The concurrence of hydrocephalus and craniosynostosis

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The clinical course and pneumoencephalographic findings of 14 patients with the associated anomalies of craniosynostosis and hydrocephalus are reviewed. Postmortem examination in two cases, one of which had aqueductal stenosis, confirmed the presence of hydrocephalus. Eight of the 14 had associated anomalies of the extremities consistent with the diagnosis of Apert's syndrome and six patients had dull to normal intelligence. Various types of sutural involvement were present including isolated closure of the sagittal suture. The hydrocephalus, which appears to be an associated anomaly rather than a direct consequence of the craniosynostosis, is most often communicating, but stenosis and atresia of the aqueduct may be present. No single pathogenetic mechanism seems responsible for the abnormal ventricular enlargement, but when the dilation becomes progressive, surgical intervention may be indicated.

Key Words: craniosynostosis • hydrocephalus • increased intracranial pressure

A decade or more ago, we encountered a patient with extreme hydrocephalus who had, in addition, craniosynostosis. Pneumoencephalography demonstrated that aqueductal narrowing was responsible for the hydrocephalus. Shortly thereafter, the presence of aqueductal atresia was confirmed by postmortem study of a second child who also suffered from the concurrence of these malformations. These findings led to a search of the literature for reports of similar experiences, but at that time no such cases were discovered. Moreover, no mention of hydrocephalus was found in several reports of large series of patients treated surgically for craniosynostosis. On the other hand, air contrast studies had seldom been performed on these patients, and, although minor degrees of hydrocephalus might have been missed, symptomatic hydrocephalus could hardly have escaped notice. This suggested that hydrocephalus complicates craniosynostosis only infrequently. Nevertheless, our own experiences over many years have led us to carefully scrutinize patients with craniosynostosis in two large medical centers and in several institutions for retarded children. The results of our studies show clearly that hydrocephalus may complicate various forms of craniosynostosis and that the hydrocephalus may be communicating or noncommunicating.

Case Material

The majority of patients in this report were encountered in routine pediatric neu-
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rology practice at two major medical centers: Massachusetts General and St. Louis Children's Hospitals. A few were discovered by review of hospital statistical data, and several were found at various state hospitals for the retarded where the authors served as consultants. Special attention was paid to those patients in whom the head size and external configuration of the skull or radiographs suggested the possibility of hydrocephalus complicating the craniosynostosis. The case material is therefore highly selected and does not provide data regarding the frequency with which these disorders concur. Except for the two cases studied postmortem, at least one pneumoencephalographic study was accomplished in each case.

In a few instances hydrocephalus was suspected clinically but pneumoencephalograms were not obtained; such cases were excluded. During the period of time when these cases were being collected, normal pneumoencephalograms were obtained in many other patients with craniosynostosis; these have also been omitted from this presentation. Patients whose sutures became fused after cerebrospinal fluid (CSF) diversion procedures for primary hydrocephalus have been excluded as well as those who had deformed ventricular systems secondary to abnormal skull configurations as noted by Dandy and Laitinen.

Results

Table 1 lists the pertinent data concerning the 14 patients (8 females, 6 males) studied. Eight of the 14 had associated malformations of the extremities characteristic of Apert's syndrome. The presence of hydrocephalus was confirmed by air study in 12 and by postmortem examination in two. Two of the 14 patients had aqueductal stenosis while in the others no definite obstruction of the cerebrospinal fluid pathways was demonstrated. Six patients were of dull-normal to normal intelligence but the remaining eight patients were moderately to severely retarded.

Case Reports

Case 1

Examination. This girl presented a grotesque appearance when examined at 8½ years of age. Her head was extremely elongated in the vertical plane with the anterior superior portion lacking a cranial vault and transilluminating completely. The edges of the frontal and parietal bones extended only two-thirds of the distance from base to vertex. The posterior portion of the head was flattened. Although the head circumference was only 56.5 cm, the tragus-to-tragus distance over the vertex measured 60 cm. The eyes were wide-set, divergent, and bulging; the eyelids covered the globes incompletely. There was a severe exposure keratitis. The patient visually followed objects held at a distance of 1 to 2 feet. The bridge of the nose was flat. The maxilla was underdeveloped with a prominent mandible. Associated skeletal defects were absent. Her developmental age was approximately 14 months. A pneumoencephalogram demonstrated aqueductal stenosis and generalized craniosynostosis (Fig. 1).

