EXTENSIVE DEVELOPMENTAL DEFECT OF THE CEREBELLUM ASSOCIATED WITH POSTERIOR FOSSA VENTRICLEOCELE

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ABSTRACT

1. A case is described in which an extensive cerebellar cortical defect with modification of collateral roof and brain stem nuclei, periventricular leukomalacia in the cerebral hemispheres, and an anomalous midline thalamic fusion were associated in a neonate with severe hydrocephalus and a massive rhombic roof ventriculocele.

2. The positional interrelationships of the principal types of neurons in the defective cerebellar cortex were normal, implying that the pathologic process intercepted normal development after the 5th fetal month. The cytoarchitectonic and topographic features of collaterally modified nuclear structures and the quality of histopathologic reaction were consistent with this inference.

3. The topographic distribution of the cortical defect is most plausibly explained by perfusion failure in the end fields of perfusion of the principal cerebellar arteries. It is suggested that this perfusion failure was due to compression or torsion of arteries by the massive ventriculocele. Hydrocephalic force with mural compression and ischemia probably accounted for the leukomalacia in the cerebral hemispheres. Hydrocephalus may have played a role in the abnormal thalamic fusion via dienecephalic compression.

4. The hydrocephalus appeared to have resulted from obstruction to CSF circulation at the level of the roofing membrane of the 4th ventricle. The ventriculocele was a massive hydrocephalic expansion of this membrane. The cause of the hydrocephalus was obscure. The outflow foramina were not patent but no internal morphological evidence bears upon whether or not the hydrocephalus preceded the normal opening of the foramina.

INTRODUCTION

Developmental malformations involving extensive portions of the human cerebellar cortex have been described repeatedly since Combette (18) drew attention to an extreme example in 1831. The Dandy-Walker malformation is probably the most commonly encountered (7, 13, 15, 17, 19, 32, 36, 39, 46, 49). Here the defect is predominantly vermian, involving particularly the posterior

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This investigation was supported in part by Public Health Service International Postdoctoral Research Fellowship I F0 5 TW 017301 and by NICHD grant HD 01147 from NIH. Dr. Caviness in a Research Scholar of the Joseph P. Kennedy, Jr. Memorial Foundation.

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ventral region of the vermis. In general this malformation is associated with hydrocephalus, which causes a midline dorsal expansion, or ventriuoleole, of the rhombic roof (13). Compression of adjacent regions of the developing cerebellum by the expanding ventriuoleole has been suggested to be the primary cause of the cerebellar defect (13, 15). This formulation is supported by the observation that a defect identical to the Dandy-Walker malformation in humans arises in the hydrocephalic mouse, hy¹, as a consequence of compression of the developing inferior midline vermis by a hydrocephalic expansion of the roofing membrane of the 4th ventricle (9, 10, 14).

Less commonly, extensive defects of the cerebellum may involve the hemispheres predominantly but encroach upon a substantial portion of the vermis as well (11, 16, 37, 43, 52). The etiology of malformations with this topography is less well understood than that of the Dandy-Walker malformation. By some they are considered to be the result of primary agenesis, that is, as a consequence of some primary abnormality of neurons during the earliest developmental stages (16). By others these are thought to be the consequence of an intercurrent destructive pathologic process acting much later in development (32, 37). The present study is a morphologic analysis of such a specimen with an extensive bilateral hemispheric and vermal defect. The cerebellar abnormalities in this specimen, as in the Dandy-Walker malformation, are most plausibly attributed to compression by a massive ventriuoleole which in turn has developed as a consequence of hydrocephalus. The different topography of the defect is probably related to an unusual asymmetric position of the ventriuoleole.

MATERIALS AND METHODS

The brain, a segment of thoracic spinal cord, and the ventriuoleole were fixed in 10% formalin, embedded in celloidin and sectioned serially in the coronal plane at 35 μ (54). Every 10th section was stained by the Nissl method and the adjacent section by the Loyez method. Every 100th section was stained with hematoxylin-eosin. Age-matched controls and earlier embryonic specimens were sectioned and stained in the same way.

Drawings were made with a calibrated Leitz drawing tube attachment. The lengths of the inferior olivary and the dentate nuclei were estimated on the basis of the thickness and the number of pertinent sections.

Case History

This female infant was delivered by a cesarean section at 36 weeks gestation, after labor had begun spontaneously with the fetus in a breech position. The mother was a 21 year old gravida 2, para 0, abortus 1. She had been diabetic, requiring insulin, since age 15.

