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Prolonged Survival With Hydranencephaly: Report of Two Patients and Literature Review

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Infants with hydranencephaly are presumed to have a reduced life expectancy, with a survival of several weeks to months. Rarely, patients with prolonged survival have been reported, but these infants may have had other neurologic conditions that mimicked hydranencephaly, such as massive hydrocephalus or holoprosencephaly. We report two infants with prenatally acquired hydranencephaly who survived for 66 and 24 months. We reviewed published reports to ascertain the clinical and laboratory features associated with survival of more than 6 months. This review demonstrates that prolonged survival up to 19 years can occur with hydranencephaly, even without rostral brain regions, with isoelectric electroencephalograms, and with absent-evoked potentials. Finally, the ethical aspects of these findings, as they relate to anencephaly and organ transplantation, are discussed. **© 2000 by Elsevier Science Inc. All rights reserved.**

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Introduction

Hydranencephaly is a rubric used to describe a group of brain malformations that vary in regards to their putative time of onset, pathogenesis, and organization of any brain remnant that may persist [1]. Although remnants of nonfunctioning cortex can be present, the hallmark is the extensive reduction in brain matter that has been replaced with cerebrospinal fluid. Facial features are uniformly normal, which distinguishes hydranencephaly from other major central nervous system anomalies [1]. Typically, hydranencephaly occurs prenatally and is related to either a developmental or encephaloclastic process, often of infectious, toxic, or genetic origin, that affects the major vessels of the anterior circulation [1-3]. Postnatal insults can also cause a similar pathologic and neuroimaging appearance [4].

To the best of our knowledge a survival analysis of infants with hydranencephaly has not been performed. Pediatric neurology texts report that infants with hydranencephaly typically have a markedly reduced life expectancy, being either stillborn or dying within a few weeks or months after birth [5,6]. Although prolonged survival has rarely been reported, specific neuroimaging or neuropathologic details that permit either confirmation of the diagnosis or ascertainment of a putative pathophysiologic feature to account for the prolonged survival are often lacking. In the era before computed tomography (CT) and magnetic resonance imaging, cases of prolonged survival attributed to hydranencephaly may have actually represented other neurologic conditions with a preserved cortex, such as massive congenital hydrocephalus, subdural collections, or holoprosencephaly.

We report two infants who have survived with hydranencephaly for 66 and 24 months. We review published reports on long-term survivors, with particular attention to the clinical and laboratory features that may be associated with such survival. Finally, the ethical and legal ramifications of hydranencephaly as they relate to anencephaly and the modification of current brain death criteria for the purpose of organ transplantation are discussed.

Case Reports

Patient 1. The first patient was a 5-year, 6-month-old male who was born (weight = 4,100 gm) at term after an uncomplicated pregnancy. Neonatal generalized seizures were treated with phenobarbital. CT scanning demonstrated a complete absence of the cerebral hemispheres, which had been replaced with cerebrospinal fluid. The bilateral thalamus, brainstem, and cerebellum were intact. At 3 months of age a ventriculoperitoneal shunt was placed without any changes in the CT appearance (Fig 1). The most recent CT scan at 5 years of age demonstrated no change. Electroencephalography at 3 years of age exhibited marked background suppression. A neurologic examination at 5 years, 6 months of age demonstrated no definite awareness of the environment, although

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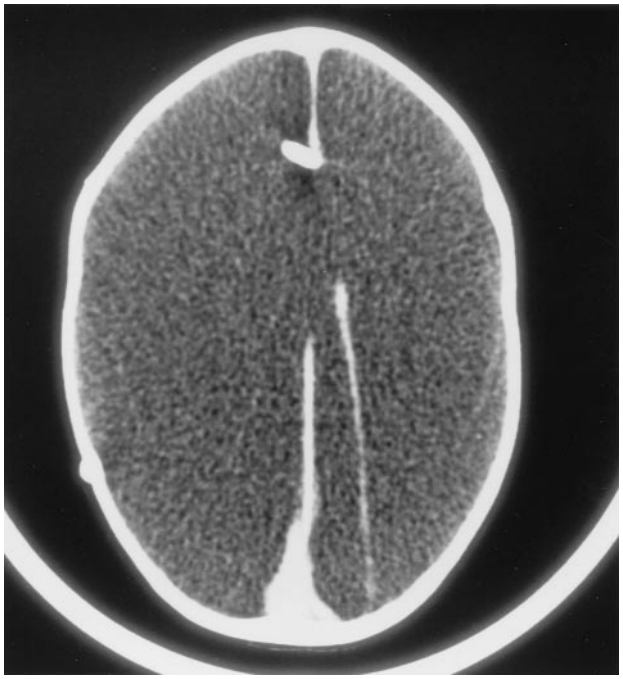

