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Holoprosencephaly Classified by Computed Tomography

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Five cases are presented to demonstrate the computed tomographic (CT) spectrum of holoprosencephaly. The classifications of alobar, semilobar, and lobar types A and B holoprosencephaly are each represented, with an additional case of semilobar holoprosencephaly complicated by a subdural effusion.

The classification of the holoprosencephalic brain has been modified from that of Kundrat [1] in 1882 to a proposal by Probst [2] in 1979. The most useful classification for the radiologist, however, is the 1963 classification of DeMyer and Zeman [3]. With the aid of the computed tomographic (CT) scanner, the diagnosis of holoprosencephaly can be made and subdivided into alobar, semilobar, or lobar, types A and B. This gives valuable early information to the clinician and avoids confusion with other cerebral abnormalities. We report five children in whom the diagnosis of holoprosencephaly was made on the basis of the plain films, clinical examinations, and CT scans on G. E. 8800 scanners.

Case Reports

Case 1

A newborn boy had a right-sided cleft lip and cleft palate. He had an elevated herpes titer that was believed to have been acquired transplacentally. At 4 months of age, a ventriculo-peritoneal shunt was inserted for increasing head size. He was readmitted at age 14 months with sepsis, and he died. An autopsy was not performed.

The CT scan of the brain at 1 day of age showed a crescent-shaped cerebral mantle that filled the anterior part of the cranial cavity and enveloped a central monoventricle (fig. 1). The caudal part of the cranium was occupied by a dorsal cyst. The midbrain and the elements of the posterior fossa were seen. The rest of the brain was absent. The density measurements in the monoventricle were those of cerebrospinal fluid.

Case 2

A 6-day-old girl was born to a 33-year-old diabetic mother. Apgar scores were 3 at 1 min and 1 at 5 min. Her head was microcephalic (27 cm circumference), and her forehead slanted backward. Chromosomal karyotype revealed a deletion of 13 with translocation of 22. CT revealed a brain that contained more brain parenchyma than had case 1, with development of the temporal lobes (fig. 2). There was a monoventricle and a small dorsal cyst. The thalami were fused.

Case 3

A 1-year-old girl, seen first at 2½ months of age, was a product of a full-term pregnancy. Her head circumference was 32 cm, which is below the third percentile. She had abnormal milestones of development and progressive severe spasticity of both legs. No cleft deformities

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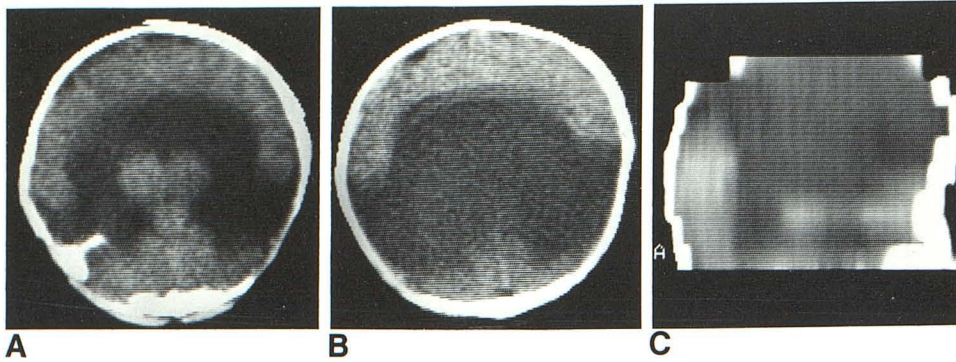


Fig. 1.—Case 1. Alobar holoprosencephaly. **A**, Axial CT scan demonstrating fused thalami, crescent-shaped anterior cerebral mantle, and monovertricle. **B**, Higher axial image with large dorsal cyst and anterior cerebral mantle. **C**, Sagittal reconstruction demonstrates above features. A = anterior.

