Hydranencephaly

Contents

Hydranencephaly is a severe central nervous system disorder, characterized by complete or almost complete absence of cerebral cortex with preservation of meninges, basal ganglia, pons, medulla, cerebellum, and falx. Cerebral hemispheres are completely or partially destroyed and transformed into membranous sacs containing cerebrospinal fluid (Greco et al. 2001). Hemihydranencephaly is an extremely rare brain condition in which the vascular occlusion is presumed to be unilateral. Hydranencephaly occurs in less than 1 in 10,000 births (To and Tang 1999).

Synonyms and Related Disorders

Fowler syndrome; Hemihydranencephaly

Genetics/Basic Defects

1. Maternal risk factors
    1. Intercurrent infections
        (i) Toxoplasmosis
        (ii) Rubella
        (iii) Cytomegalovirus
        (iv) Herpes simplex
    2. Exposure to irradiation
    3. Exposure to teratogenic agents
        (i) Warfarin
        (ii) Estrogens
        (iii) Valproic acid
        (iv) Drug abuse: cocaine
    4. Twin-twin transfusion
    5. Intrauterine death of a monozygotic co-twin leading to vascular disruption of cerebral tissue
    6. Alloimmune and idiopathic thrombocytopenia
    7. Von Willebrand disease
    8. Congenital factor X and factor V deficiencies leading to hemorrhage into various congenital tumors
2. Presumably resulting from intrauterine bilateral internal carotid artery occlusion
    1. The structural defects occurring during the 4th and 6th months of gestation, after neuronal migration (Greco et al. 2001)
    2. Occurring between the 8th and 12th weeks, based on fetal ultrasound data, histopathologic findings, embryogenic vascular development, and postnatal CT and MRI findings (Cecchetto et al. 2013)
3. May be associated with porencephaly and congenital hydrocephalus

H. Chen, *Atlas of Genetic Diagnosis and Counseling*,
DOI 10.1007/978-1-4939-2401-1_262

4. Fowler (proliferative vasculopathy and hydranencephaly-hydrocephaly) syndrome (Fowler et al. 1972; Meyer et al. 2010):
    1. An autosomal recessively inherited prenatal lethal disorder characterized by hydranencephaly
    2. Brain stem, basal ganglia, and spinal cord diffuse clastic ischemic lesions with calcifications
    3. Glomeruloid vasculopathy of the central nervous system and retinal vessel
    4. A fetal akinesia deformation sequence with muscular neurogenic atrophy
    5. Associated with mutations in *FLVCR2* (feline leukemia virus subgroup C receptor 2)

Clinical Features

1. Markedly reduced life expectancy
    1. Stillborn
    2. Dying within a few weeks or months after birth
    3. Rare reports of prolonged survival (McAbee et al. 2000; Bae et al. 2008)
2. First year of life
    1. Typically marked by medical emergencies (Merker 2008)
        1. Uncontrolled epileptic seizures
        2. Pulmonary sequels to reflux and aspiration
        3. Unregulated intracranial pressure (hydrocephalus)
        4. Problems with temperature regulation
    2. Other features
        1. Macrocephaly
        2. Hyperirritability
        3. Retardation
        4. Transillumination
3. Survivors after first year of life
    1. The previously mentioned problems brought under control by medication, shunting, and other interventions
    2. Cases reported with diagnosis of developmental or persistent vegetative state (The Multi-society Task Force on the Persistent Vegetative State 1994)
    3. Cases reported exhibiting a responsiveness to surroundings incompatible with the classification vegetative state (Shewmon et al. 1999)
    4. Merker (2007) provided a detailed examination of functional reasons for expecting individuals with early and drastic (even complete) loss of cortical tissue to display forms of coherent responsiveness to their surroundings incompatible with a diagnosis of vegetative state.

Diagnostic Investigations

1. Transillumination of the skull (Alexander et al. 1956; Levin 1957; Barozzino and Sgro 2002)
    1. Used as a screening procedure for infants with macrocephaly and those suspected of having the following:
        1. Hydranencephaly
        2. Subdural effusion
        3. Subdural hematoma
        4. Hydrocephalus
        5. Porencephaly
        6. Increased intracranial pressure
        7. Skull fracture
        8. Nutritional deficiencies
    2. Has become a somewhat forgotten tool with advancements in and increased availability of neuroimaging techniques, but sometimes even a simple otoscope placed in the appropriate position can provide clinical "enlightenment."
2. CAT angiography (Jordan et al. 2004): A fast and safe way to assess the vascular anatomy of newborn babies with significant cerebral anomalies
3. MRI of the brain: better delineation of detail anatomy of the brain
    1. Absence of cerebral mantle (temporal and occipital lobe remnants commonly present)
    2. Falx cerebri partially or completely intact
    3. Thalamus and hypothalamic mesencephalic structures usually preserved
    4. Brainstem usually atrophic
    5. Cerebellum always intact

