Dorsal third ventricular cyst: an entity distinct from holoprosencephaly

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The treatment and subsequent developmental progress of six children with dorsal third ventricular cysts are described. This cystic malformation has a radiological appearance which is superficially similar to that of the dorsal cyst of alobar holoprosencephaly, especially when the third ventricular cyst is large. Indeed, previous reports have identified this abnormality as a form of holoprosencephaly. However, careful study reveals that the dorsal third ventricular cyst is a distinct entity both developmentally and clinically. The six patients in this series were effectively treated with shunts, and their subsequent developmental progress was assessed by means of the Pre-screening Developmental Questionnaire-Revised as well as the Bayley Scales of Infant Development. The nomenclature and differences between this entity and the holoprosencephalies are reviewed. The authors conclude that dorsal third ventricular cysts have a developmental and clinical course more similar to that of arachnoid cysts than to that of the holoprosencephalies.

KEY WORDS • corpus callosum • alobar holoprosencephaly • interhemispheric cyst • abortive holoprosencephaly • ventricular cyst • dorsal cyst • children

Agenesis of the corpus callosum was first described in 1812 by Reil.\(^9\) In 1934, Davidoff\(^6\) and Dyke\(^7\) characterized the pneumoencephalographic (PEG) appearance with the first case diagnosed in a live patient. Authors agree that isolated agenesis of the corpus callosum causes no significant neurological deficits.\(^6\) Rather, the frequently associated abnormalities seem to produce the attendant clinical symptoms. Among these associated abnormalities is a 23% incidence of cystic malformations: 8.8% in the interhemispheric fissure, 5.7% on the convexity (porencephalic), and 4.8% unspecified.\(^1\)

A cystic structure is occasionally found dorsal to the third ventricle in agenesis of the corpus callosum. This abnormality has the elements of a large interhemispheric fluid cavity associated with partial or complete agenesis of the corpus callosum, in the presence of a complete interhemispheric fissure and lateralization of the ventricles. It has been denoted by several terms: diencephalic cyst,\(^2\) dorsal cyst,\(^3\) interhemispheric arachnoid cyst,\(^4\) midline porencephalic cyst,\(^4\) and interhemispheric intradural cyst.\(^5\) Due to its radiological similarity to the dorsal cyst of alobar holoprosencephaly, this entity has frequently been considered a form of holoprosencephaly, and some have associated with it the same poor prognosis.

We consider that the interhemispheric cyst associated with agenesis of the corpus callosum, which we term “dorsal third ventricular cyst,” is an entity distinct from the holoprosencephalies both developmentally and clinically. We present six patients with this disorder and give a brief review of previously reported cases to make the point that the prognosis in these patients, once their cysts are effectively decompressed, may be better than previously thought.

Clinical Material and Methods

Patient Population

Between June, 1986, and April, 1990, six children (three boys and three girls) were diagnosed at our institution as having dorsal third ventricular cysts (Table 1). Their age at diagnosis ranged from neonatal (three cases) to 13 years. All but one had been referred to a pediatric neurosurgeon (W.J.O.) for evaluation of hydrocephalus and progressive macrocrania. One patient (Case 5) had no medical problems prior to suffering the generalized seizure that led to his diagnosis.

Imaging and Surgery

The radiological evaluation consisted of brain computed tomography (CT) scans and magnetic resonance (MR) imaging. The initial procedure was placement of a ventriculoperitoneal (VP) shunt, unless the radiological studies indicated the presence of septations in the cyst. In that event, ventricular exploration and creation of a communication of all cystic cavities were performed prior to placement of a VP shunt.
Dorsal third ventricular cyst

TABLE 1
Clinical characteristics of six patients with dorsal third ventricular cyst

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex</th>
<th>Age</th>
<th>Presentation</th>
<th>Complications</th>
<th>Follow-Up Period</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>15 mos</td>
<td>failed shunts</td>
<td>none</td>
<td>37 mos</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>7 days</td>
<td>hydrocephalus</td>
<td>residual cyst after 2 mos</td>
<td>20 mos</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>3 mos</td>
<td>&quot;holoprosencephaly&quot;</td>
<td>ventriculitis</td>
<td>29 mos</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>1 day</td>
<td>hydrocephalus</td>
<td>reseptation after 2 mos</td>
<td>64 mos</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>13 yrs</td>
<td>seizure</td>
<td>none</td>
<td>29 mos</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>5 days</td>
<td>hydrocephalus</td>
<td>chronic subdural hematoma</td>
<td>19 mos</td>
</tr>
</tbody>
</table>

