Gliosis of the Aqueduct

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The ventricles of the central nervous system develop as expansions of the central canal of the primitive neural tube. Segments of the canal remain relatively small and form the central canal of the spinal cord and the aqueduct of Sylvius. The aqueduct is normally about 1.3 sq. mm. in cross-section and varies in form from round or oval to T-shaped. It is lined by a single, continuous layer of ependymal cells resting on a stratum of neuroglial tissue.

Spiller1 first described in a 19-year-old male a condition in which hydrocephalus was associated with "occlusion of the aqueduct of Sylvius . . . by proliferation of the neuroglia". Subsequent observers2-8 have reported this lesion in virtually all age groups. Schlapp and Gere6 described an infant, born with hydrocephalus at seven months' gestation, in whom the aqueduct was reduced to "a minute slit, about which an active proliferative process may be made out, while at either end of the opening there is a well advanced gliosis". A possible inflammatory etiology was suggested by the presence, elsewhere in the nervous system, of perivascular cuffing with lymphocytes. At the other extreme of life, Drachman and Richardson7 described a 72-year-old housewife who died with myelomonocytic leukemia and was found to have markedly dilated third and lateral ventricles. The aqueduct was reduced to 0.4 mm. in area and "the ependymal lining was interrupted at several places, the gaps being filled in by mounds of dense glial fibres containing astrocytic and a few microglial nuclei".

All of the described cases have a strikingly similar morphology, even though different etiologic factors may be involved. The most commonly cited cause is disruption of the ependymal lining by an inflammatory process. An unrecognized intrauterine meningitis or a clinically unapparent infection later in life may be followed by slow occlusion of the aqueduct by proliferating subependymal astrocytes. Patients with aqueduct gliosis usually present with signs and symptoms of increased intracranial pressure.

In this report, two new instances of aqueduct gliosis will be presented, together with a summary of the diagnostic criteria for this interesting pathologic entity.

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lined by ependymal cells, but were mainly composed of fibrous astrocytic tissue. The original aqueduct wall was outlined by a ring of small groups of ependymal cells, some of which formed minute tubules or rosettes. The original aqueduct lumen contained masses of astrocyte cell bodies and fibres (Fig. 3). The astrocytes varied slightly in size and shape, but there was no nuclear hyperchromatism or mitoses. The appearance was one of benign hyperplasia of the astrocytes with disruption and scattering of the ependymal lining of the cerebral aqueduct. Anterior to the residual lumen of the aqueduct there was a small hemorrhagic focus (Fig. 4) surrounded by edema and swelling. Occasional ependymal granulations were present in the walls of the lateral ventricle; none were observed in the fourth ventricle.

There was no evidence of meningeal fibrosis or of old hemorrhage which could be related to the previous head injury. An apparent complete functional closure of the aqueduct occurred, which produced an acute increase in intracranial pressure and coma.

**Case 2.**—A 14-year-old girl was admitted to hospital on January 2, 1965. She complained that at school she had been unable to see the blackboard clearly for three months. The blurring of vision was worse in the early morning on arising and was occasionally accompanied by an aching pain in the forehead. Past history included attacks of "infectious mononucleosis" at ages 5, 8 and 12.

She was an alert, well-nourished girl. Her blood pressure was 125/85 mm. Hg. There was mild myopia, enlarged blind spots and early papilledema bilaterally. She was unable to converge her eyes. Otherwise, examination was unremarkable.

Skull films revealed mild spreading of the coronal suture. Bilateral carotid arteriography on January 4 showed elevation of the anterior cerebral arteries indicating moderate dilatation of the lateral ventricles. A pneumoencephalogram on January 8 outlined the fourth ventricle, but no air passed into the third or lateral ventricles. A ventriculogram outlined markedly dilated lateral ventricles and a moderately dilated third ventricle. Positive contrast studies revealed obstruction of the aqueduct 3-4 mm. from its upper end.

On January 8 a shunt was installed between the right lateral ventricle and the subarachnoid space. The patient was given one bottle of whole blood during the procedure. Postoperatively her papilledema lessened.

On January 28 she began to vomit and lumbar CSF obtained on February 3 had a protein of 194 mg. %
with 700 lymphocytes and 2700 polymorphonuclear leukocytes per c.mm. No growth was obtained on culture. Daily lumbar puncture was done and by February 21 the protein was 34 mg. % with 2 lymphocytes and 7 polymorphonuclear leukocytes per c.mm. The shunt was considered blocked and was replaced on February 22 with a ventriculostial Pudenz valve shunt. One bottle of whole blood was given during the procedure. The patient again did well for about three weeks.

Vomiting, confusion and papilledema reappeared on March 12 and the ventricular end of the shunt was found to be blocked and was replaced.

On March 15 the patient was slightly jaundiced, and by March 17 the jaundice had deepened. She became drowsy and irritable and complained of abdominal pain. Her condition deteriorated rapidly. Upper gastrointestinal hemorrhage occurred and she died on March 18.