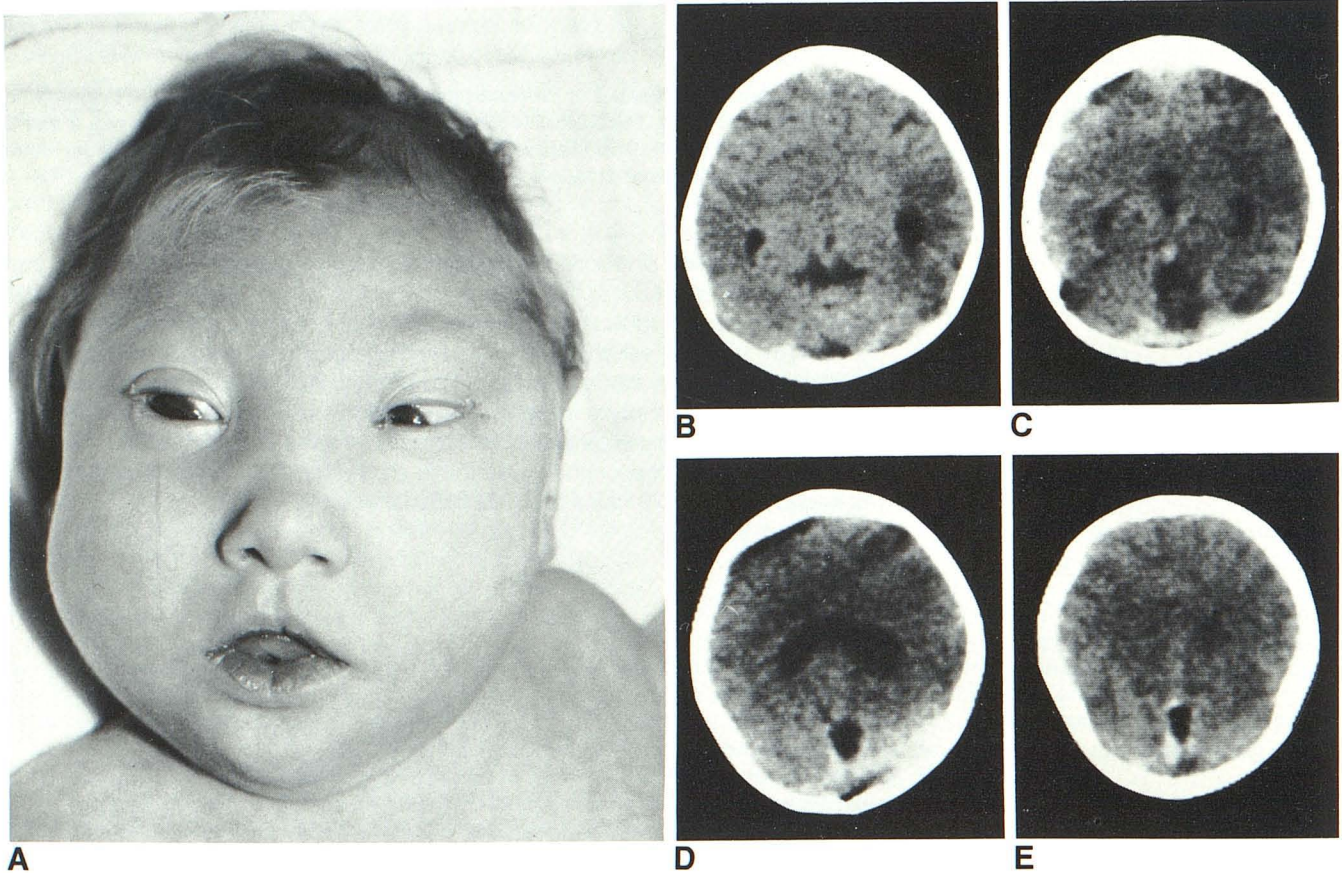


Fig. 2.—Case 2. Semilobar holoprosencephaly. **A**, Facial abnormality with microcephaly. Ascending axial CT scans demonstrate temporal lobe development (**B** and **C**) and persistent monovertricle, dorsal cyst, and absence of hemispherization (**D** and **E**). Coronal reconstruction (not shown) demonstrated thalamic fusion.

were apparent. On CT, a midline continuity of the frontal neocortex was seen (fig. 3). There was still a monovertricle with lateralization of the posterior aspects. A small dorsal cyst seemed to communicate with the ventricle. There was a spleniumlike posterior termination of the infolded brain. The thalami were separated.

Case 4

A 3-day-old boy had a severe cleft palate and lip, right enophthalmos, and microphthalmia. His head circumference was 39 cm and decreased to 37 cm after ventriculoperitoneal shunt. His mother also

had a history of cleft palate. CT revealed large lateral ventricles, common anteriorly but separated posteriorly (fig. 4). The septum pellucidum was absent, and there was a rudimentary corpus callosum. The falx was complete superiorly and a small dorsal cyst was seen posteriorly.