From the 10th week of gestation until delivery she had received daily hydrodiuril, thyroid hormone, and supplementary vitamins and weekly deluteval (hydroxyprogesterone caproate) and estradiol valerate. Because of urinary tract infection, she had taken Kynex (sulfamethoxypyridazine) from the 25th week. She had also been given mercuhydrin weekly from the 28th week. Her blood type was O, Rh negative, but no anti-Rh antibody was demonstrated in
CEREBELLAR DEFECT WITH VENTRICLEOCELE

her serum during the pregnancy. There was no family history of neurological disease.

The infant weighed 6 lbs, 12 ozs. at birth. The Apgar score was two after the first 3 minutes and seven 8 minutes after delivery. A 12 × 10 × 8 cm cystic mass, entirely covered by normal integument but transilluminating, was present in the occipital region (Fig. IA). The skull was otherwise normal in configuration with no diastasis of sutures. One umbilical artery was absent. The heart, lungs, and abdominal viscera were normal. The external genitalia were hypoplastic, with a cleft elitoris, small labia majora and minora, and no demonstrable hymenal orifice. The lower extremities were somewhat small though of normal configuration.

X-rays confirmed that the shape of the skull was normal and that it was not enlarged. An unencephalized soft tissue mass extended through a defect in the occipital bone. The vertebral column below the first lumbar level and the sacrum and coccyx were absent. The iliac bones preformed in the midline. The pelvis was hypoplastic, but the hip joints were normal. The infant’s blood was type O, Rh positive; however, a Coombs test was negative.

Throughout the first day of life the infant maintained normal cry, color and respirations. There were sustained clonic movements in the left arm. Urine dribbled constantly from the urethra, sphincteric tone was poor and there were spontaneous movements of the trunk below the waist or of the legs. On the second day of life her temperature climbed to 101° F. (rectally) and respirations became laborious with intercostal retraction. An electroencephalogram at this time was abnormal with generalized high voltage slow activity. The following morning she expired after a convulsive gasp.

General Autopsy and Gross Description of the Brain (BLIH % A64-57)

The general autopsy was remarkable for moderate patchy atelectasis of the lungs, a small uterus and absent vagina. The heart and great vessels and the abdominal viscera were normal, and both ovaries were present. A description of the bony anomalies of the lower vertebral column and pelvis was not recorded.

The occipital cystic structure entered the posterior fossa through a 1.5 cm defect in the occipital bone above the foramen magnum. It proved to be an expansion of the velum medullare which issued from the right lateral recess of the 4th ventricle. The foramina of Luschka and Magendie could not be identified within the velum medullare. Within the posterior fossa the ventriculocele was reflected asymmetrically over the right cerebellar hemisphere and was adherent to the underlying cerebellar cortex. There was no extension above the tentorium. In its extrusion through the occipital bone it was invested by the dura of the posterior fossa. It was readily separable from and not continuous with the overlying normal integument. Otherwise, no abnormality of the meninges or the intracranial arterial tree was noted.

With the exception of the cerebellum, the gross configuration of the brain was normal. Although the gyri of the cerebral hemispheres were somewhat flattened,
Fig. 1A. Photograph of infant with ventriculocele covered by normal integument, normally formed but slightly small legs, and anomalous external genitalia. 1B. Cerebellum and medulla. There is normal foliation in anterior vermis (v) and the floccular and adjacent hemispheric regions ventromedially along the horizontal fissure (h). Damage is moderate to severe in the nodulus (n) and in the simplex lobe anterior to the posterior superior fissure (ps). The convolutional pattern of the dentate (d) is poorly developed on the right more than on the left; that of the inferior olivary nuclei (io) better developed on the left. The ventriculocele issues from the right lateral recess of the enlarged 4th ventricle by a pedicle lined by low cuboidal ependymal cells (p). Dense gliosis borders the ventricle (arrow). An asterisk marks the area photographed at higher magnification in Figure 3A. Cresyl violet × 63. 1C. Cerebral hemisphere and mesencephalic-pontine junction. Massive dilation of the occipital horn of the right lateral ventricle and enlargement of aqueduct with decreased bulk of griseum pontis. Choroid plexus (c) is atrophic. Cresyl violet × 2.3.
they were normal in pattern and size. The cerebellum was reduced in size and asymmetrical, with the right side smaller than the left. Although much of the surface was abnormally smooth and hard with a gray appearance, islands of evidently normally developed cortical folia were present bilaterally as in the region of the flocceulus. The brainstem and diencephalon were not remarkable. No description was recorded of the gross appearance of the spinal cord, the spinal roots, peripheral nerves or muscles.