Follow-Up Evaluation

The follow-up period averaged 33 months (range 19 to 64 months). All patients were examined at 6- to 12-month intervals with at least one postoperative CT scan obtained. The Denver Prescreening Developmental Questionnaire, Revised (PDQ-R) was administered by telephone to the mothers of the youngest five children. (The oldest child was outside the age range for PDQ-R assessment.) This evaluative tool tests development in four areas (personal/social, gross motor function, fine motor-adaptive function, and language) and assigns to each of these an approximate age at which a "normal" child would perform these skills. The age level at which the child performed in each of the four areas was divided by the patient’s chronological age to produce a normalized percentage. Care was taken to validate the answers to the questions asked in the telephone interview. Detailed descriptions of the children’s behavior were requested to prevent overoptimistic parental interpretation from influencing the scoring. The Bayley Scales of Infant Development (BSID), a frequently used standardized test of developmental achievement, was given to two of the patients to verify concordance with the PDQ-R. The case histories of these two patients follow.

Illustrative Cases

Case 2

This baby boy was delivered at term by Caesarean section with the prenatal diagnosis of hydrocephalus. The pregnancy was complicated only by hydrocephalus. The infant’s Apgar scores were 9 and 9 at 1 and 5 minutes.

Examination. The infant’s head circumference was 44 cm (above the 98th percentile for his age) and the cranial sutures were widely diastatic. There was normal tone and spontaneous movement of all four extremities. The Moro, grasp, and sucking reflexes were normal.

A CT scan showed a very large midline cyst with multiple intracranial cavities. An MR image revealed that the cyst had displaced the cortex into a thinned peripheral mantle (Fig. 1a to c). Both lateral ventricles were displaced posteriorly and inferiorly, and the interhemispheric fissure was present to the left of midline. Intrathecal injection of contrast medium filled the lateral ventricles but did not communicate with the midline cyst.

Operation. The patient underwent a right parietal craniectomy at the age of 7 days. When the dura was opened, cystic cavities were immediately encountered. Multiple loculations were found, some containing clear fluid and others yellowish fluid. All visible septations were lysed. A cystoperitoneal shunt utilizing a low-pressure Hakim valve was inserted to complete the procedure. The cyst wall was arachnoid in origin.

Postoperative Course. The patient developed focal left-sided motor seizures which were treated with phenobarbital and phenytoin. Otherwise he did well, with a 1.6-cm decrease in head circumference. Two months after surgery, the shunt became obstructed. A CT scan performed after instillation of intraventricular dye revealed the presence of a residual midline cyst as well as a large subdural cavity. The cyst was made to communicate with the lateral ventricles and a new VP shunt was placed. The subdural space was shunted with a separate catheter and connected to the common peritoneal catheter.

At 20 months of age, the patient’s CT scan showed re-expansion of the cortex to fill the intracranial space (Fig. 1d). The child had met or exceeded all milestones for language and social development as evaluated by the PDQ-R (Fig. 2). However, he exhibited mild developmental delays in fine and gross motor skills, likely related to a marked right hand preference. These results were confirmed by the BSID, which showed mental development at the 20-month age level and motor development at the 16-month age level.

Case 3

This 3-month-old girl was referred for evaluation of progressive macrocrania and holoprosencephaly. A diagnosis of lobar holoprosencephaly had been made at birth on the basis of a CT scan. The family had been advised of the likely prognosis and had chosen nonaggressive treatment. Despite the child’s physical problems she thrived and was referred for evaluation. She also had a number of congenital anomalies including choanal atresia, right clubfoot, syndactyly, and a seizure disorder.

Examination. The child had gasping respirations and could not support her head. The head circumference was 44 cm (above the 98th percentile for her age group). The metopic and sagittal sutures were widely patent and scalp veins were prominent. Hypertelorism and micrognathism were prominent. Movements of all four extremities were spontaneous, and tone was normal. There was withdrawal in response to painful stimuli. The child did not clearly respond to light or noise.

Magnetic resonance images were obtained revealing a large midline dorsal cyst extending toward the vertex.
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**FIG. 1.** Case 2. a-c: Magnetic resonance T₁-weighted images at birth showing a large midline cyst with multiple intracranial compartments. The lateral ventricles can be seen displaced posteriorly and inferiorly (arrows). Note the interhemispheric fissure (open arrow, a) and falx (arrowhead, c). There is agenesis of the corpus callosum. (Sagittal image taken 35 mm left of midline.) d: Computerized tomography scan obtained after shunt revision demonstrating a decrease in cyst volume. The falx posteriorly (arrow) and interhemispheric fissure anteriorly (open arrow) are clearly seen.