4. EEG for seizures
5. Comprehensive molecular test for Fowler syndrome (Sanger sequencing and HDT array deletion duplication) for FL/VCR2 mutation is available clinically

Genetic Counseling

1. Recurrence risk
   1. Sporadic occurrence
      1. Patient's sib: not increased
      2. Patient's offspring: not reported due to reduced life expectancy
   2. Autosomal recessive inheritance (Fowler syndrome)
      1. Patient's sib: 25%
      2. Patient's offspring: low unless the spouse is affected
2. Prenatal diagnosis (Lam and Tang 2000)
   1. Ultrasonography
      1. Hydranencephaly is suspected when there is a large fluid collection in the head with no recognizable cerebral cortex.
      2. During the early stages of disease, hydranencephaly is characterized by the presence of a large intracranial saclike structure containing homogeneous echogenic material, representing blood and necrotic debris secondary to massive liquefaction of the developing cerebral hemispheres (Sepulveda et al. 2012).
      3. Differentiated sonographically from holoprosencephaly by identifying the presence of dural attachments and distinctly separate thalami (McGahan et al. 1988)
      4. In severe hydrocephalus, a rim of cerebral cortex around the cystic cavity and enlargement of the 3rd ventricle may be visualized.
   2. Fetal MR imaging (Ghosh et al. 2013) shows normal-appearing brain stem, cerebellum, portions of the occipital and temporal lobes, and unfused thalami with the remainder of the supratentorium all representing fluid
   3. Molecular genetic analysis for Fowler syndrome
3. Management: symptomatic

References

Alexander, E., Jr., Davis, C. H., Jr., & Kitahata, L. M. (1956). Hydranencephaly: Observations on transillumination of the head of infants. *AMA Archives of Neurology Psychiatry, 76*, 578–584.

Bae, J. S., Jang, M. U., & Park, S. S. (2008). Prolonged survival to adulthood of an individual with hydranencephaly. *Clinical Neurology and Neurosurgery, 110*, 307–309.

Barozzino, T., & Sgro, M. (2002). Transillumination of the neonatal skull: Seeing the light. *Canadian Medical Association Journal, 167*, 1271–1272.

Cecchetto, G., Milanese, L., & Giordano, R. (2013). Looking at the missing brain: Hydranencephaly case series and literature review. *Pediatric Neurology, 48*, 152–158.

Fowler, M., Dow, R., White, T. A., et al. (1972). Congenital hydrocephalus-hydranencephaly in five siblings, with autopsy studies: A new disease. *Developmental Medicine and Child Neurology, 14*, 173–188.

Ghosh, P. S., Reid, J. R., Patno, D., et al. (2013). Fetal magnetic resonance imaging in hydranencephaly. *Journal of Paediatrics and Child Health, 49*, 335–336.

Greco, F., Finocchiaro, M., Pavone, P., et al. (2001). Hemihydranencephaly: Case report and literature review. *Journal of Child Neurology, 16*, 218–221.

Jordan, L., Raymond, G., Lin, D., et al. (2004). CT angiography in a newborn child with Hydranencephaly. *Journal of Perinatology, 24*, 565–567.

Lam, Y. H., & Tang, M. H. Y. (2000). Serial sonographic features of a fetus with hydranencephaly from 11 weeks to term. *Ultrasound in Obstetrics and Gynecology, 16*, 77–79.

Levin, J. C. (1957). The value of transillumination in the diagnosis of hydranencephaly. *Journal of Pediatrics, 50*, 55–58.

McAbee, G. N., Chan, A., & Erde, E. L. (2000). Prolonged survival with hydranencephaly: Report of two patients and literature review. *Pediatric Neurology, 23*, 80–84.

McGahan, J. P., Ellis, W., Lindfors, K. K., et al. (1988). Congenital cerebrospinal fluid-containing intracranial abnormalities: A sonographic classification. *Journal of Clinical Ultrasound, 16*, 531–544.

Merker, B. (2007). Consciousness without a cerebral cortex: A challenge for neuroscience and medicine. Target article, peer commentary, and author's response. *Behavioral and Brain Sciences, 30*, 63–134.

Merker, B. (2008). Life expectancy in hydranencephaly. Editorial. *Clinical Neurology and Neurosurgery, 110*, 213–214.

