THE EPENDYMAL LINING OF THE CAVUM SEPTI PELLUCIDI:
A HISTOLOGICAL AND HISTOCHEMICAL STUDY* † ‡

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The cavum septi pellucidi, which is present in the fetus (La Roche (1)), disappears at the time of birth. Our observations indicate 3 variants in the formed brain: 1. complete closure of the cavum with formation of a single septum pellucidum (over 50 per cent); 2. complete closure, grossly, but evidence of loose tissue in the central portion (about 25 per cent); 3. frank cavum septi pellucidi (under 25 per cent) (2).

In cases which belong to group 2, the remnants of the cavum are located mostly in the anterior portion of the septum, less frequently in the central portion, and are found least in the posterior portion (obliterated cavum Vergae). The cells in this vascularized area are clumped and show a low grade of differentiation (fig. 1).

In cases which belong to group 3, the comparison of the ventricular and caval lining does not reveal any differences (fig. 2). The lack of morphological differences between the cells which line the cavum and those which line the ventricle is deduced from such observations as those of an uninterrupted, single layer of epithelial cells which are either cylindrical, cuboidal, or flat. Less pertinent is the presence or absence of cilia since it represents an unreliable criterion in human autopsy material.

METHOD AND MATERIAL

For this study, close to 100 cases, in which a cavum septi pellucidi was observed, have been examined. Hematoxylin and eosin and phosphotungstic acid hematoxylin stains and variants of Hortega's silver carbonate technic were used on fixed material. In addition, 15 cavums from individuals ranging in age from prematurity to seventy years were fixed in buffered formalin at 4°C for less than 24 hours, cut on freezing microtome at 15μ, and examined for LD (Lactate Dehydrogenase), BOH (Beta-Hydroxy Butyric Acid), DPNH (Beta-Diphosphopyridine Nucleotide), G-6-PD (Glucose-6-Phosphate Dehydrogenase), and AP (Alkaline Phosphatase).

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Fig. 1. Loose tissue and cell rests in the central portion of a closed septum pellucidum, 17 months old infant. Hematoxylin and Eosin stain.

Fig. 2. Lateral wall of a cavum septi pellucidi with caval lining (right) and ventricular lining (left), 38 months old child. Hematoxylin and Eosin stain.

Fig. 3. Cavum lined by a single layer of cuboidal epithelium, 62 years old individual. Hematoxylin and Eosin stain.

Fig. 4. Cavum lined by flat and cuboidal epithelium, 75 years old individual. PTAH stain.

Fig. 5. Cavum lined by flat and cuboidal epithelium, 65 years old individual. PTAH stain.

RESULTS

In evaluating the results, only the juxtapositioned areas of the lining of cavum and ventricle as shown in Figure 2 have been used. This method was adopted because of variations in the appearance of ependyma in different areas of the ventricular system and also because of the simplicity of such an examination, since both areas lie in the same low-power microscopical field.
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Figures 3 to 5 represent examples of lining of the cavum. In Figure 3 part of the lining, formed by a single layer of cuboidal, epithelial cells, is preserved. The cells in Figure 4 are flattened or cuboidal. The ependyma covering the cavum in Figure 5 is single layered and consists of flat or cuboidal cells with occasional cilia. This type of ependymal caval lining is frequently found in adults. The appearance of cilia in the lining of the cavum, as illustrated distinctly in Figure 4, and partly in Figure 5, is not a frequent occurrence in the majority of cases; but where it was found in the adjacent lining of the lateral ventricle, it was also observed in the lining of the cavum.

In the premature and newborn infant, the lining is of a more complex nature. Figure 6 illustrates the ventricular lining in a four-day-old infant. Part of this ventricular lining is interrupted and replaced by subependymal glial elements. It can be observed that the ependymal elements, reaching the ventricular surface, lose their glial characteristics, and morphologically resemble ependymal cells. Figure 7 from a one-day-old male shows the lining of the cavum. As in the ventricle, the single layer of cells is distinct with some cells having a single, long, thin process which reaches deep into the brain substance. In the newborn this is one of the features of either the ventricular or caval lining.

A comparison of the lining of cavum and ventricle in adults adds further evidence of their morphological identity. Figures 8 and 9 are from a 65-year-old patient. The cavum (figs. 8 and 8a) is covered by a single layer of epithelial cells with round, large nuclei and processes reaching into the underlying cerebral tissue. The lining of the ventricular surface, (figs. 9 and 9a) has an identical appearance. There is, however, a difference in the density of the subependymal layer in the ventricle and in the cavum. The subependymal layer in the ventricle is dense and contains numerous astroglial elements and their processes. The subependymal layer of the cavum is loose having few cells. Regressive changes can be observed in the epithelial layer of the cavum in the form of amyloid bodies (fig. 8a) as well as in the ventricular lining (fig. 9a). Cilia at this age are difficult to demonstrate, and the small “processes” visible in Figure 8 (cavum) and Figure 9 (ventricle) are apparently the result of protein precipitates from the ventricular fluid.

