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Hydranencephaly: Insights into Pathophysiology and Management

Abstract

Hydranencephaly is a rare and severe form of congenital disorder in which there is absence of cerebral cortex which is replaced by fluid. The presentation is in the form of hydrocephalus and developmental delay. There are various reports on possible etiopathogenesis and management. However, the overall prognosis is grim and clinicians especially in low and middle-income countries like Nepal often face a clinical judgement dilemma regarding management options to offer to the patient family. The ethical issue whether to offer cerebrospinal fluid diversion or not is always there. This review is aimed at discussing the various aspects of management of this pediatric neurosurgical problem.

Key words: Hydranencephaly, Management, Pathophysiology, Prognosis

Introduction

Hydranencephaly (HE) is the term used to describe conditions in which the "encephaly" or brain tissue is almost replaced by "hydro" or water. In its severe form there may be complete absence of cerebral cortex but in many cases a thin rim of non-functional cerebral cortex may be present. The midbrain, cerebellum, thalami, basal ganglia, and choroid plexus are usually not involved.[1]

It is often thought to be due to occlusion of bilateral internal carotid arteries in-utero during second trimester.[2] The estimated incidence is around 1 per 10,000 live births.[3] However, it is difficult to find an accurate incidence due to similarity with other conditions like hydrocephalus and holo-prosencephaly.

There may be a rarer form with hemi hydranencephaly.[4] Among the series of patients reported in literature, the series described by Adeloye is the largest, involving 15 patients with HE.[5]

Owing to the absence of functional cerebral cortex, higher mental functions are universally affected. Regarding survival, most children die during first year of life but survival of patient up to 32 years has been reported.[6] Survival probably depends upon the degree of nursing care the patient receives and associated manifestations like epilepsy.[3]

Etiopathogenesis

The condition was first described by Cruveilhier in 1835. The term hydranencephaly was probably first introduced by Spielmeyer in 1905.[7]

Many scientists are of the view that the pathogenesis is due to occlusion of bilateral supra-clinoidal Internal carotid artery (ICA) in the early fetal life.[8] Absence of flow in ICA on angiography is an evidence in many if not all patients. In all cases in which blood flow in ICA is seen, it is hypothesized that the vessels might have probably recanalized after the damage was inflicted. Another evidence is the relative preservation of a portion of brain supplied by the posterior cerebral arteries. Many patients are seen to have some preservation of occipital lobe structures. It is difficult to explain the presence of fronto-basal cortex in some patients, however, according to some authors, the ophthalmic arteries, which are direct anastomoses between the external and internal carotid arteries, might partially supply these regions during early internal carotid artery occlusion.[8]

The ICA occlusion probably occurs early during 8 to 12 weeks of gestation as suggested by absence of the carotid canals in patients and preservation of falx. The loss of blood flow probably leads to necrosis of brain matter and encephalomalacia replacing it with CSF. [6] Other possible etiology includes intrauterine infection like CMV, toxoplasmosis, rubella etc. leading to massive brain necrosis and cavitation.[9,10]

Regarding genetic link up, most patients have an unremarkable karyotype. However, triploidy (XXY) has been seen in some patients.[6]

Toxic exposures, such as cocaine abuse, sodium valproate and smoking have also been reported. HE has been associated with young maternal age and has been described in association with rare syndromes [11,12,13,14]. HE has also been seen in monochorionic twin pregnancies, in which the death of one twin provoked a vascular exchange to the living twin through the placental circulation and may have caused hydranencephaly in the surviving fetus.[15,16]

Clinical Presentation

In pregnancy there are no abnormal clinical features like decreased fetal movements. Most of the infants are born with a normal head size which keeps on increasing with time or even a normal size. (Figure 1) The choroid plexus continues to produce CSF but the absorption mechanism is ill developed. [4]

Many affected children die in-utero. Neurological or clinical signs may not be evident at birth; leg and arm movements as well as sucking and swallowing reflexes may be present. However, subtle signs, like feeble cry, difficulty with feeding, hypotonia or wide anterior fontanelle may be present. Many kids die before their first birthday. In those who survive long, visual impairment, spastic diplegia and cognitive delay are seen. Many babies present with seizure or seizure-like episodes and irritability. Hearing is usually preserved with cases of sensorineural hearing loss have been reported.[17] 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.[18] Certain behaviors like yawning, crying, smile as well as turning head to sound or painful stimuli can occur which are presumably related to reflexes associated with brainstem or diencephalon, rather than cortical function.[19]