**FIG. 2.** Graph showing Prescreening Developmental Questionnaire, Revised (PDQ) scores represented as a percentage of chronological age. Language scores were near-normal in all patients except one (Case 3), whose score may have been influenced by ventriculitis and 3 months of nontreatment prior to shunting. Skills tested: PS = personal/social; FMA = fine motor-adaptive; GM = gross motor; LAN = language.

(Fig. 3a to c). Both lateral ventricles were present and displaced away from the midline. Neither the falx nor the corpus callosum could be identified.

**Operations.** The patient underwent placement of a medium-pressure cystoperitoneal shunt. The pathology of the cyst wall was consistent with arachnoid. Eighteen months after the initial shunt placement, the patient developed an abdominal pseudocyst which required externalization of the shunt. The cerebrospinal fluid ultimately became infected and antibiotic therapy was required for several weeks before a new shunt could be placed.

**Postoperative Course.** With decompression of the cyst, there occurred a re-expansion of the cortex. The true ventricular relationships were revealed on a postoperative CT scan (Fig. 3d). There was a complete interhemispheric fissure with extension past the normal location of the corpus callosum. The lateral ventricles continued to be displaced laterally, without a wide communication between them. Clinically, it became apparent that the child was not blind; however, hearing could not be confirmed.

At 29 months of age, the infant performed at approximately one-third her chronological age in all four areas on the PDQ-R. Formal developmental assessment with the BSID confirmed these results, revealing profound delays in motor function such as the inability to hold her head upright. Combined with the child’s severe sensory impairment, this resulted in a motor developmental level of less than 1 month of age. Mental development rose to a ceiling of 7 to 8 months due to the child’s ability to cooperate in back-and-forth games with her parents.

**Results**

**Developmental Assessment**

Figure 2 shows the PDQ-R results for the six patients. Although one patient (Case 5) was not tested due to his age, his functional status both at school and at home were clearly normal pre- and postoperatively, and PDQ-R scores were assigned to him accordingly. All but one of the patients (Case 3) had language scores that were essentially normal. This is in contrast to gross motor, fine motor-adaptive, and personal/social scores, which lagged behind.

On detailed questioning, it became evident that some of the poor scores in the personal/social category were secondary to poor motor skills. That is, a child might have had the cognitive ability and desire to dress himself but lacked the motor skills to button his shirt. This was certainly true in Cases 3 and 6; both patients demonstrated certain personal and social skills beyond those indicated by their PDQ-R scores.

**Surgical Results**

All six patients had decompression of their cysts and hydrocephalus as determined by postoperative CT scans. Head circumferences became normal with time.
Dorsal third ventricular cyst

Fig. 3. Case 3. a–c: Magnetic resonance T1-weighted images at 3 months of age demonstrating a large cyst posteriorly in the interhemispheric fissure. The lateral ventricles are clearly seen (arrows), as is an anterior portion of interhemispheric fissure (arrowhead, at). There is agenesis of the corpus callosum. d: Computerized tomography scan obtained 1 month after shunt placement showing expansion of the cerebral cortex and decompression of the midline cyst. The interhemispheric fissure (arrow) can now be seen fully.

unless shunt failure developed. There were a total of four complications in the series (Table 1). One patient had a residual cyst which required reoperation (Case 2, see above), one patient developed septations necessitating ventricular exploration; there was one case of a chronic subdural hematoma and one case of ventriculitis (Case 3, see above).

Discussion

Prognosis

These six patients illustrate the spectrum of dorsal third ventricular cysts. Five of the six patients had normal or near-normal scores in the area of language development after decompressive surgery. In contrast, fine motor and, to a lesser extent, gross motor skills lagged behind. Notably, the poorest scoring patient (Case 3) was the one patient who had prolonged non-treatment of her symptomatic hydrocephalus. In addition, she was the only patient with ventriculitis in the series. The two BSID scores confirm the results obtained by the PDQ-R.

Clearly, there is a potential for near-normal neurological development in these children if decompressive shunting is performed early. This suggests that cortical distortion is secondary to the cysts' mass effect and is not a primary defect of cerebral development, similar to the situation in arachnoid cysts. Indeed, the language scores rather than motor scores were the most consistently normal area of function in these patients, which is the opposite of the result one might expect if there were an intrinsic defect of cortical, and thus, cognitive development. Further follow-up study is needed to establish if language performance continues to progress. Nevertheless, these results argue that similar cystic malformations should be shunted early and aggressively to reduce the mass effect of the cyst quickly.