**Pathologic-Anatomic Analysis from Whole Brain Serial Sections (RPSL-NP No: W-170-64)**

The topologic relationships of major structures were normal. Principal fiber tracts were readily identified, and the maturity of myelination was judged normal with reference to age-matched controls. Except where specified, cytoarchitectonic features were not remarkable with respect to neuronal shape and density and the relative positions of different types of cells. Especially in the brain stem and the central gray matter of the spinal cord (the latter judged in a few available sections), there was a general increase in astrocytes. There were no foci of neuronophagia or inflammatory infiltration, and the histologic appearance of vessels was not remarkable. The principal abnormalities included the ventriculocele and those situated within the ventricular system, the cerebellum and certain of its related brain stem nuclei, the central white matter of the cerebral hemispheres and the fused midline region of the thalamus.

**Ventriculocele and Ventricular System.** The cavity of the ventriculocele communicated with the 4th ventricle via a narrow pedicle which issued from the right lateral recess of the ventricle. The truncated pedicule is illustrated in a single plane of section (Fig. 1B). Near the ventricle the pedicule (Fig. 1B) was lined on its inner aspect by low cuboidal ependymal cells, more remotely from the ventricle by delicate mesothelial cells heavily invested by vascular connective tissue. It was bound by dense glial-mesenchymal adhesion to the superior surface of the right cerebellar hemisphere. At all points the extracranial sector of the ventriculocele was separated from overlying ectoderm by subcutaneous tissue.

The connective tissue investment of the rhombic roof was only mildly increased. There were no inflammatory infiltrates and no adhesions to adjacent arachnoidal or rhombencephalic structures. No foramina could be identified in serial sections. The occluded left lateral recess is visible in Fig. 1B. The 4th ventricle was widely flared with separation of the obex beyond the caudal limit of the area postrema. Rostrally the aqueduct was widely patent in all levels as was the dorsal channel of the third ventricle leading to the aqueduct. Much of the third ventricle was obliterated below the dorsal channel, however, by an anomalously extensive midline thalamic fusion. Only a small channel was patent below the fusion. The foramina of Monro and the lateral ventricle were widely dilated, the latter cavities varying in their distention between 6 and 8 × normal, as estimated planimetrically, in all coronal sections (Fig. 1C). The central canal of the thoracic spinal cord was similarly widely dilated in the
form of an isosceles triangle, with the apex directed dorsally into the plane of the median raphe, though fully contained within neuroglial tissue.

The ependymal lining of the entire ventricular system was largely denuded, with only scattered islands of flattened ependymal cells remaining. Ependymal cells were found in the distended dorsal portion of the central canal of the spinal cord. The perimeter of the ventricular system was universally densely gliotic. The choroid plexuses were small and fibrotic and the secretory cells somewhat flattened. No hemosiderin pigment was evident in these cells in either the hematoxylin-cosin or cresyl violet preparations.

Cerebellum. The cerebellum was small, comparable in size to that of the cerebellum of a fetus of 24–26 weeks, and the right side was smaller than the left (Fig. 1B). The topography of the damage has been reconstructed from serial sections in Fig. 2A [schematic convention and terminology of Jansen and Brodal (29) and Angevine, Mancall, and Yakovlev (5)]. The cortex of the inferior caudal quadrant of the right side, including much of Crus II of the

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Fig. 2A. Mercator’s projection of the cerebellum, with all principal fissures included. Stippled area defines the topography of the defect; intensity of stippling parallels the severity of the defect; maximum intensity represents complete absence of the cortex. 2B. Mercator’s projection of the cerebellum with primary, horizontal and secondary fissures included. Cross-hatched areas represent end fields of perfusion between the medial (sm) and lateral (sl) branches of the superior cerebellar arteries and the anterior (ai) and posterior (pi) inferior cerebellar arteries.
ansiform lobule and the paramedian and biventer lobules, and a small portion of the cortex of Crus II on the left were absent. Cortex over much of the remaining cerebellum was severely modified in its structure. Normal cortex remained only in the flocculi and adjacent ventromedial ansiform lobules along the banks of the horizontal fissure, the paraflocculi, ventromedial biventer lobules along the banks of the secondary fissure, and the rostral regions of the anterior lobe.