In some cases, the caval ependyma forms a single layer without any relationship to the subependymal glia (fig. 10). In others, the interrelationship between the caval ependyma and the subependymal glia can be seen (fig. 11). The proximity of both cellular types suggests a possibility of glial participation in formation of the ependymal lining.

Further comparison between the ventricular surface (fig. 12) and that of cavum (fig. 12a) shows that it is impossible to differentiate between the cells lining each. The number of subependymal cells, and in older individuals the abundance of amyloid bodies, permits indirect identification of the ventricular lining since in the caval subependyma such are scarce. Similarly, in Figures 13 and 13a the cells, lining both ventricle and cavum, are flattened, bipolar elements which can be identified as ependyma. A higher magnification of the ventricular lining shows ependymal processes reaching into the brain substance.
Fig. 6. Incomplete lining of ventricle, partially replaced by subependymal elements. 4 day old infant. Silver stain.

Fig. 7. Cava1 surface lined by a single layer of cells, some of which have distinct long process. 4 day old infant. Silver stain.

Fig. 8 and 8a. Lining of cava1; single layer of epithelial cells with processes. 65 years old individual. PTaH stain.

Fig. 9 and 9a. Ventricular lining; cuboidal cells form an incomplete lining and an amyloid body is present. 65 years old individual. PTaH stain.

Fig. 10. Lining of cava1 by dense, single-layered, cuboidal cells which show little relation to subependymal gia. 65 years old individual. PTaH stain.

Fig. 11. Cava1 lined by a single layer of ependymal cells which show a close relationship to subependymal elements. 57 years old individual. Silver stain.
Fig. 12. Ependymal lining of a ventricle. 65 years old individual. Hematoxylin and Eosin stain. 12a. Ependymal lining of a cavum. 65 years old individual. Hematoxylin and Eosin stain.

Fig. 13. Flattened ependymal lining of a ventricle. 42 years old individual. Silver stain. 13a. Flattened ependymal lining of a cavum. 42 years old individual. Silver stain.

Fig. 14. Ventricular lining; some cells have processes. 41 years old individual. Silver stain. 14a. Lining of a cavum by a single layer of cuboidal cells, some of which have distinct processes. 41 years old individual. Silver stain.

Fig. 15. Flattened, cuboidal cells form a continuous lining of a ventricular surface. 75 years old individual. PTAH stain. 15a. Flattened and cuboidal cells form the lining of a cavum. 75 years old individual. PTAH stain.

Fig. 16. Ventricles lined by multi-layered, poorly differentiated cells, some of which are distinctly unipolar. Premature infant. Silver stain.

Fig. 17. Lining of cavum composed of multi-layered, poorly differentiated cells; some uni-, bi-, and multipolar cells can be distinguished. Premature infant. Silver stain.
(fig. 14). Figure 14a shows a single layer of cuboidal cells lining a cavum. In Figures 15 and 15a the ependymal lining of the cavum and of the ventricle are compared. Cilia can be observed in each, but are much more pronounced in the lining of the ventricle.

Additional findings are demonstrable in children's brains. Figure 16 shows numerous elements arranged in several layers along the ventricular cavity. The astroglial elements are seen in the white matter. Some of the cells on the surface have a single process reaching deep into the brain tissue. Figure 17 shows the lining of the cavum from a premature infant; the astrocytes can be observed in the white matter. The ependymal cells of the cavum are distinct. Some cells possess both astroglial and ependymal characteristics.

In Figure 18 the relationship between the ependymal cells lining the ventricular cavity, the underlying deep layer of astroglial cells, and the intermediate layer composed of undifferentiated cells is shown. These undifferentiated elements may be: a. multipolar, apparently astrocytic elements; b. bipolar cells with some ependymal characteristics; or c. unipolar and distinctly ependymal cells located close to the surface. The same relationship is present around the cavum. The transition from astroglial cells of the white matter to the bizarre morphology of the intermediate cells and subsequently to the ependymal cells of the cavum surface is demonstrated in a 2-day-old infant (fig. 19). Cells of the intermediate type are illustrated in Figures 20 and 21, each from the cavum lining of a 1 day old child. In Figure 20 the ependymal lining is adjacent to bi- and multipolar (apparently pluripotential) cells of the subependymal tissue. In Figure 21 the lining of the cavum is absent; there are only a few cells among the glial fibers which cover the surface. This suggests that the glial cells, upon reaching the surface of the cavum, undergo a morphological change. The subependymal layer consists of well differentiated astrocytes and cells smaller than those covering the surface. These small cells are bi- or multipolar with processes running parallel to the ventricular surface (fig. 22). Figures 23 and 24 illustrate the surface cells, the intermediate types, and the astroglia surrounding a cavum of a 2 day old infant.