Meyer, E., Ricketts, C., Morgan, N. V., et al. (2010). Mutations in *FLVCR2* are associated with proliferative

vasculopathy and hydranencephaly-hydrocephaly syndrome (Fowler syndrome). *The American Journal of Human Genetics, 86*, 471–478.

Sepulveda, W., Cortes-Yepes, H., Wong, A. E., et al. (2012). Prenatal sonography in hydranencephaly. Findings during the early stages of disease. *Journal of Ultrasound in Medicine, 31*, 799–804.

Shewmon, D. A., Holmes, G. L., & Byme, P. A. (1999). Consciousness in congenitally decorticate children: Developmental vegetative state as self-fulfilling prophecy. *Developmental Medicine and Child Neurology, 41*, 364–374.

The Multi-society Task Force on the Persistent Vegetative State. (1994). Statement on medical aspects of persistent vegetative state (first of two parts). *New England Journal of Medicine, 330*, 1499–1508.

To, W. W., & Tang, M. H. Y. (1999). The association between maternal smoking and fetal hydranencephaly. *Journal of Obstetrics and Gynaecology Research, 25*, 39–42.

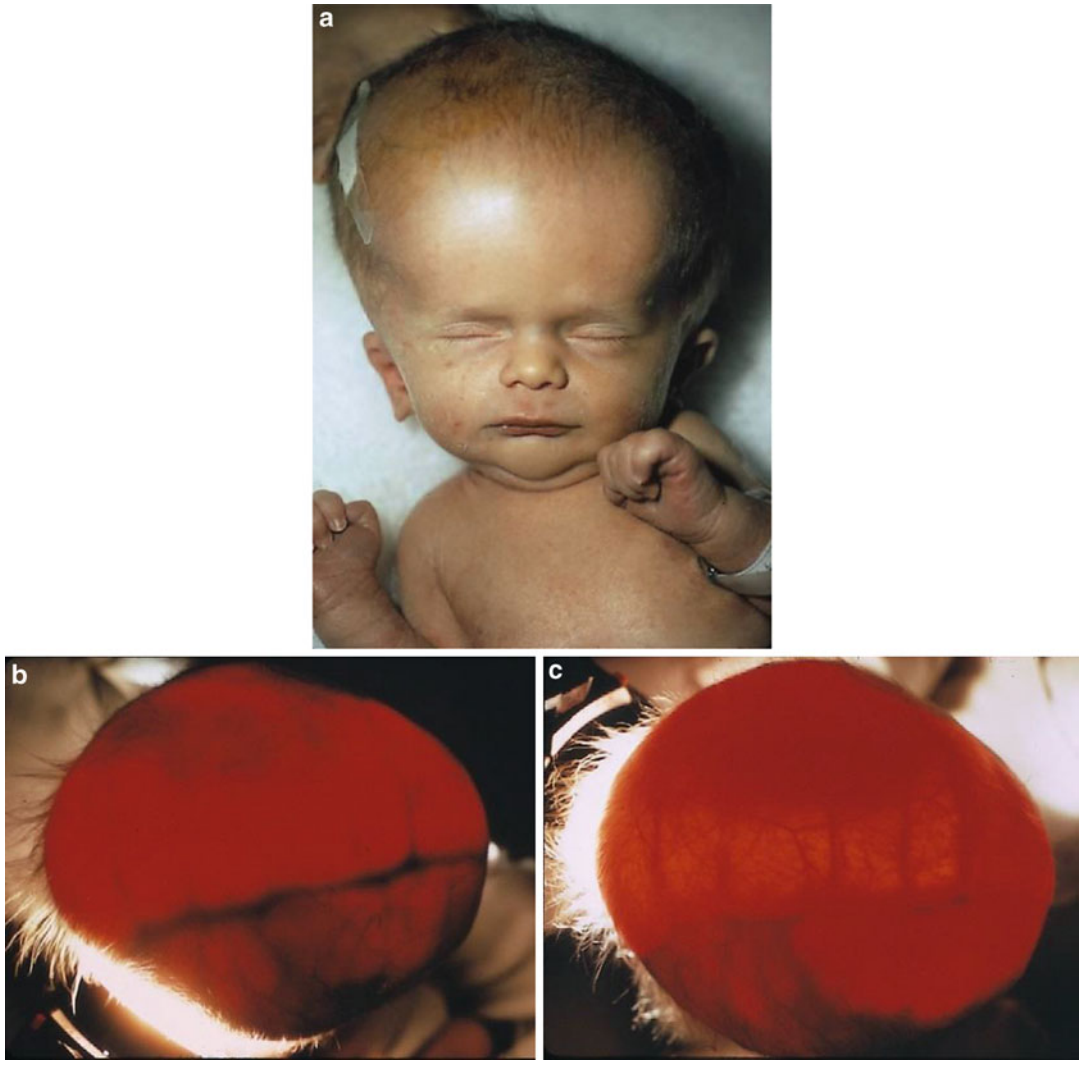

Fig. 1 (**a**, **b**, **c**) Transillumination of the skull in a neonate with hydranencephaly in a dark room shows the light illuminates the entire brain from the forehead through the back of the head. The transillumination is most drastic