Figure 1: Six months old girl with large head suggesting hydrocephalus

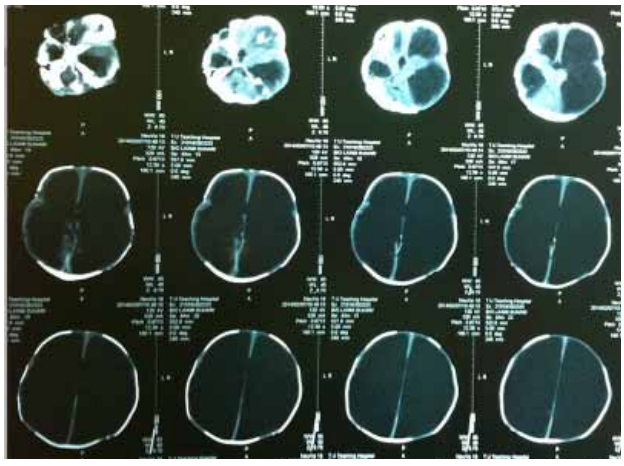

Figure 2: Plain CT head showing near absence of cortical mantle with remnants in frontal and temporal part suggestive of hydranencephaly

Diagnosis

Fetal ultrasound can usually diagnose the condition in late second trimester. Early diagnosis as early as 12 weeks have been reported. [20] Fetal diagnosis is suspected when there is a large fluid filled cavity without any recognizable cortical mantle and thalamus and brainstem structures protruding in the cavity.[8]

In infancy, non-contrast Computed Tomography (CT) scan can suggest diagnosis in presence of absent or thin cortical mantle with varying amount of scattered cerebral cortical matter (Figure 2). Magnetic Resonance Imaging (MRI) can help in better understanding the condition. MRI reveals an almost total parenchymal absence, replaced by cerebrospinal fluid and frequently containing remnants of the occipital area and orbitofrontal regions. The falx is usually present, with the preservation of cerebellar hemispheres, thalamus and brainstem. Magnetic resonance phase contrast images may demonstrate atretic or hypoplastic ICA.[21]

The differential diagnosis of severe hydrocephalus and alobar holoprosencephaly need to be ruled out as far as possible. Differentiating with severe hydrocephalus may be particularly difficult. Hydrocephalus has a better prognosis so it is very important to separate these two entities. In HE, the cortical mantle may be absent unlike in hydrocephalus which has mantle though thinned out. Electroencephalogram (EEG) changes may be helpful. Some authors are of the opinion that HE has "flat EEG" and presence of any electrical activity other than from occipital area is suggestive of severe hydrocephalus.[22]

However, as per Iinuma et al electrical activity can be demonstrated using referential derivation[23]. If the electrical activity originates from only rudimentary caudal structure, most of the EEG activity by referential derivation will be the same and the activity by bipolar derivation will show very low voltage because of the differential amplification of the same activity from remote generators all leads.

Loss of cortical activity with preservation of brainstem function is confirmed by Brainstem auditory evoked responses (BAER) and in some cases a total absence of visual evoked potential can be detected in HE.[24]

Alobar holoprosencephaly can be distinguished by the absence of falx and presence of partial fusion of thalamus. The head size is not large and facial dysmorphism is also seen. [4]

Prognosis and Ethical issues

The fate of kids with HE is universally doomed. Most of them die before birth and many before one year of birth. [4] There are reports of prolonged survival as long as 32 years in some of these patients.[4] The exact factors contributing to prolonged survival have not been identified. Some hypothesis regarding presence of rostral cortex, functioning hypothalamo-pituitary adrenal axis, presence of EEG activity have not been uniformly accepted. The circuits necessary for maintenance of temperature, blood pressure, and cardiorespiratory functions are, at least in part, functional in prolonged survivors. [3]

Although thalamic circuits, considered by some to play a role in consciousness, are more likely to be intact in patients with hydranencephaly 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.[3,25]

Documentation of prolonged survival in infants with HE has important medical, ethical, and legal ramifications. 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.

There are also cases of HE exhibiting a responsiveness to their surroundings incompatible with the classification of vegetative state. [26]

There are issues related to the modification of brain death criteria for purposes of organ procurement for infants with anencephaly, yet may be analogous to infants with HE. 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.[27]

Treatment

Considering the outcome of kids with HE, treatment options need to be discussed with the family in detail. The futility of surgery in improving the cognitive functions should be balanced against the stabilization of raised intracranial pressure and head size. Ventriculo-peritoneal (VP) shunt procedure is an option but may need multiple revisions due to leakage from burr hole site and absorption problems in the peritoneum.

Choroid plexus coagulation via endoscopic method has been attempted and had shown promising results. [28,29] Shitsama and colleagues have shown good results in 50% (5 out of 10) of HE patients who underwent endoscopic choroid plexus ablation and did not need a VP shunt.[29]

Surgical treatment should at least be proposed to the family of patients with severe intracranial hypertension giving them the possibility to choose this option. Medical management of epileptic fits, nutritional support and regular physiotherapy should be instituted.

Conclusions

HE is a rare disease with a majority suffering in-utero death. Early diagnosis and differentiating from conditions with better prognosis are important. Management options and universal poor prognosis should be well explained to the parents on whom the onus of care till the child survives lies. The management protocols till date are highly individualized. There are ethical issues regarding abortions if diagnosed early as less severe forms can have prolonged survival.

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