Figure 1. Noncontrast computed tomography scan demonstrates absence of cortical tissue with replacement with cerebrospinal fluid. Shunt tube is evident.

he would slowly turn his head ipsilaterally to sounds, music, and venipuncture. Brainstem auditory–evoked potentials were normal. He could make sounds and smile. His head circumference was 52.5 cm. He had roving eye movements, with cortical blindness and no blink response to light or threat. Pupils did not react to light but changed position with prolonged changes in room light intensity. Severe bilateral optic atrophy was present. Feeding was by way of a gastrostomy tube because he would gag on minute amounts of liquid. Truncal hypotonia with spasticity of all the extremities was evident. His temperature control was generally good, although rare episodic hypothermia did occur. Sleep apnea was present.

Patient 2. A 2-year-old male was transferred to our hospital from the Caribbean, where he had been living in a foster-care setting. The details of his birth are unknown. His neurologic examination demonstrated a head circumference of 98 cm; ulceration of the skin over the parietal area was present because of the massive head circumference. He had no definite awareness of his environment. The pupillary response to light was minimal; he did not fix or follow visually and had no visual response to threat. Bilateral optic atrophy was present. Downward deviation of the eyes and horizontal nystagmus with a downward rotatory component was evident. Bilateral corneal and gag reflexes and spontaneous respirations were present. He had spastic quadriparesis. Episodes of opisthotonos occurred. Electroencephalography demonstrated marked background suppression. CT revealed an absence of the cerebral hemispheres, which had been replaced with cerebrospinal fluid, although a very thin cerebral mantel at the medial frontal, parietal, and occipital areas was evident. The brainstem and cerebellum were intact. A ventriculoperitoneal shunt was placed to control the head growth and to assist in nursing care. No change occurred in the CT appearance after shunt placement.

Literature Review

English language reports were identified by a Medline search and were included if either the pathologic findings or neuroimaging features by CT or magnetic resonance imaging with sufficient details for analysis were provided. To eliminate the possibility of including patients with massive hydrocephalus, cases were excluded if the neuroimaging findings suggested hydranencephaly but the patient had not undergone shunt placement, unless the diagnosis was confirmed by angiography or pathologic examination. Cases of acquired hydranencephaly or hemihydranencephaly were also excluded. Reports of patients who survived for 6 months or more were analyzed.

Discussion

Documentation of prolonged survival in infants with hydranencephaly has important medical, ethical, and legal ramifications. First, the information is essential for appropriate parental counseling not only about the possibility of prolonged survival but also for decision-making about medical treatment that may prolong survival but ultimately will be futile for improved neurodevelopmental outcome. Second, issues related to the modification of brain death criteria for purposes of organ procurement for transplantation have focused on infants with anencephaly, yet may be analogous to infants with hydranencephaly. To date, little attention has focused on the specific documentation of infants with neurologic conditions associated with the severe neurologic impairment and outcome that are analogous to anencephaly.

The literature review demonstrated that prolonged survival of up to 19 years can occur with hydranencephaly, without improved neurologic outcome. However, clinicians should be aware that no definitive set of features predictive of such prolonged survival could be determined from this review. As expected, prolonged survival was associated with relative preservation of subcortical, brainstem, and cerebellar regions, although one patient did have absence of the pontine corticospinal tracts. Conversely, significant abnormalities of the brainstem and thalamus have been demonstrated in many, but not all, infants who die within days to weeks of birth [1,7]. This finding implies that the circuits necessary for maintenance of temperature, blood pressure, and cardiorespiratory functions are, at least in part, functional in prolonged survivors.