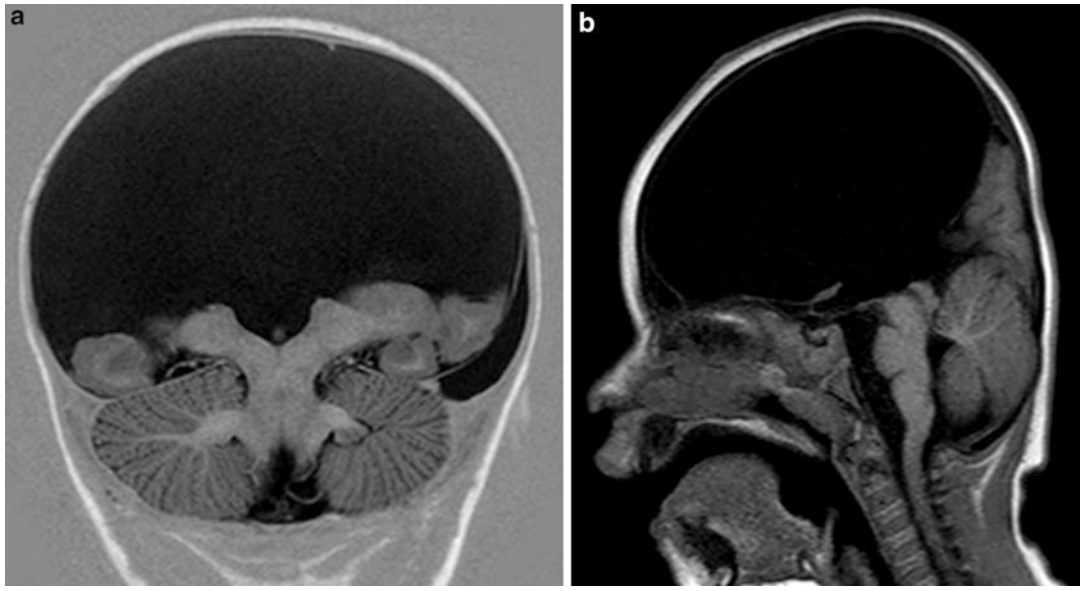

Fig. 2 (**a**, **b**) These two MRI images of the brain was from 1-year-old girl with seizures. Coronal image shows complete absence of the cerebral hemispheres with the exception of some portions of the inferior temporal lobes. The cerebellum is normal (**a**). The sagittal image shows absence of most of the cerebrum with a portion of occipital lobe present. Brainstem appears diffusely atrophic (**b**). The separated bilateral thalami are present (Courtesy of Dr. Grace Guo)