Extensive areas of cerebellar cortex seemed to be excessively convoluted, with extension deep into the central medullary region (Fig. 1B). Despite severe distortion and reduction in width, however, the affected cortex contained the principal types of neurons seen normally. Furthermore, lamination was normal (Fig. 1B, 3). As in normal cortex, a layer of granule cells was situated adjacent to the central white matter. Above the internal granular layer was a layer of Purkinje cells. Favorable sections, even in deeply infolded areas, demonstrated normal uniform radial alignment and polarity of the Purkinje cells, with radially ascending apical processes (Fig. 3). A well developed molecular layer, richly endowed with migrating granule cells, separated the Purkinje cell layer from the external granule cell layer. Where the width of the cortex is reduced, it was generally at the expense of external and internal granule layers as well as the molecular layer.

There were no Purkinje cell heterotopias in the central white matter. Aggregates of cells, apparently isolated, proved in serial section to be continuous with the cortex.

*Roof Nuclei and Brain Stem Nuclei with Cerebellar Connections.* Cytoarchitectonic abnormalities were conspicuous in the dentate nuclei and in certain of the brain stem nuclei with cerebellar connections (Fig. 4B, C) [for review of structural interrelationships see Jansen and Brodal (29) and Larsell and Jansen (33)]. The size and convolutional pattern of the left inferior olivary and right dentate nuclei approximated the values for a normal fetus at 5–6 months; measurements from the right olive and left dentate were closer to those of a 6–7 month fetus.

There was a close correspondence between the severity of abnormality within a given region of the inferior olivary complex and the region of cerebellar cortex to which it projects (Fig. 4). Thus, the severely modified ventral lamina of the principal olive, which was largely devoid of neurons, particularly on the left, corresponded to the severely damaged posterior inferior quadrants of the right cerebellar hemisphere; the severe changes in the medial accessory olives, also associated with severe neuronal loss, corresponded to the severely damaged portions of the posterior vermis. In contrast, the well preserved, normally cellular rostral poles of the principal olivary nucleus and dorsal accessory olive corresponded to the undamaged anterior lobe of the cerebellum in its lateral and midline vermal aspects, respectively. Similarly, the normally presented rostral poles of the medial accessory olives, which are also normally cellular, corresponded to the normal flocculi. Finally, changes of an intermediate degree of severity within the remainder of the principal nucleus were matched by
extensive, moderately severe damage in the remainder of the cerebellar hemisphere.

*Cerebral Hemispheres.* Patchy bilateral foci of necrosis were scattered throughout the central white matter in the form of an arc, dorsolateral to the ventricles. They were largest and most numerous near the center of the hemispheres along their rostro-caudal axes, but scattered lesions were also present along both the caudal and the rostral extremities of the lateral ventricles.
Fig. 4A. Drawings of sequential coronal levels of the inferior olivary nuclear complex, proceeding horizontally and vertically from the most rostral level in the upper left to the most caudal level in the lower right. Left olive lies on viewer's right. Shaded areas define sectors of cell loss; the area of darkest shading represents complete loss of neurons. 4B & C Higher power photograph of right (B) and left (C) inferior olivary complex, near the level of Figure 1C. Cresyl violet × 19.
Generally they were confined to the inner aspect of the corona radiata. More extensive lesions penetrated the internal sagittal strata, but none extended into the periventricular zone of gliosis. All were bordered by zones containing reactive astrocytes and macrophages, and showing proliferation of capillaries.

Diencephalon. Midline fusion was seen in two separate zones in the diencephalon. The anterior diencephalic wall was fused from the level of the lamina terminalis, with fusion continuing between the diverging columns of the fornix below the hypothalamic sulcus. A more massive fusion involved the anterior 7 mm of the thalamus, with conjunction not only of the midline thalamic nuclei but of the medial aspects of the anterior ventral and medial dorsal nuclei as well. The zone of fusion was homogenously cellular without evident nuclear partitioning. The lateral aspects of the involved nuclei, in contrast, were normal cytoarchitectonically and normal in size, as determined planimetrically.

Spinal Cord. No tissue was available for examination from the lower portions of the spinal cord, which would have been involved in the caudal dysplasia. At the thoracic level, no abnormalities were evident in the available sections, with the exception of the dilated central canal. Clarke's columns and the dorsal spino-cerebellar tracts were normal.