The subependymal cells are close to the ventricular wall. These cell nests can form a tube (fig. 25). The small tubes may be separated from one another (fig. 26); a single nest might be located close to the ventricular surface, which

Fig. 18. Lining of a ventricle composed of multiple layers of cells, many of which have distinct, long, deep-reaching processes. Premature infant. Silver stain.

Fig. 19. Lining of a cavum, which is almost single layered; some cells have ependymal characteristics; others are bipolar spongiosplastic; others are multipolar astrocytes. 4 day old infant. Silver stain.

Fig. 20. Lining of cavum; a single layer of chiefly multipolar cells; distinctly elongated bipolar elements constitute an intermediate form between the ependymal and subependymal layers. 4 day old infant. Silver stain.

Fig. 21. A single-layered lining of a cavum which is not separated from the subependymal cells which are multi- and bipolar. 4 day old infant. Silver stain.

Fig. 22. Lining of cavum; mature, single-layered, dense lining. The subependymal area is filled by bipolar, spongiosplastic-like elements; fibrillary-astrocytes are present in deeper layers of the white matter. 4 day old infant. Silver stain.

Fig. 23. Cavum lining; incomplete but dense lining. The underlying cells consist of various transitional types. 4 day old infant. Silver stain.
Figs. 18 to 23.
lacks its ependymal covering (fig. 27). The ependymal cells in the stroma may also be found close to the caval surface either scattered (fig. 28) or in small clumps (fig. 29).

A study of the enzymatic activity in the linings of cavum and ventricle offers additional data of importance. Figure 30 is from a premature infant who died at birth; gestation age was estimated at 36 weeks. The ventricular lining (DPNH) showed a dense, low-cuboidal layer of cells with distinct cilia and with processes which reached into the cerebral substance. The activity of ependymal layer was definitely higher than that of the subependymal glial elements. Figure 30a shows cells lining a cavum in the same case. The pattern of these cells is loose and has a similar arrangement to that observed in Figure 19. The DPNH activity of these cells, which reached the surface or are close to it, is definitely higher than that of cells remaining in the deeper layers. Although there is no definite dense lining, these cells resemble the cells of the ependyma lining the ventricle in degree of their activity.

In the same case an examination of the alkaline phosphatase activity shows an active, dense cellular layer and the presence of a highly active membrane in the ventricle (fig. 31). The alkaline phosphatase activity of the cells lining the cavum (fig. 31a) is lower as compared to the cells lining the ventricle, but it is definitely higher as compared to the cells in the deeper layers. This difference between the linings of the cavum and the ventricle disappears in the brains of older children and in adults.

Figure 32 shows lactate dehydrogenase activity in a tangential section of the lining of the ventricle; Figure 32a is a partially tangential section and illustrates a definite single layer of epithelial, cuboidal cells lining a cavum. The LD activity in cells lining a cavum and those lining a ventricle is equally high in each; cilia are not found in either. The LD activity in such cells in adults, in another case, is little different in the lining of the ventricle (fig. 33) and in the caval lining (fig. 33a). Cells, lining both cavities, exhibit equal activity that is higher than that of the cells located in the deeper layers. The possibility that other glial elements may readily assume the characteristics of ependymal cells upon reaching the surface and form the surface cell layer is rendered unlikely by the findings illustrated of DPNH activity in Figure 34. The cavum (C) is lined by cuboidal cells which show high DPNH activity. This high activity is in contrast to the much lower activity of astrocytic elements covering the adjacent