Episodes classified as seizures occurred in Patient 1 and have been reported in hydranencephaly with or without prolonged survival [7]. Similar events have been described in infants with other major forebrain anomalies, such as anencephaly and atelencephaly [8]. Although one might infer that the presence of seizures connotes the preservation of sufficient cortex needed for prolonged survival, it is more likely that these episodes are primarily a brainstem-release phenomenon [9].

Certain clinical and electrophysiologic features should not be used as predictors of the length of survival (Table 1). For instance, preservation of the rostral cortex was not needed for prolonged survival because many survivors had only remnants of the occipital lobes. In addition the cellular architecture of the preserved occipital region was

Table 1. Summary of studies

Study	Age/Sex	Means of Diagnosis	Brain Findings	Other Organ Abnormalities	Behavioral Features	Neurophysiology
Velasco et al. [16], 1997	14 mo/M	CT, angiography	Complete loss of telencephalon with partial sparing of thalamus; bilateral internal carotid occlusion; cerebellum, hypothalamus normal		Spontaneous movement; crying seizures (tonic, apneic, lip-smacking); Lennox-Gastaut syndrome? (but no EEG slow spike-and-wave)	EEG: generalized fast; absent vertex waves; disrupted sleep spindles; bitemporal and bifrontal generalized paroxysms BAER: all components absent
Hashimoto et al. [11], 1992	7 yr/M	CT	Remnant right occipital lobe; BS and cerebellum intact	No circadian rhythym of cortisol secretion	Normal REM sleep	EEG: low amplitude and near isoelectric; right occipital sharp VER: absent SSER: defect in cortical wave ERG and BAER: normal
Hanigan et al. [18], 1988	6 mo/F	MRI	Small occipital lobes present; BS, pons, and cerebellar vermis intact			ERG and BAER: normal VER and MLR: absent SSER: absent cortical potential
Lee et al. [10], 1986	18 yr/F	CT, angiography	Frontal, occipital, pasasaggital remnants; posterior fossa intact	Abnormal anterior pituitary function	Smiled, cried; generalized seizures?	EEG: low amplitude frontal and central; posterior theta; occipital spike/polyspike in sleep
Sutton et al. [19], 1980	6 mo/NR 7 mo/NR 11 mo/NR 18 mo/NR		All with minimal occipital lobes	All blind and deaf	Developmental age 1 mo	3/4 isoeletric (occasional occipital spikes noted but specifics NR); 1 EEG NR
Mosier et al. [20], 1978	9 mo/M	Postmortem examination	Occipital and inferior temporal lobes normal; thin cerebral mantle with polymicrogyria; optic nerves hypoplastic; BS, posterior diencephalon, and cerebellum normal			EEG: right frontal isoelectric
Takagi et al. [21], 1976	15 mo/F	Postmortem examination	Cortex: glial tissue without ganglion; occipital, diencephalon, BS, cerebellum normal	Hypoplasia of adrenals	Convulsion?	
Deiker et al. [15], 1976	19 yr/F	Postmortem examination	No preserved cortex or white matter in either hemisphere		Transient guttural vocalizations and head turning; eye blinking	Serial EEGs: isoelectric; transient 15 Hz spindles at 9 yr
Halsay et al. [22], 1971	27 mo/NR	Postmortem examination	Posterior temporal and parieto-occipital lobes atrophic; thalamus, BS, BG, and cerebellum normal; spinal cord: small CTS			
Ulwan et al. [23], 1970	4 yr/F	Postmortem examination	Specifics NR	Fibrinous pericarditis (shunt-related?)		Serial EEGs: isoelectric
Hoffman and Liss [24], 1969	7 yr, 6 mo/F	Postmortem examination	Occipital, insular, hippocampal, and temporal remnants; BS, cerebellum, and spinal cord normal except for absent medullary pyramids and small peduncles; small caliber, patent, anterior and middle cerebral arteries	Heart, adrenals, thymus, and kidneys weight <20–30% expected; no abnormalities noted	Age 2 yr, 6 mo: "learned to drink from a cup" when propped in sitting position	
Barnet et al. [17], 1966	6 mo/M	Postmortem examination	Small occipital lobes with polymicrogyria; midbrain, BS, BG, and cerebellum were normal; pons: absent CTS	Small patent ductus arteriosus; no other major malformations were found	Blinked and cried to flashing and bright light; startled, cried and eyes widened to auditory stimuli; seizures	EEG: isoelectric with low amplitude after photic ERG: normal VER: became abnormal as stimuli rate increased BAER: absent