Comment. This patient demonstrates the concurrence of craniosynostosis and non-communicating hydrocephalus secondary to aqueductal stenosis. This case and Case 2 were the first encountered with these defects. Aqueductal stenosis was demonstrated, but as later experience showed, this finding is exceptional.

Case 9

A 10-month-old Negro boy was first evaluated because of respiratory distress. He was delivered after a normal pregnancy but exophthalmus and a large head were noted at birth, and an air study a few days later demonstrated hydrocephalus. He was rehospitalized at 2 months of age because of an upper respiratory infection. His head circumference then was 41 cm, and a repeat pneumoencephalogram showed further enlargement of the ventricles; no air was visualized in the posterior fossa or over the cerebral hemispheres.

Examination. On admission at 10 months of age the patient weighed 6.3 kg and his head circumference was 44 cm. Developmentally, he was functioning at the 6-month level. The skull was peculiarly shaped; the forehead sloped posteriorly, the eyes were wide-set and prominent. The nasal bridge was flat and the palate highly arched. Bony ridges were palpable over the coronal and metopic sutures. Visual fields and acuity, within the limits of testing, were normal. The
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optic discs were pale. There was spontaneous vertical nystagmus with associated fluttering of the eyelids, and upward gaze was limited. On lateral gaze there was horizontal nystagmus with a rotatory component. Muscular tone and movements were normal but there was scissoring of the legs when extended with the patient supported vertically. Plantar and palmar grasping reflexes and tonic neck reflexes were present. Pneumoencephalography demonstrated dilated cisterns in the posterior fossa and normal sulci over the convexities of the cerebral hemispheres behind the coronal suture; air failed to enter the ventricular system.

At 11 months of age, a plastic repair of the cranium was carried out. A postoperative pneumoencephalogram (Fig. 2) showed moderately dilated ventricles with no evidence of obstruction to the passage of air. The patient’s current status is unknown as he has been lost to follow-up examination.

Comment. The mechanism of the hydrocephalus in this case was not elucidated. Although intracranial pressure was increased, there was no evidence of cerebral atrophy producing the dilated ventricular system as previously postulated. Technical factors may have been responsible for the failure of air to enter the ventricular system during the preoperative pneumoencephalogram.

Case 10

A 4-week-old baby girl was evaluated for premature closure of the sagittal suture and a large head. At birth, the head had been noted to be large with a circumference of 41 cm. Development during the first month of life was normal.

Examination. At 4 weeks, the head circumference was 43 cm, and the skull was increased in its anteroposterior diameter. The sagittal suture was closed and ridged to palpation. The scalp veins were dilated, and there was frontal bossing. Except for hyperreflexia and increased tone in the legs, the neurological examination was normal.

A ventriculogram demonstrated moderate enlargement of the lateral and third ventricles with no evidence of obstruction to the flow of air. Cortical atrophy was present over the right parietal region.

The sagittal synostosis was corrected surgically. The patient continues to develop normally at 2½ years of age, but her head circumference is 52 cm and of hydrocephalic contour.

Comment. In this case of isolated sagittal suture synostosis, hydrocephalus was present from birth and progressed after plastic repair of the sagittal suture. This suggests that the cerebral defect was independent of closure of the sagittal suture, but that the growth of the cranium was limited by the restricting cranial defect.

Case 13

First Examination. This baby boy was evaluated at 7 months of age because of a large head and syndactyly of the fingers and toes, associated with pre- and postaxial polydactyly. In addition to the abnormalities of the phalanges, there was flattening of the nasal bridge, mild hypertelorism and macrocrania, and a head circumference of 47 cm. His development was minimally retarded. Skull radiographs demonstrated the patency of all cranial sutures, and pneumoencephalography revealed the presence of mild communicating hydrocephalus.

