ORIGINAL RESEARCH

Hydranencephaly: exploring the role of CT features in the diagnosis of 22 cases

Hui Zhang[1], Patrick Manda[2], Tianze Sun[1], Blessed Kondowe[2], Dong Wang[3]*, Jin Shang[1]*

1. Department of Medical Imaging, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, 710061, China
2. Radiology Department, Mzuzu Central Hospital, Mzuzu, Malawi
3. Department of Radiology, Xi'an Children's Hospital, Xi'an, Shaanxi, China

***Corresponding Author:** Dong Wang, Jin Shang; E-mail: 463501291@qq.com, shangjin01@qq.com

Abstract

Objective

To delve into the clinical and CT imaging manifestations of hydranencephaly, a rare congenital post-neurulation disorder occurring during the second trimester, characterized by the destruction of cerebral hemispheres and cranial cavity filled with cerebrospinal fluid (CSF). This research aims to enhance our understanding of hydranencephaly and establish a standard for its imaging diagnosis.

Methods

A retrospective analysis was conducted using the brain CT images and clinical data of 26 pediatric patients diagnosed with hydranencephaly.

Results

At birth, the primitive reflexes were generally preserved in these infants, who exhibited a spectrum of symptoms including progressive enlargement of head circumference, epilepsy, cerebral palsy, intellectual disability, developmental delay, lethargy, convulsive spasms, and varying degrees of visual and auditory impairment. These infants may also present with other congenital malformations or abnormalities. The primary CT imaging findings revealed complete or near-complete absence of bilateral cerebral hemispheres, replaced by CSF. Specifically, there were 5 cases of complete absence of cerebral hemispheres, with minimal residual brain tissue observed in 17 cases. Bilateral ventricles were approximately normal in 3 cases and completely absent in 19 cases. Falx cerebri was incomplete or/and displaced in 12 cases, and 3 cases were concurrent with Dandy-Walker syndrome.

Conclusion

Hydranencephaly is a congenital disease characterized by destruction of the cerebral hemispheres. CT scan can provide accurate and reliable imaging evidence for the diagnosis of hydranencephaly.

Keywords: Hydranencephaly; Congenital cerebral malformation; Severe hydrocephalus; Computed Tomography

Introduction

Hydranencephaly is a congenital cerebral defect characterized by extensive destruction of the cerebral hemispheres, which are subsequently replaced by a sac filled with cerebrospinal fluid (CSF)[1-3]. The incidence may vary from 1 in 10,000 to 1 in 5,000 (0.01% - 0.02%) pregnancies. There is no significant difference between males and females. In developed countries, prenatal diagnostic procedures are highly sophisticated, and termination of pregnancy is often chosen upon confirmation, leading to a scarcity of reports analyzing the clinical and CT imaging features of hydranencephaly. However, in Malawi, a country in Southeast Africa, this malformation is not uncommon. During the author's tenure at the Radiology Department of Mzuzu Central Hospital in Malawi, from January to September 2024, a retrospective analysis was conducted on 22 pediatric patients diagnosed with hydranencephaly. The findings are summarized as follows.

Methods

General Information

The study enrolled 22 pediatric patients, all definitively diagnosed through non-contrast cerebral CT scans. Among them, there were 8 males and 14 females, yielding a male-to-female ratio of 4:7. The patients presented at ages ranging from 2 weeks to 13 months, with a median age of 8 months. The mothers' ages at delivery ranged from 18 to 42 years, averaging at 28.41 years, and all denied any relevant family history of the condition. This study was approved by Mzuzu University Research Ethics Committee (MZUNIREC) (Approval Number: MZUNIREC/DOR/24/137), and consent in written form was waived.