DISCUSSION

Complex structural anomalies of the cerebellum and its collateral roof and brain stem nuclei were associated in the present case with hydrocephalus and a massive rhombic roof ventriculocoele. Morphologic evidence suggests that the hydrocephalus was initiated as early as the first trimester of gestation. Cerebrospinal fluid circulation appeared to have been blocked by obstruction at the rhombic roof. None of the outflow foramina were patent. Presumably these foramina, which normally open between the 8th and 12th weeks of gestation (12, 53), failed to develop, for reasons not known. The onset of hydrocephalus may have dated from this time or, perhaps, may have occurred even earlier [as has been suggested to be the case in the Dandy-Walker malformation by Brodal (13); Brodal and Hauglie-Hanssen (15); and Hart, Malamud and Ellis (26)].

The dilated 4th ventricle was continuous with the ventriculocoele, and the wall of the ventriculocoele was an expansion of the rhombic roof. As in the Dandy-Walker malformation, this presumably came about as a consequence of hydrocephalic force. Although there is no morphologic evidence as to why this occurred asymmetrically from the right lateral recess rather than in the dorsal midline, it is perhaps possible that an incomplete breakthrough of the right foramina of Luschka created a weakness that favored expansion in that area.

The cytoarchitectonic features of the malformed cerebellar cortex suggest that the cerebellar abnormality itself originated considerably later than the time of origin of the hydrocephalus. Despite the fact that the cortex was excessively convoluted and reduced in width with reduced numbers of granule cells, the relative positions of granule cells and Purkinje cells were normal. Furthermore, the Purkinje cells were uniformly aligned and normally polarized,
even in the most severely abnormal areas. Cytoarchitectonic features normally depend upon cellular interactions which are not completed until the latter part of the 5th to the early part of the 6th month of gestation. Only by that time have the postmigratory granule cells formed a well defined internal granule cell layer subjacent to a precisely aligned Purkinje cell layer, as was found in the present case (42).

Quite different cytoarchitectonic patterns might have been expected had cerebellar development been disrupted at an earlier stage of development. For example, when the cerebellar cortex of experimental animals is mildly or moderately damaged by irradiation during the earliest phases of granule cell migration, Purkinje cells become misaligned and tend to be scattered throughout the zone of postmigratory granule cells (1–3, 28). This cytoarchitectonic abnormality has also been encountered in humans, as in the case of van Bogaert and Radermecker (51)—see their figure 6. In their case the fetus was subjected to irradiation during the 4th and 5th fetal months—the period during which granule cell migration begins (42). Alternatively, disruption before the 5th or 6th month might have produced Purkinje cell heterotopias. Presumably this anomaly occurs when the disrupting event occurs after the Purkinje cells have migrated radially beyond the zone of the roof nuclei, that is, some time after 13–14 weeks (42), though we know of no human case in which this cytoarchitectonic abnormality has actually been correlated with an externally timed event. However, Purkinje cell heterotopias have been observed in mice when the cerebellum is compressed during the period of Purkinje cell migration [Brodal, Bonnevie and Harkmark (14)—see their figure 19a].

The morphologic features of the inferior olivary and dentate nuclei also support the view that the cerebellar cortex in the present case developed normally until well into the second trimester. Its efferent connections with the cerebellar cortex are known from experimental work to be essential to the survival and differentiation of the cells of the inferior olive (26). Observations from the present case seem to illustrate the dependence of the growth and development of the convolutions of the dentate upon its afferent connections with the cerebellar cortex. The overall size and richness of the convolutions of the left inferior olive and the right dentate nucleus approximated that of the normal embryo during the 6th fetal month. That of the contralateral olive and dentate, structurally related to the less abnormal left side of the cerebellum, approximated the structure of the normal at the 6th to 7th fetal month.

Whereas the cytoarchitectonic features of the abnormal cerebellar cortex and collateral nuclei would place the events leading to cerebellar malformation no earlier than the 5th to 6th fetal month, these events may actually have occurred even later, in the early part of the third trimester. The gliosis and mesenchymal tissue reaction in abnormal cortical regions is not typical of that of human specimens which are damaged before the 7th to 8th fetal month. Astrocytes are not even identifiable in the cortex of the cerebellum with the electron microscope until the 5th to 6th fetal month (42).

If the hydrocephalus had originated during the first trimester, the ventriculo-
P. Evrard and V. S. Caviness, Jr.