Second Examination. The patient was next evaluated at 26 months of age. In the interim, synostosis of the coronal suture had developed. Repeat pneumoencephalography demonstrated progression of the communicating hydrocephalus with dilatation of the posterior portion of the third ventricle and absence of the posterior portion of the corpus callosum (Fig. 3). There was no evidence of cerebral atrophy. Technetium-albumin cisternography demonstrated normal CSF flow patterns. Strip craniectomy for correction of the coronal suture synostosis was followed by an uneventful course.

Comment. Development of craniosynostosis beyond the neonatal period in association with syndactyly has not previously been reported. In this case the hydrocephalus was present prior to the appearance of closure of the coronal suture on radiographs and continued to progress during the development of the synostosis. No clue as to the mechanism of hydrocephalus was obtained by the cisternography since the flow pattern of the injected isotope was normal.

Discussion

The association of craniosynostosis and
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age, Sex</th>
<th>Cranium Shape and Radiographic Findings</th>
<th>Measurements*</th>
<th>Other Deformities</th>
<th>Pneumoencephalographic Findings</th>
<th>Neurological Status</th>
<th>Surgery</th>
<th>Postmortem Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8 yrs 8 mos F</td>
<td>decreased AP diameter; increased vertical diameter</td>
<td>HC 56.5 cm; tragus-tragus 60 cm (over vertex)</td>
<td>—</td>
<td>aqueductal stenosis with gross enlargement of ventricular system</td>
<td>marked proptosis; decreased vision; developmental age 14 mos</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>10 mos F</td>
<td>prominent frontal and temporal regions</td>
<td>HC 38 cm at 4 mos; birth wt 1300 gm</td>
<td>sydactyly of fingers, toes</td>
<td>severe retardation</td>
<td>—</td>
<td>aqueductal atresia, cortical mantle varied from 2-10 mm</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>5 mos M</td>
<td>increased vertical diameter; decreased AP diameter; synostosis of coronal sutures</td>
<td>.sydactyly of fingers, toes</td>
<td>—</td>
<td>? retarded</td>
<td>—</td>
<td>brain wt 650 gm, dilatation of lateral and 3rd ventricles; patent aqueduct; corpus callosum absent posteriorly</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>10 yrs F</td>
<td>increased vertical diameter; bulging temporo-mandibular regions with narrow waist above this, followed by enlargement of calvarium to the vertex</td>
<td>HC 49.5 cm; tragus-tragus 42 cm</td>
<td>sydactyly of fingers, toes</td>
<td>generalized ventricular enlargement especially of the frontal and temporal horns of the lateral ventricle</td>
<td>severe retardation</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>5 yrs F</td>
<td>increased vertical diameter; narrow transverse diameter</td>
<td>HC 49 cm; tragus-tragus 35 cm</td>
<td>—</td>
<td>enlargement of the right lateral ventricle and large supra- pineal recess</td>
<td>severe retardation</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>6</td>
<td>9 yrs M</td>
<td>increased vertical diameter; decreased AP diameter</td>
<td>HC 50 cm; tragus-tragus 40 cm</td>
<td>sydactyly of fingers, toes</td>
<td>generalized ventricular enlargement</td>
<td>proptosis with limited eye movements; severe retardation</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>7</td>
<td>4 yrs M</td>
<td>increased transverse diameter; decreased AP diameter; synostosis of coronal sutures</td>
<td>HC 48 cm</td>
<td>sydactyly of fingers, toes</td>
<td>constriction of subarachnoid space in upper cervical and foramen magnum regions; enlargement of lateral ventricles with disproportionately severe involvement of temporal and parietal regions</td>
<td>proptosis; dull normal intelligence</td>
<td>cranioplasty at 4 yrs</td>
<td>—</td>
</tr>
<tr>
<td>8</td>
<td>3½ yrs M</td>
<td>increased transverse diameter; decreased AP diameter</td>
<td>sydactyly of fingers, toes</td>
<td>moderate generalized ventricular enlargement and absence of septum pellucidum</td>
<td>severe retardation</td>
<td>—</td>
<td>—</td>
<td></td>
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</tbody>
</table>