CT Examination

Volumetric scanning was performed using the NeuViz 16 Essence CT scanner, independently developed and manufactured by Neusoft Medical. Patients were positioned in the supine posture. An appropriate field of view (FOV) was selected for the CT volumetric scanning, with a tube voltage of 100 kV, tube current of 280 mA, rotation time of 0.75 s/r, and a scan duration of 3 ~ 4 s. The original data acquisition was set at a slice thickness of 16 mm × 0.625 mm, with a collimation of 40 mm. Continuous scanning was conducted at a slice thickness of 5 mm without intervals, a pitch of 1.00, window level of 40 HU, and window width of 85 HU. All patients received 0.5 mg/kg of diazepam via retention enema for sedation 20 minutes prior to the scan.

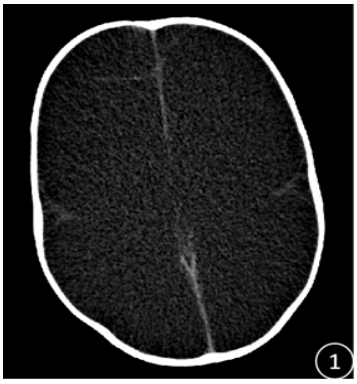

Figure 1 Non-contrast axial CT image shows that both cerebral hemispheres are absent, brain cavity is filled by cerebrospinal fluid, with no visible brain tissue

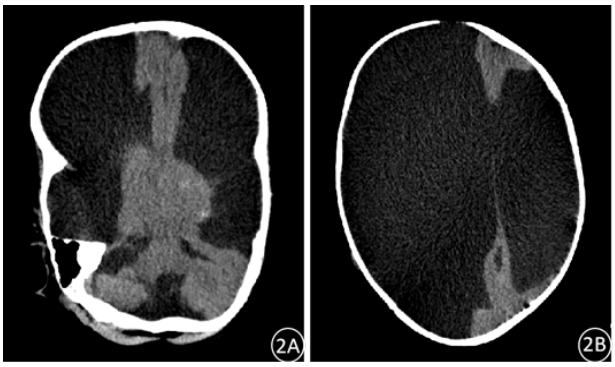

Figure 2 Hydranencephaly with Dandy-Walker syndrome

Female, 12 months old. Non-contrast axial CT image shows partial absence of the inferior cerebellar vermis, the fourth ventricle communicating with the cistern magnum, and atrophy of the right cerebellar hemisphere, consistent with Dandy-Walker syndrome (A). Non-contrast axial CT image shows almost complete absence of both cerebral hemispheres, with only a small portion of brain parenchyma intact in the bilateral frontal and occipital lobes (B).

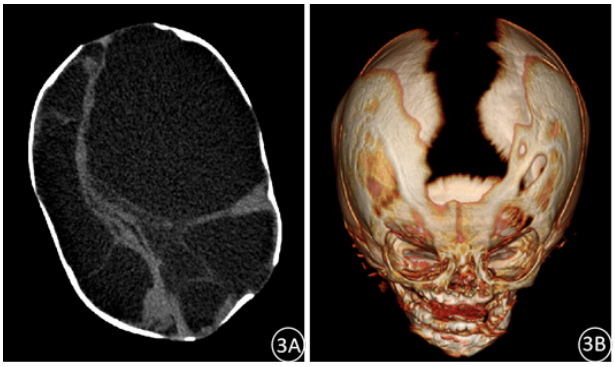

Figure 3 Hydranencephaly with displacement of the falx cerebri and increased intracranial pressure

Female, 11 Months old. Non-contrast axial CT image shows that the falx cerebri is displaced to the right (A); three-dimensional volume rendering reconstruction of the skull CT showed separated cranial sutures and enlarged anterior and posterior fontanelles, indicating increased intracranial pressure (B).

No contrast-enhanced scans were performed.