Abbreviations:

BAER = Brainstem auditory evoked response
BG = Basal ganglia
BS = Brainstem
CC = Corpus callosum
CT = Computed tomography
CTS = Corticospinal tract
EEG = Electroencephalogram
ERG = Electroretinogram
MLR = Auditory middle latency response
MRI = Magnetic resonance imaging
NR = Not reported
SSER = Somatosensory evoked response
VER = Visual evoked response

abnormal in some patients. Also, both normal and abnormal neurophysiologic tests can occur with prolonged survival. For example, the presence of electroencephalographic activity was not needed for prolonged survival because many patients had an isoelectric or near isoelectric electroencephalographic recording. Similarly, absent visual- and brainstem- and abnormal somatosensory-evoked potentials were evident in prolonged survivors.

Some have suggested that hypothalamic-pituitary-adrenal function is essential for prolonged survival [1]. However, abnormal hypothalamic-pituitary function can occur [10,11]. Prolonged survival might also be expected to correlate with the absence of associated malformations in other organs. In fact a small patent ductus arteriosus and hypoplasia of the adrenals were the only non–central nervous system organ malformations observed, and these occurred in two separate patients. However, an extensive evaluation for non–central nervous system malformations may not have been performed in all patients.

An ongoing debate relates to a proposal to modify the current brain death criteria for infants with anencephaly so that their organs can be more readily procured for transplantation. The rationale for such modification is based on several factors believed to be unique to anencephaly. First, a functioning cortex is always absent and there never was, nor is there currently, any reasonable chance for achieving a conscious or cognitive state. Second, these infants have been considered near death because of their reduced life expectancy [12].

Critics of such brain death modification have raised two arguments. First, there is concern of a slippery slope, a controversial theory that contends that the use of organs from anencephalic infants might lead to the use of organs from others with severe neurologic impairment. Some have rejected the slippery slope argument because of the uniqueness of infants with anencephaly resulting from their lack of both consciousness and the potential for future consciousness [13]. Second, there is the possibility of prolonged survival with anencephaly, which refutes the point that these infants are near death [14].

Both arguments are analogous to anencephaly and to prenatally acquired hydranencephaly. An infant in a hydranencephalic state lacks a functioning cortex, and a hydranencephalic state is associated with a lack of consciousness and cognitive state. Although thalamic circuits, considered by some to play a role in consciousness, may be more likely to be intact in patients with hydranencephaly than with anencephaly, the patients with prolonged survival were not reported to have any improvement in consciousness or awareness. Such prolonged survival is more likely to be associated with a more preserved brainstem, aggressive nursing care, or a combination of both. Thus the major supporting argument for modification of brain death criteria should be based on the lack of consciousness from birth and the inability to ever gain consciousness or awareness, which is unique to infants with these two conditions. The use of an extremely reduced life span, which occurs with various neurologic conditions, as a criterion for anencephalic or hydranencephalic infants to be considered morally acceptable organ donors should be eliminated.

Finally, certain behaviors observed in our first patient and others, such as head turning to sound and painful stimuli, [15] have been reported in hydranencephaly and are presumably related to brainstem/diencephalic, rather than cortical, function. Other behavioral manifestations, such as yawning, crying, and smiling, can occur [16,17]. Parental counseling is essential about these behaviors to prevent any false hope about improved neurodevelopmental outcome.

References

[1] **Halsey** J. Hydranencephaly. In: Vinken P, Bruyn G, Klawans H, eds. Handbook of clinical neurology. Amsterdam: Elsevier Science, 1987:337-53.