Nomenclature

Previous reports have frequently labeled similar large cystic malformations as a type of holoprosencephaly on the basis of ventricular configuration and/or association with defects in the corpus callosum, a categorization that derives from the original classification scheme for the holoprosencephalies devised by DeMyer and Zeman. In their 1963 paper, these authors formulated the term "holoprosencephaly" to better represent a group of abnormalities which had previously been called the "arhinencephalies." They intended the term to indicate "the fundamental defect, the tendency for the prosencephalon to remain as a whole, as a simple vesicle incompletely transformed into a complex di- and telencephalon with lobes and hemispheres."

Kundrat argued as early as 1882 that agenesis of the corpus callosum was essentially a form of arhinencephaly. This similarity of agenesis of the corpus callosum with holoprosencephalies, especially when associated with a cyst, was addressed by DeMyer and Zeman. They concluded that agenesis of the corpus callosum should not be routinely grouped with the holoprosencephalies. Rather, "since defects of the corpus callosum undoubtedly result from a variety of mechanisms, many examples of callosal defect are not related to holoprosencephaly."

On the surface, such a distinction appears easy to make. The defects of holoprosencephaly are believed to arise from a failure of the prosencephalon to diverticulate fully into the telencephalon and diencephalon, a process that normally occurs sometime in the first 2 weeks after conception. In its most severe form, failure of the brain to diverticulate results in a single midline ventricle surrounded by an unbroken sphere of cortex. On the other extreme, one may find only a single gyrus of the frontal lobes fused across the midline. In either case, the sine qua non is some degree of incomplete diverticulation.

DeMyer and Zeman implied in their 1963 work that PEG evidence of "midline continuity of frontal neocortex" would distinguish between these two abnormalities. Unfortunately, they included in their classification scheme a subtype of the lobar form, IIIb(5), "[w]ith complete separation of the neocortex across the middle . . . olfactory bulbs present, dorsal cyst, hypoplasia of the corpus callosum." This seemed to allow patients
with full development of their interhemispheric fissures to be classified as holoprosencephalic, provided there was a characteristic dorsal cyst and hypoplasia of the corpus callosum. It is this last, mildest subtype of lobar holoprosencephaly that has led to confusion.

Yokota, et al.,21 have written a critical review on the definition of holoprosencephaly. They concluded that wide ventricular communication does not necessarily signify the common ventricle or the failed lateral migration of holoprosencephaly. Similar radiographic evidence can be found in the absence of the septum pellucidum and in the presence of large interhemispheric cysts. Furthermore, they noted that DeMyer and Zeman5 did not use their own cases to formulate the IIIb(5) subtype of lobar holoprosencephaly. Rather, they cited several cases from the literature, cases that on further review were found to be completely hemispheric, not holoplastic. Thus, Yokota, et al.,21 stated “To make the definitive diagnosis of holoprosencephaly, the essential finding of midline continuity of the forebrain should be proved.”

We agree with the view that brain malformations with complete separation across the midline should not be grouped with the holoprosencephalies. To do so leads to confusion concerning prognosis, and confers on the holoprosencephalies too vast a disease spectrum. DeMyer and Zeman5 had only PEG studies, autopsy specimens, and surgical specimens upon which to base their classification of holoprosencephalies. Since then, CT and MR imaging have been developed, providing a more reliable means of assessing midline fusion. As a result, it is now known that a number of abnormalities produce ventricular configurations similar if not identical to those described with the lobar holoprosencephalies, yet with full hemispheric division.

**Differentiation From Holoprosencephaly**

There are a number of characteristics that distinguish these dorsal third ventricular cysts from each other and the holoprosencephalies (Table 2). Davidoff and Dyke8 and Hyndman and Penfield10 described the angular “bicornuate” appearance and parallel arrangement of the ventricular horns in agenesis of the corpus callosum. Holoprosencephalies tend instead to have very rounded ventricular horns and contiguous, almost fused lateral ventricles. Most commonly, holoprosencephalies are characterized by microcephaly and hypotelorism, while patients with agenesis of the corpus callosum will usually be either normal or abnormal in the opposite direction in these respects. Jeret, et al.,14 in a comprehensive literature review of callosal agenesis, found a 20% incidence of hypotelorism, but not a single case of hypotelorism.

Fitz1 noted that the falx is present in callosal agenesis, although occasionally incomplete because of secondary cysts. In contrast, Osaka and Matsumoto15 reported that the absence or incompleteness of the falx strongly suggests a holoprosencephaly. Because of the failure of diverticulation, no falx develops in lobar holoprosencephalies. Callosal development, on the other hand, normally occurs in the 12th to 18th week, after the falx has developed.13,16 Hence, in their view, insults occurring during the time of callosal development should leave an intact falx.