It is likely that cerebellar development reaches substantial proportions by the 6th to 7th month, the time when cerebellar development appears to have been disrupted, as judged from internal morphologic criteria. This is a period of rapid volumetric increase in the cerebellum (42), and it would appear most plausible that cerebellar development was disrupted by the effects of the ventriculocoele. To some extent damage may have been the result of direct compression, because the area of most severe abnormality, where cortex was absent, lay immediately subjacent to the ventriculocoele, in the right posterior lateral aspect of the hemisphere. However, direct compression does not account for the full extent of the cortical defect, which extended well beyond the region of direct contact with the ventriculocoele. The topography of the abnormality corresponded more closely to the distal fields of perfusion of the principal cerebellar arteries, as schematically represented by Stephens and Stillwell (47) and Krayenbühl and Yasargil (31) in Fig. 2B. Consistent with this formulation is the fact that the distribution of the major cerebellar arteries during the 5th to 6th fetal month is essentially the same as that of the adult (25). This observation suggests that the effects of direct compression by the ventriculocoele were both augmented and extended by a more widespread failure of arterial perfusion. Presumably this was an indirect consequence of the mass, mediated by compression or torsion effects of the ventriculocoele upon the arterial supply to the cerebellum. Perfusion failure mediated by mechanical occlusion of vessels is, of course, regularly encountered in adult neuropathology. A common example is occipital lobe infarction due to posterior cerebral artery occlusion during the course of tentorial neocerebral herniation. It also occurs in other regions of the brain, including the cerebellum, in association with tumors and with increased intracranial pressure from other causes (34, 37).

Malformations of the cerebellum which are similar in their topographic extent to the present case comprise a well known class of developmental anomaly. The topography may be virtually identical, involving much of the hemispheres and part of the vermis as well (11, 16, 37, 43, 52). Commonly the pattern is similar but less extensive (8, 16, 23, 37, 50). Rarely, the involvement may be even more extensive, but there is usually sparing of parts of the flocculus and adjacent portions of the hemisphere at the base of the horizontal fissure (6, 41, 48). Marburg (37) recognized that the distribution of such abnormalities corresponded to the distal fields of perfusion of the principal cerebellar arteries, and suggested that their pathogenesis might be due to infarction secondary to perfusion failure. The ventriculocoele offers a plausible cause of perfusion failure in the present case. Other defects of similar distribution are more difficult to explain, but may be associated with transient failure of systemic fetal circulation occurring, perhaps, as a consequence of intrauterine asphyxia, infection or other reasons not well understood at this time. The fact that cerebellar defects such as these are occasionally associated with porencephaly and microgyria of the forebrain (37) supports this view. Commonly, such forebrain malformations also lie in the distal perfusion fields of the principal cerebral arteries (34).
Certain other abnormalities in the present case may also have been due to the indirect effects of hydrocephalus. The leukomalacia distributed in an arc dorsal and lateral to the lateral ventricles in the forebrain presumably also was the result of perfusion failure, with infarction due to critical occlusion of the terminal vascular capillary fields which have this jurisdiction (21). This finding is a common one in severe hydrocephalus (45), and hydrocephalic compression of capillaries in the juxtaventricular zone has been demonstrated to be its mechanism in experimental animals (20).

The anomalous thalamic fusion found in this case may also have been secondarily related to hydrocephalus. Such fusions have been encountered in other conditions, including the Chiari malformation (4), occipital encephalocele (30) and hydranencephaly (34), malformations in which general dilation of forebrain ventricles during gestation is a frequent common denominator. It is possible that excessive apposition of the medial thalamic surfaces, during or even after the period of normal thalamic fusion between the 4th and 5th fetal months (22), occurred as a consequence of diencephalic compression by the expanded forebrain vesicles, with fusion secondary to this apposition.

The morphologic nature of the lower spinal cord and vertebral column anomaly would have been of considerable interest had the material been conserved at postmortem examination. In its clinical and radiologic features the abnormality was typical of the caudal regression anomaly (40). There is a heightened association of this anomaly with maternal diabetes, and the present case is included in a recent study of this relationship (44). The mechanism of origin of such a malformation in the present case must remain obscure. It is of interest, however, to consider that tissue compression and destruction mediated ultimately by the hydrocephalus could have occurred here as elsewhere in the central nervous system in this specimen, in a manner analogous to that suggested by Gardner (24) to occur in the Chiari malformation and in related dysraphic states.

REFERENCES