Case 5

A 4-day-old boy with macrocephaly (45.3 cm circumference) was born of a normal pregnancy and cesarean delivery due to breech presentation and fetal-pelvic disproportion. No facial abnormalities

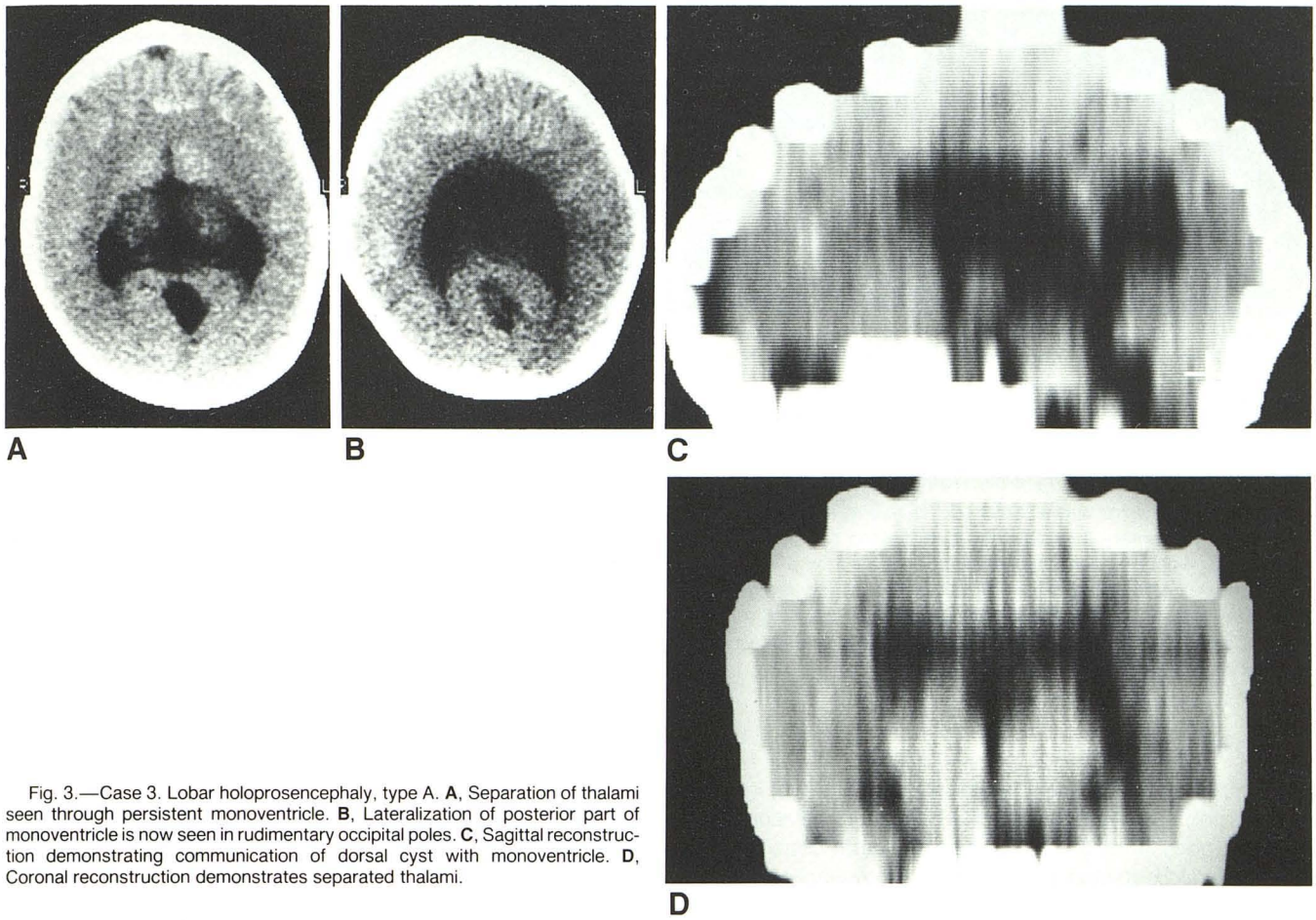


Fig. 3.—Case 3. Lobar holoprosencephaly, type A. **A**, Separation of thalami seen through persistent monoventricle. **B**, Lateralization of posterior part of monoventricle is now seen in rudimentary occipital poles. **C**, Sagittal reconstruction demonstrating communication of dorsal cyst with monoventricle. **D**, Coronal reconstruction demonstrates separated thalami.