[2] **Rais-Bahrami** K, Naqvi M. Hydranencephaly and maternal cocaine use. Clin Pediatr 1990;29:729-30.

[3] **Gershoni-Baruch** R, Zekaria D. Deletion (13)(q22) with multiple congenital anomalies, hydranencephaly and penoscrotal transposition. Clin Dysmorphol 1996;5:289-94.

[4] **Lindenberg** R, Swanson P. Infantile hydranencephaly—A report of five cases of infarction of both cerebral hemispheres in infancy. Brain 1967;90:839-50.

[5] **Menkes** J, Till K. Malformations of the central nervous system. In: Menkes J, ed. Textbook of child neurology, 5th ed. Baltimore: Williams & Wilkins, 1995:307-8.

[6] **Ashwal** S. Congenital structural defects. In: Swaiman K, Ashwal S, eds. Pediatric neurology, 3rd ed. St. Louis: Mosby, 1999:273-4.

[7] **Ferguson** JH, Levinsohn MW, Derakshan I. Brainstem seizures in hydranencephaly. Neurology 1974;24:1152-7.

[8] **Danner** R, Shewmon DA, Sherman MP. Seizures in an atelencephalic infant: Is the cortex essential for neonatal seizures? Arch Neurol 1985;42:1014-6.

[9] **Mizrahi** EM, Kellaway P. Characterization and classification of neonatal seizures. Neurology 1987;37:1837-44.

[10] **Lee** B, Low P, Kwok R, Tan C, Tan S. Hydranencephaly-radiologic features and anterior pituitary function—A case report. J Singapore Pediatr Soc 1986;28:250-3.

[11] **Hashimoto** T, Fukada K, Endo S, et al. Circadian rhythm in patients with hydranencephaly. J Child Neurol 1992;7:188-94.

[12] **Medearis** D, Holmes L. On the use of anencephalic infants as organ donors. N Engl J Med 1989;321:391-3.

[13] Council on Ethical and Judicial Affairs, American Medical Association. The use of anencephalic neonates as organ donors. JAMA 1995;273:1614-8.

[14] **McAbee** G, Sherman J, Canas J, Boxer H. Prolonged survival of two anencephalic infants. Am J Perinat 1993;10:175-7.

[15] **Dieker** T, Bruno R. Sensory reinforcement of eyeblink rate in a decorticate human. Am J Mental Def 1976;80:665-7.

[16] **Velasco** M, Velasco F, Gardea G, Gordillo F, DeLeon A. Polygraphic characterization of the sleep-epilepsy patterns in a hydranencephalic child with severe generalized seizures of the Lennox-Gastaut syndrome. Arch Med Res 1997;28:297-302.

[17] **Barnet** A, Bazelon M, Zappella M. Visual and auditory function in a hydranencephalic infant. Brain Res 1966;2:351-60.

[18] **Hanigan** W, Aldrich W. MRI and evoked potentials in a child with hydranencephaly. Pediatr Neurol 1988;4:185-7.

[19] **Sutton** LN, Bruce DA, Schut L. Hydranencephaly versus maximal hydrocephalus: An important clinical distinction. Neurosurgery 1980;6:35-8.

[20] **Mosier** M, Lieberman M, Green W, Knox D. Hypoplasia of the optic nerve. Arch Opthalmol 1978;96:1437-42.

[21] **Takagi** M. Hydranencephaly-report of a case. Bull Tokyo Med Dent Univ 1976;23:109-13.

[22] **Halsay** J, Allen N, Chamberlin H. The morphogenesis of hydranencephaly. J Neurol Sci 1971;12:187-217.

[23] **Ulwan** O, Hambraeus L, Andersson-Hjort G. Studies on the amino acid pattern of cerebrospinal fluid in a case of hydranencephaly before and after shunt operation. Neuropediatrics 1970;2:325-34.

[24] **Hoffman** J, Liss L. Hydranencephaly: a case report with autopsy findings in a 7 year old girl. Acta Paediatr Scand 1969;58:297-300.