*HC = head circumference.
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age, Sex</th>
<th>Cistern</th>
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<th>Surgery</th>
<th>Postmortem Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>4 days M</td>
<td>synostosis of coronal and metopic sutures</td>
<td>HC 41 cm</td>
<td>generalized ventricular enlargement</td>
<td>paltor of optic discs; vertical nystagmus with fluttering of eyelids</td>
<td>—</td>
</tr>
<tr>
<td>10</td>
<td>1 mo F</td>
<td>synostosis of sagittal sutures; increased AP diameter</td>
<td>HC 41 cm (at birth)</td>
<td>HC 43 cm</td>
<td>moderate enlargement of lateral &amp; third ventricles, cortical atrophy over right parietal region</td>
<td>normal</td>
</tr>
<tr>
<td>11</td>
<td>1 mo F</td>
<td>synostosis of lambdoid and lateral portions of coronal &amp; squamous sutures</td>
<td>HC 33 cm</td>
<td>HC 44 cm</td>
<td>communicating hydrocephalus with marked dilatation of lateral and third ventricles</td>
<td>moderate retardation</td>
</tr>
<tr>
<td>12</td>
<td>2 mos F</td>
<td>synostosis of all sutures</td>
<td>HC 33 cm</td>
<td></td>
<td>slight dilatation of lateral ventricles</td>
<td>normal</td>
</tr>
<tr>
<td>13</td>
<td>7 mos M</td>
<td>patent sutures radiographically</td>
<td>HC 47 cm</td>
<td>HC 51 cm</td>
<td>slight communicating hydrocephalus</td>
<td>developmental quotient 80</td>
</tr>
<tr>
<td>14</td>
<td>1 mo F</td>
<td>synostosis of the coronal sutures</td>
<td>HC 39 cm</td>
<td>HC 49 cm</td>
<td>slight dilatation of lateral ventricles and enlarged cisterna magna</td>
<td>developmental quotient 85</td>
</tr>
</tbody>
</table>

**TABLE (1 continued)**
FIG. 1. Case 1. Pneumoencephalogram demonstrating air in the fourth ventricle and a distorted aqueduct, but none in the third or lateral ventricles. The lateral ventricles were almost certainly enormous as judged by the size and total transillumination of the head.

hydrocephalus was first noted at least five decades ago, but was not discussed in several large, recent reviews of premature closure of cranial sutures. Park and Powers described an autopsied case in which there was moderate internal hydrocephalus but concluded that this must be unusual since none of their other patients had abnormally large head circumferences. However, this reasoning may not be valid in cases of craniosynostosis since the shape of the skull is abnormal and consequently the circumference may not be a true reflection of brain volume. False impressions are obtained when the circumferences of synostosed skulls are plotted on percentile grids composed from normally shaped craniums. In scaphocephaly, the circumference is falsely increased in comparison to the volume, while in brachycephaly it is decreased. This discrepancy is readily apparent when comparing three rectangles: 4 × 16, 13 × 4.9, and 8 × 8; in each instance the area is 64 while the perimeters are 40, 35.8, and 32 respectively. Indeed, in the case of coronal synostosis cited by Park and Powers, the head circumference was said to be less than normal. In scaphocephaly, the apparently increased head circumference may contribute to the belief that the rate of head growth exceeds normal.

Other authors have also noted the concurrence of these conditions. Laitinen reported that of 23 patients with craniosynostosis in whom pneumoencephalography was performed, three were found to have enlarged ventricles. Of Bertelsen's 48 patients in whom air contrast studies were performed, 12 demonstrated moderate to pronounced ventricular dilatation but of this total, seven examinations were interpreted as showing cortical atrophy. Enlarged ventricles secondary to cerebral atrophy must be distin-

guished from true hydrocephalus. The cases reported by McLaurin and Matson to have slight to moderate ventricular enlargement by pneumoencephalography are suspect for this reason since many of them also had deep subarachnoid spaces over the cerebral surfaces, which may have been indicative of cerebral atrophy. In Andersson and Gomes' series, hydrocephalus was demonstrated in two patients, one of whom had aqueductal stenosis. A recent survey of craniosynostosis in the Amish by Cross and Opitz revealed one case of communicating hydrocephalus in a patient with Crouzon's disease.