At autopsy the direct cause of death was found to be massive hepatic necrosis with multiple visceral hemorrhages. Examination of the brain revealed minimal dilatation of the third and lateral ventricles with a patent Pudenz valve shunt. The upper end of the cerebral aqueduct was irregular in outline and tapered rapidly within 4 mm. to a pinpoint lumen. The fourth ventricle was not dilated.

Microscopically, the lumen of the upper aqueduct was encroached upon by small tufts of neuroglial tissue which protruded through gaps in the ependymal lining (Fig. 5). Further along, the neuroglial ingrowth left only a minute lumen. The extent of the original aqueduct was indicated by a ring of ependymal cells in small nests (Fig. 6). The tissue ingrowth was composed of histologically benign astrocytes (Fig. 7). There was no evidence of recent or remote inflammation. However, ependymal granulations were prominent in the lateral ventricles and the upper part of the fourth ventricle.

**DISCUSSION**

Aqueduct gliosis can be distinguished from other types of abnormally small aqueduct only by microscopic examination of the midbrain. The characteristic findings are: (1) benign hyperplasia of fibrous subependymal astrocytes; (2) disruption and fragmentation of the ependyma, some cells

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**Fig. 4.—Case 1. Recent edema and hemorrhage into the gliial mass at the point of maximal narrowing of the aqueduct. (L.F.B., H.F.S. × 50.)**

**Fig. 5.—Case 2. Tufts of neuroglial tissue encroaching upon the lumen of the upper end of the aqueduct through areas devoid of ependyma. (L.F.B., H.F.S. × 50.)**

**Fig. 6.—Case 2. Site of maximal narrowing of the cerebral aqueduct, with the original triangular lumen partly outlined by nests of dark-staining ependymal cells. (L.F.B., H.F.S. × 50.)**
remaining in the original location and some being pushed inward; (3) encroachment upon the lumen of the aqueduct; and (4) absence of inflammatory cell infiltration around the aqueduct.

Other lesions of the aqueduct of Sylvius may cause hydrocephalus and simulate aqueduct gliosis. In congenital stenosis the aqueduct is small but is lined by intact ependyma with no proliferation of the surrounding neuroglia. Congenital "forking" is similar to stenosis except that there may be multiple minute channels, some ending blindly, instead of a single small aqueduct. In congenital septum formation a thin membrane totally or partially occludes the lumen of the aqueduct. Head trauma, meningitis or cerebral infarction may result in aqueduct occlusion by CSF emboli consisting of blood clot, fibrin masses or infarct debris. Neoplasms, particularly pinealomas and astrocytomas of the quadrigeminal plate, may compress the aqueduct; indeed there may be difficulty in distinguishing gliosis from a low-grade astrocytoma.

Ependymitis is distinguished by the presence of acute or chronic inflammatory cell infiltration around the aqueduct.

The etiology of aqueduct gliosis is unknown. It is postulated that the ependyma is disrupted by an unknown factor and regenerates poorly; repair is attempted by the subependymal astrocytes, which proliferate and occlude the lumen of the aqueduct. Some authors have suggested that the astrocyte proliferation is the cerebral counterpart of the segmental obliteration of the central canal of the spinal cord, which commonly occurs after puberty. Others believe that the condition results from intracranial meningitis or an unrecognized granular ependymitis later in life. They cite the frequent observation of ependymal granulations in the lateral, third and occasionally the fourth ventricles as evidence. Russell has shown that ependymal granulations are commonplace in dilated ventricles, and thus must be interpreted with caution. Their presence in the non-dilated fourth ventricle, as in our second case, may be more suggestive of a previous ependymitis. A developmental anomaly is suggested by the observation of coexistent meningomyelocele, Arnold-Chiari malformation or other anomalies in some cases.

In aqueduct gliosis, a ring of scattered ependymal cells around the zone of neuralgial proliferation indicates that the aqueduct has once been of normal size but has undergone secondary narrowing. The early remittent episodes and later continuous symptomatology indicate that the condition is progressive.

In Case 1 it cannot be established whether or not the head trauma was associated with a transient communicating hydrocephalus which caused aqueduct dilatation, ependymal disruption and astrocytic proliferation. Similarly, in Case 2, it can only be speculated that the recurrent attacks of "infectious mononucleosis" were episodes of low-grade meningitis or ependymitis. Whatever the etiology of these and other cases described in the literature, it is apparent that the gliosis continues long after all evidence of the original causal factor has disappeared. In this respect the lesion is similar to neoplasia. However, there is also a time lag between stimulus and stricture in other more common locations, such as the esophagus, bile duct, ureter or urethra.

**Summary**

Two cases of gliosis of the aqueduct of Sylvius are presented. Gliosis is an acquired condition in which the aqueduct is constricted by proliferation of fibrous astrocytes and is distinct from developmental stenosis: a narrow aqueduct of otherwise normal structure. Both conditions may cause internal hydrocephalus. While hydrocephalus due to aqueduct gliosis may appear in the newborn, the symptoms may not arise until adolescence or middle age.

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**References**