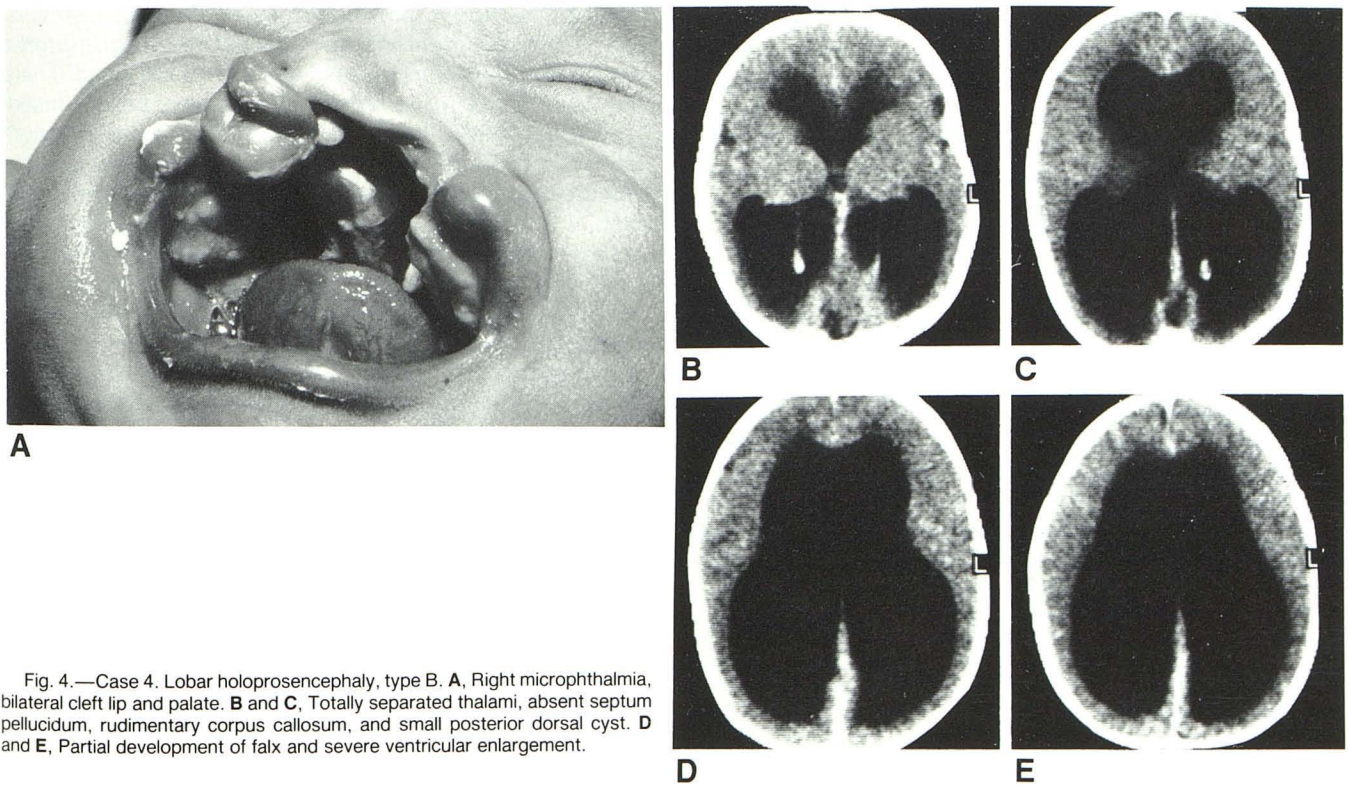


Fig. 4.—Case 4. Lobar holoprosencephaly, type B. **A**, Right microphthalmia, bilateral cleft lip and palate. **B** and **C**, Totally separated thalami, absent septum pellucidum, rudimentary corpus callosum, and small posterior dorsal cyst. **D** and **E**, Partial development of falx and severe ventricular enlargement.

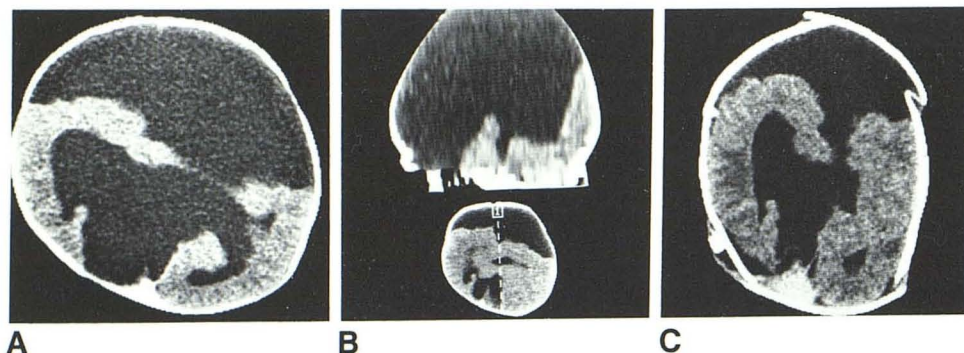


Fig. 5.—Case 5. Semilobar holoprosencephaly complicated by subdural effusion. **A**, Thin membrane separates anterior subdural effusion from posterior monoventricle. **B**, Sagittal reconstruction. (Brain in retroflexed position.) **C**, Post-shunt CT scan with reduction of subdural hygroma and more anterior position of holosphere.