Isolated premature closure of the sagittal suture is often thought to be of no consequence except for the cosmetic deformity. While this may be the situation in the majority of patients, cases of increased intracranial pressure and scaphocephaly have been cited. Cerebrospinal fluid pressures, when measured, have ranged from 200 to 310 mm; patients have had papilledema, optic atrophy, blindness, and radiographic findings on plain skull films consistent with increased pressure, i.e., widening of open sutures, erosion of the dorsum sellae, and increased digital markings. The mechanism responsible for the increased pressure has not been considered in detail, but hydrocephalus may be responsible in some cases. Andersson and Gomes reported a patient with sagittal synostosis and aqueductal stenosis. Another of their cases with increased intracranial pressure and scaphocephaly had a normal pneumoencephalogram. Therefore, progressive hydrocephalus may not be responsible for all cases of intracranial hypertension and sagittal synostosis. However, the hydrocephalus need not be progressive as exemplified by some of our cases and by the lack of examples of progressive head enlargement in other large series of cases. Consequently, slightly increased intracranial pressure in association with craniosynostosis may be transient and due to a relatively mild form of ventricular enlargement which later becomes compensated.

The mechanisms responsible for the hydrocephalus have not been clearly elucidated. Various theories include interference with cerebrospinal fluid flow from obstructed or cramped pathways, bending of the aqueduct, or stoppage of venous flow. However, our demonstration of a normal cerebrospinal fluid flow pattern on radioisotope cisternography in one case and the progression of hydrocephalus after craniectomy in another, when a mechanical obstruction should have been relieved, indicate that other pathogenetic mechanisms must be considered. In several series reported earlier, dilated ventricular systems were observed but often attributed to an atrophic process secondary to increased intracranial pressure, a direct consequence of the craniosynostosis itself. That this mechanism cannot be invoked in all cases is clearly demonstrated by

Fig. 3. Case 13. Repeat pneumoencephalogram performed after the development of craniosynostosis. Left: Lateral view. Right: Anteroposterior view.
our patients who developed progressive hydrocephalus after surgical correction of the craniosynostosis, had continued enlargement of an abnormally shaped head beyond that needed to accommodate a normal-sized brain, and had hydrocephalus secondary to aqueductal stenosis. Hypoplasia of the chondrocranium with basilar deformity resulting in compression of outflow tracts of the fourth ventricle has been incriminated as the mechanism responsible for the ventricular enlargement in the most severe form of craniosynostosis associated with hydrocephalus, the kleeblattschädel or cloverleaf skull syndrome.5,5

In most cases the hydrocephalus appears to be associated with the premature synostosis rather than a direct consequence of it. Communicating or noncommunicating forms of hydrocephalus may be present and the abnormal ventricular enlargement may progress even after surgical treatment of the cranial defect. The noncommunicating hydrocephalus may be due to true aqueductal stenosis or perhaps to a functional insufficiency as demonstrated by one of our cases in which dilatation of only the lateral and third ventricles was found in spite of a patent aqueduct at autopsy.

The etiology of premature closure of cranial sutures is unknown. A faulty development of the blastemal mesenchyme which is destined to form the sutures was postulated by Park and Powers15 and is a plausible explanation. Experimentally, the condition has been produced by mechanical trauma to the sutural area,14 and by giving large amounts of Vitamin D to pregnant rabbits, which results in the appearance of the malformation in the offspring.9 There seems to be little clinical applicability of the experimental models to the condition as it is commonly seen in humans except for the association of premature synostosis in the syndrome of supravalvular aortic stenosis and the rachitid diseases including hypophosphatasia.

The evaluation and therapy of craniosynostosis should include consideration of the possibility of concomitant hydrocephalus, and, when this is progressive, ventricular shunting procedures are warranted and could reduce or prevent the mental retardation and neurological sequelae accompanying the syndrome. Unfortunately, well-documented examples of this are rare, and mental retardation may occur despite early recognition and treatment of the hydrocephalus and craniosynostosis.

Summary

Fourteen cases with concurrent hydrocephalus and craniosynostosis have been reviewed. The hydrocephalus, which was communicating or noncommunicating, appeared to be associated with but independent of the premature closure of the cranial sutures. The ventricular enlargement often was progressive and contributed to the neurological sequelae and mental retardation.

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References

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