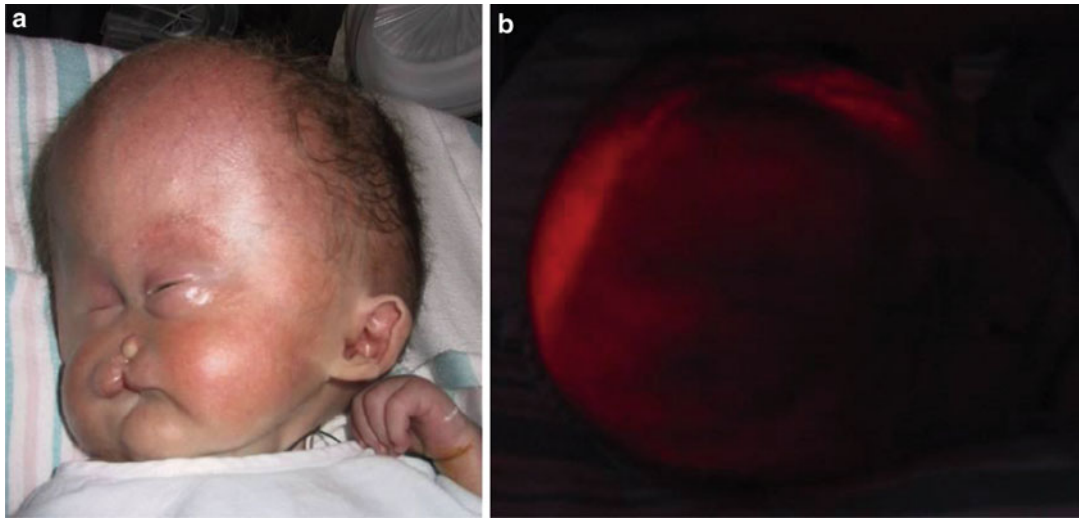

Fig. 3 (**a**, **b**) Transillumination of the skull in a neonate with alobar holoprosencephaly, difficult to differentiate from hydranencephaly

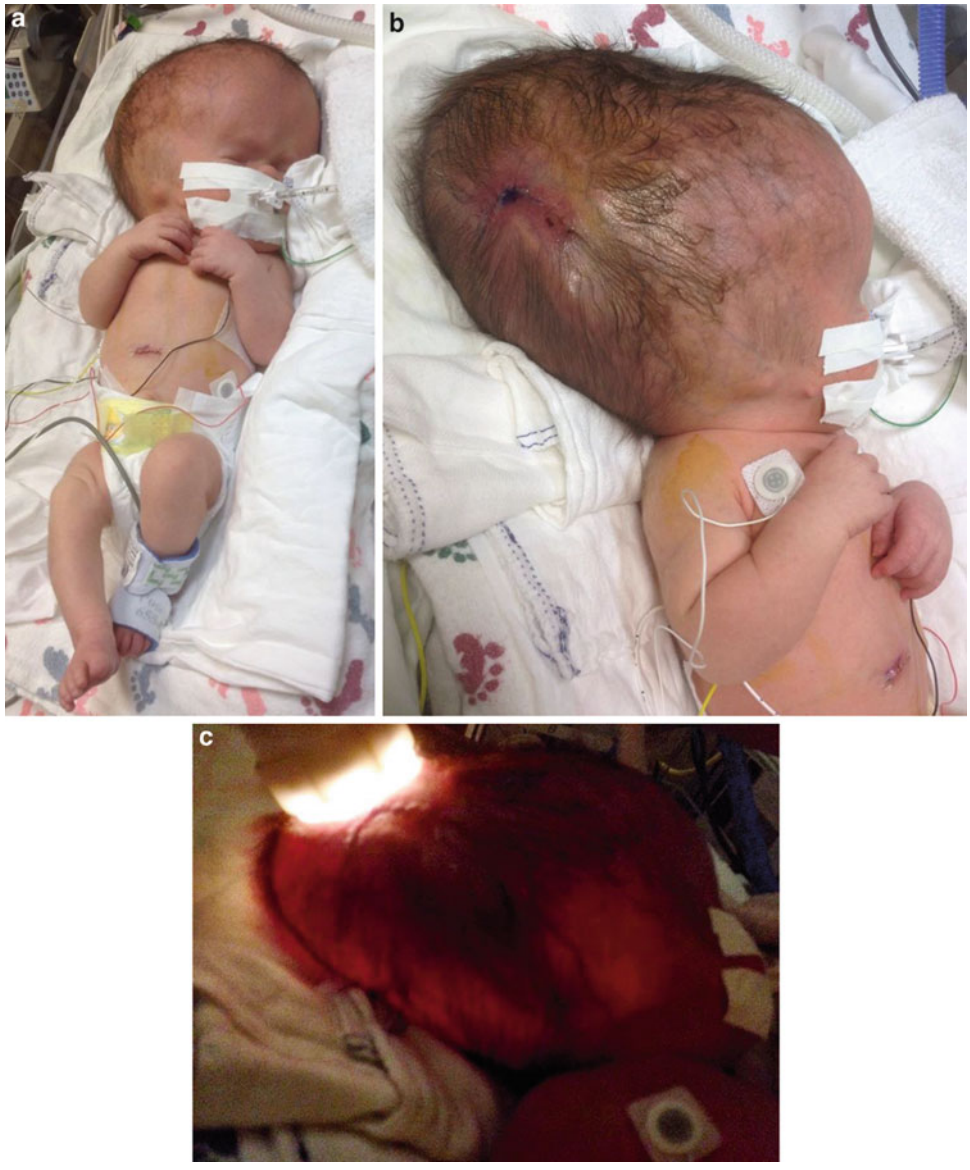

Fig. 4 (**a**, **b**, **c**) Transillumination of the skull in a neonate with massive hydrocephaly, difficult to differentiate from hydranencephaly