were detected. CT at 4 days of age revealed a large subdural effusion anteriorly and superiorly (fig. 5). A thin membrane separated this from the cortical mass, which was retroflexed. There was a monoventricle, which had rudimentary lateralization. The thalami appeared fused. This was semilobar holoprosencephaly complicated by a large subdural effusion. After a ventriculoperitoneal shunt and drainage of subdural hygroma, his head size decreased to 41 cm. The postoperative CT examination revealed diminution of the subdural hygroma and a more anterior position of the holosphere.

Discussion

The holoprosencephalies represent early embryologic defects. At the 4–5 week stage of embryologic development, the brain goes from a three vesicular stage, consisting of prosencephalon, mesencephalon, and rhombencephalon, to the five vesicular stage of telencephalon, diencephalon, mesencephalon, metencephalon, and myelencephalon. The major defect is the failure of differentiation of the prosencephalon into the telencephalon and diencephalon, which represent the adult brain cerebral convexities. This is at the time when the facial primordia appear around the stomodeum or primitive mouth. The unpaired frontonasal elevation results from proliferation of mesenchyma ventral to the developing brain. It is for this reason that the holoprosencephalies are commonly associated with facial abnormalities [4].

The etiology of the holoprosencephalies is still unknown. Suggested causal agents are hypoxia and diaplacental infection. One of our cases had an elevated herpes titer. Holoprosencephalic malformations have been shown in sheep afflicted with *Veratrum californium* [5]. Hereditary patterns of prosencephaly are still not fully understood. However, there have been familial occurrences [6, 7], reports of afflicted monozygotic and dizygotic twins [8, 9], and association with cleft-palate families [10]. The predominant cerebral malformation in trisomy 13–15 seems to be holoprosencephaly [10]. The radiologic evaluation of an infant suspected of holoprosencephaly should include CT. Angiography and pneumoencephalography were used previously [11].

We believe that with axial and reconstructed CT imaging, the holoprosencephalies can be subgrouped into alobar, semilobar, and lobar. The Probst [2] classification would require more anatomic definition.

Alobar holoprosencephaly is the lowest order of differentiation of the prosencephalon. A mantle of cerebral tissue is present anteriorly around a large monoventricle, and a dorsal sac is present. There is an association with multiple craniofacial anomalies [12]. Orbital hypotelorism, absence of the nasal septum, medial and bilateral cleft lip and palate, microphthalmia, enophthalmia, micrognathia, trigonocephaly, cyclopia, and cebocephaly may be associated [13]. These infants rarely survive more than 1 year.

Semilobar holoprosencephaly is an intermediate category. There is clearly more brain parenchyma, particularly temporal lobe development, and the monoventricle persists. There is no falx cerebri or corpus callosum. The thalami are fused. The facial abnormalities may or may not be present. These infants are usually microcephalic.

Lobar holoprosencephaly, types A and B, is the most developed of the holoprosencephalies. Clinically, these infants are the most viable and may or may not have facial abnormalities. The type A lobar holoprosencephaly has lateralization of the monoventricle and, posteriorly, a spleniumlike termination. The anterior part of the brain is still fused. There may be a posterior falx cerebri. The thalami are not fused. Type B has further hemispherization. The corpus callosum may be rudimentary as opposed to the other holoprosencephalies, in which it is absent. The thalami are separate, and there is frequently a posterior interhemispheric cyst, which can aid in differentiation of this entity from hydrocephalus.

One of our cases had an associated subdural effusion. This can make the diagnosis and classification more difficult. The holospheric brain, lacking vascular fixation and normal falcine attachment to the cranium, can be retroflexed by such an effusion. This would not occur in a hemispherized brain.

We believe that the holoprosencephalies can be diagnosed and subclassified by CT. Our cases 1–4 are representative of the types classified by DeMyer and Zeman [3]. Facial anomalies, when present, can aid in diagnosis; but the cerebral abnormalities occur without characteristic facial anomaly.

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