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Fig. 24. Cavum; early formation of ependymal lining with various types of transitional cells in underlying layer. 2 day old infant. Silver stain.
Fig. 25. Subependymal ependymal cell rests forming a tube. 20 months old infant. PTAH stain.
Fig. 26. One large, and two small, ependymal cell tubules beneath ventricular surface. 20 month old infant. van Gieson stain.
Fig. 27. Subependymal compact cluster of primitive ependymal cells. 4 year old child. PTAH stain.
Fig. 28. Clumps of undifferentiated ependymal cells close to the cavum. 4 year old child. PTAH stain.
Fig. 29. Small clumps of undifferentiated cells under the caval lining. 4 year old child. PTAH stain.
Figs. 24 to 29.
Fig. 30. Ventricular lining. Premature infant, 36 weeks gestation. DPNH.
Fig. 30a. Lining of cavum. Premature infant, 36 weeks gestation. DPNH.
Fig. 31. Lining of ventricle. Premature infant. AP.
Fig. 31a. Lining of cavum. Premature infant. AP.
Fig. 32. Tangential section of ventricular lining. 54 year old individual. LD. 32a. In part a tangential section of the lining of a cavum. 54 year old individual. LD.
Fig. 33. Ventricular lining. 65 year old individual. LD. 33a. Lining of cavum. 65 year old individual. LD.
Fig. 34. Lining of ventricle (V) and cavum (C). 78 year old individual. DPNH.
Fig. 35. Lining of cavum. 78 year old individual. LD.
ventricular surface (V). Figure 35 illustrates the lining of the cavum in the same case which shows high LD activity.

Despite the morphological adaptation of the astrocytic elements so as to cover a denuded ventricular surface, their enzymatic activity shows that they are different from a true functional lining. The cells which form the lining of the cavum during infancy not only undergo morphological transformation and assume an appearance identical to that of ventricular ependyma but they also display functional activity like that of ependymal cells.

**DISCUSSION**

Many investigators (1–7) have made statements denying the presence of an ependymal lining in the cavum septi pellucidi, in some cases without even discussing the nature of the lining. Many of the statements, unfortunately, are quoted from textbooks (8–11) which led to a subsequent repetition of these statements.

Wolf and Bamford (12) have described cells which varied from low to a high cuboidal form which lined the cavum. None of these cells had any cilia or blepharoplaques. No evidence was found that these cells might be of mesodermal origin. The major portion of the caval surface was found to be covered by a mat of glial fibers and by some fibrillary astrocytes. They concluded that these cells, although closely resembling ependymal cells, can not be ependyma because: 1) the cavum is not part of the ventricular system; 2) the lining cells did not form a complete membrane; and, 3) no blepharoplaques were demonstrated.

Hughes, Kernohan and Craig (13) found that in 110 brains there was an overall incidence of the occurrence of a cavum of 85%, which represents the highest number reported. They found a resemblance between the cells lining the cavum and ependymal cells but did not find cilia or blepharoplaques. Their conclusion was that perhaps these cells might be immature or modified ependyma or spongioblasts modified to resemble ependymal cells.

Our comparison of the ventricular and caval lining shows that the cells in both are morphologically and functionally identical. We postulate, therefore, that both ventricle and cavum are lined by ependymal elements. This is distinct in adults and older individuals; it is less obvious in children and is absent in premature and young infants.

One of the main arguments which supports the alleged absence of an ependymal lining of the cavum septi pellucidi is based on the difference between it and the remainder of the ventricular system. In infants the ependymal lining of the cavum is incomplete or sometimes absent, but it appears later in life. As a source of this ependymal lining of the cavum we suggest two possibilities:

1) The astroglial elements are transformed into ependymal cells as they reach the caval or ventricular surface. When these cells assume the function of ependyma, they also acquire its morphological characteristics. This transformation of neuroglia into ependyma is apparently possible only under certain circumstances since it is known that destruction of the ependymal surface of the ventricle will not lead to regeneration of ependyma but rather to the formation of astroglial scars without any ependymal or ependyma-like elements in it.
2) The second possible source of ependymal cells in the cavum might be from the ependymal cell rests which occur as nests of cells or as scattered elements. We assume that a migration of these elements to the surface and their formation of a single layer is possible. This possibility is supported by the finding that the ependymal covering of the recesses of the fourth ventricle, which are close to numerous ependymal cell rests, is always intact. We assume that the abundance of ependymal cell rests may constitute a reserve from which, through migration, the ependymal lining is augmented.

Another possibility was suggested by E. C. Alvord, Jr. (14) which was that ependymal cells migrate into the cavum through a communicating foramen. This might hold true for cases in which such a communication is present. Considering the filling of the cavum septi pellucidi by air during ventriculography, this possibility should be considered a valid one. Fenestrations of the septal leaves account for this.

Cells lining the cavum septi pellucidi are not only morphologically modified glial elements but have adopted similar functional characteristics. Therefore, it should be concluded that they do not only resemble ependymal cells but that they have assumed their morphology and functions as well, thus becoming ependymal elements.

SUMMARY

A comparison of cells lining the cavum septi pellucidi and the nearby lateral ventricle was used for determining the nature of these cells. The results indicate that the epithelial cells which line the cavum, although they appear at a later age, assume all of the characteristics morphologically and functionally, of the ependymal cells which line the ventricular system.

REFERENCES