline. Third, the presence of at least two outlet points may explain why the change does not always occur in a larger tumor. To produce the

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**Fig 5.** Histologic samples obtained in an 81-year-old man. CP indicates cerebral peduncle.

A. Section shows lines corresponding to sections in B–F. B–F. Continuous thin sections show a penetrating vessel from the perforation point in the subarachnoid space (B) to the largest PV space within the upper part of the OT (F). Its maximum height is 0.7 mm. Sections show the perforation point through the OT, which corresponds to the small arrows in Figure 2. A few small PV spaces (arrowheads) are visible along the OT (myelin staining, original magnification ×25). Bracket in E = 1 mm.

**Fig 6.** Schematic representation shows a possible new mechanism for edema along the OT in pituitary-region tumors. Right, In the normal anatomy, the PV space along the OT communicates with the adjacent subarachnoid space through a thin channel medial to the OT. Left, Tumor can block this channel with mechanical, inflammatory, or adhesive processes. The PV space retains interstitial fluid and distends along the OT (dotted area).
edema, a tumor must be larger in a patient with an outlet point through the OT, rather than in a patient with the point medial to the OT. Likewise, even a small tumor may have accompanied edema when the points are located medially (8, 15). The distance between tumors and outlet points may play a role in how readily tumor causes PV spaces to be distended. Therefore, this present study has provided supportive anatomic evidence for dilated PV spaces along the OT as a formation mechanism of the edema along the OT in pituitary-region tumors (Fig 6).

In addition to such anatomic considerations, other factors, such as the extent and degree of peritumoral edema, the growth speed, the invasiveness of malignant tumors, and tumor adhesion to the surrounding tissue, influence the edema formation (8, 15). Clinicoanatomic correlation between patients with tumors in the pituitary region and healthy subjects is important, because this pattern of edema has not been pathologically proved in humans. This change may be associated with a new pattern of brain edema in addition to vasogenic, cytotoxic, osmotic, hydrostatic, and interstitial edemas (16), or it may be an unrecognized variation of one of these mechanisms. Accordingly, the clinical application of this knowledge has great potential. Because this new type of brain edema has been revealed by using MR imaging, pathologic investigations are required. An MR imaging system of higher field strength may succeed in demonstrating the detailed pathologic anatomy of this edema.

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References