One must point out, however, that while the distinct corpus callosum develops after the falx, agenesis of the corpus callosum may result from insults to the callosal precursors, elements that are already present during the development of the falx.14,16 It is therefore conceivable that a single insult could cause maldevelopment of both structures. Barkovich and Norman1 recently came to this very conclusion after a radiological study of callosal agenesis and associated defects.

Kendall15 made the point that holoprosencephalies invariably lack fornices and Fitz1 noted that holoprosencephalies have not been associated with posterior fossa cysts, while cysts in this location have been reported in callosal agenesis. Finally, the cyst is posterior to the holosphere in holoprosencephaly, not dorsal (superior) to the third ventricle, as are dorsal third ventricular cysts.

**Prior Series**

From the literature, one finds that a variety of cases have been placed in the general grouping of the holoprosencephalies on the basis of ventricular configuration, rather than consideration of midline fusion. Prognostication based on these reports is difficult, for while some cases may, in fact, be examples of lobar holoprosencephalies many others could well be large dorsal third ventricular cysts.

In 1973, Brocklehurst1 reported four cases of what he considered was a distinct clinical entity, the diencephalic cyst. The diagnoses were made from the operative and PEG findings. The PEG studies were described in two of his cases, of which the first presented with a scalp lesion and the second had a posterior fossa cyst. Both of these PEG studies showed the medial crescentic contour of the lateral ventricular wall associated with

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**Table 2**

<table>
<thead>
<tr>
<th>Differential diagnosis of dorsal third ventricular cyst from holoprosencephaly</th>
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<tr>
<td><strong>Dorsal Third Ventricular Cyst</strong></td>
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<tr>
<td>necessary features</td>
</tr>
<tr>
<td>cyst overlying missing callosal elements</td>
</tr>
<tr>
<td>complete interhemispheric fissure (no fusion)</td>
</tr>
<tr>
<td>Probst bundles (may be distorted with large cysts)</td>
</tr>
<tr>
<td>associated findings</td>
</tr>
<tr>
<td>ventricles parallel, widely separated</td>
</tr>
<tr>
<td>ventricular horns bicornuate</td>
</tr>
<tr>
<td>falx present (at least in part)</td>
</tr>
<tr>
<td>normo- or macrocephalic</td>
</tr>
<tr>
<td>hypertelorism (20%)</td>
</tr>
<tr>
<td>uniformly absent</td>
</tr>
<tr>
<td>not applicable</td>
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Dorsal third ventricular cyst

agenesis of the corpus callosum. These two patients did well after shunting and cyst excision. The other two patients (one with ventriculitis and the other with macrocephaly) were mentally disabled.

Swett and Nixon reported five cases of "agenesis of the corpus callosum with interhemispheric cysts." It is of note that all of their patients were moderately to severely retarded, and two died early in life from aspiration pneumonia. All of them possessed a falx, and the PEG study in their Fig. 2 shows a ventricular configuration identical to that of our Case 3. However, the angiograms showed anterior displacement of the anterior cerebral arteries, which suggests an incomplete interhemispheric fissure. It is interesting that the one autopsy performed revealed absence of the rhinencephalon, suggesting the case was one of holoprosencephaly. The remaining cases are indeterminate.

Rao, et al., presented what they believed was a case of interhemispheric intradural cyst of the falx. However, histopathology of the resected cyst revealed what appeared to be choroid plexus, suggesting a ventricular origin. Thus, this case was likely a cyst of the third ventricle. The child did well after shunt placement. Solt, et al., presented an adult patient with this entity who had been asymptomatic for 64 years before developing severe headaches. The CT scans showed clearly the location of the cyst directly above the third ventricle; an incomplete falx and a lack of midline fusion can be seen on the coronal views. The patient did well after cyst excision.

Conclusions

Our series of six patients illustrates that dorsal third ventricular cysts represent an entity developmentally, radiologically, and clinically distinct from the holoprosencephalies. Dorsal third ventricular cysts respond well to early decompressive shunting and, if necessary, ventricular exploration for removal of septations. If ventriculitis can be prevented, there is the potential for nearly normal neurological development, particularly with respect to language. We strongly believe that infants found to have similar large midline cystic malformations cannot be assumed to have holoprosencephaly. These children should be treated with shunt placement unless there is clear evidence for midline cortical fusion.

We have been impressed with the good outcome of patients with this abnormality in reviewing both our patients and the reports in the literature. Perhaps it was the inclusion of this group of patients that allowed DeMyer and Zeman to state of patients with lobar holoprosencephaly, "Although most will be ametere, some will have sufficient intelligence to live freely in society."

Acknowledgments

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References


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