Results

Clinical Characteristics

All mothers of the enrolled pediatric patients denied histories of smoking, alcohol abuse, drug addiction, or exposure to radiation during pregnancy. Among them, 8 mothers (38.46%) were laboratory-confirmed to be infected with the Human Immunodeficiency Virus (HIV), while the remaining mothers tested negative for HIV. Additionally, TORCH serological tests (Toxoplasma gondii, Rubella virus, Cytomegalovirus) was not conducted in any mothers or their offsprings. All patients were from singleton pregnancies. Primitive reflexes at birth, such as leg and arm movements, crying, sucking, and swallowing, were generally present. The patients predominantly exhibited progressively abnormal increases in head circumference, bulging or protrusion of the anterior fontanel, seizures, cerebral palsy, intellectual disability, developmental delay, lethargy, microcephaly, convulsions, and varying degrees of auditory and visual impairments. Most cases were involved with a combination of these clinical manifestations. Intracranial hypertension was clinically diagnosed in 13 patients, of whom 4 received CSF shunt procedures. Postoperatively, abnormal head enlargement was alleviated to varying degrees, yet no significant improvement in clinical symptoms was observed.

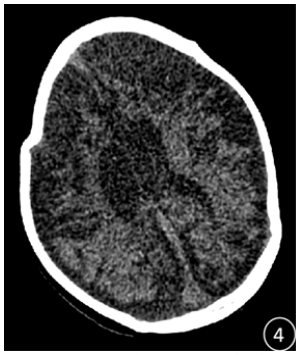

Figure 4 Hydranencephaly with normal lateral ventricles

Table 1: Radiological Manifestations on CT Imaging of the Brains of 22 Pediatric Cases with Hydranencephaly

Characteristic Features	Case Count	Percentage Representation (%)
Total Absence of Cerebral Hemispheres	5	22.73
Residual Cerebral Parenchyma within Cerebral Hemispheres	17	77.27
Residual Cerebral Areas		
Frontal Lobe	6	27.27
Occipital Lobe	3	13.64
Frontal and Temporal Lobes	3	13.64
Frontal, Temporal, and Occipital Lobes	2	9.09
Frontal and Occipital Lobes	2	9.09
Temporal and Occipital Lobes	1	4.55
Bilateral Lateral Ventricles Essentially Normal	3	13.64
Complete Absence of Bilateral Lateral Ventricles	19	86.36
Incomplete or/and Dislocated Falx Cerebri	12	54.55
Association with Other Craniocerebral Malformations		

CT Imaging Findings

In all 22 patients, the bilateral cerebral hemispheres were completely or nearly completely absent, replaced by cystic areas filled with cerebrospinal fluid (CSF) (Figure 1). Minor remnants of the frontal, occipital, temporal, and parietal lobes were observed in some cases (Figure 2B). The cerebellar tentorium, thalamus, brainstem, and cerebellar

https://dx.doi.org/10.4314/mmj.v36i5.4

hemispheres were approximately intact. The falx cerebri was present, albeit incomplete or displaced (Figure 3). Notably, incomplete or displaced falx cerebri was observed in 12 patients, 10 of which exhibited symptoms of intracranial hypertension. The bilateral lateral ventricles were completely absent in most patients with hydranencephaly, while few exceptions (Figure 4). The third ventricle was visible or partially visible, and the fourth ventricle was clearly visible without significant dilation. No obvious space-occupying lesions were observed in the third and fourth ventricles or the mesencephalic aqueduct region in any of the cases. A minority of patients had concomitant Dandy-Walker syndrome (Figure 2). The CT imaging findings of the brains of the 22 patients are summarized in Table 1.

Discussion

Hydranencephaly is a rare congenital post-neurulation disorder that occurs during the second trimester characterized by the destruction of the cerebral hemispheres, which are replaced with a membranous sac filled with CSF[4,5]. Hydranencephaly is rarely seen among developed regions due to therapeutic abortions. A study performed in the United States with the population of Texas showed an incidence rate of 1.4 to 2.8 per 100,000 live births[6]. A study in a Japanese population found an incidence of 2.1 per 100,000 live births[1]. The aim of this study is to draw attention to the clinical, radiological, and other characteristics of hydranencephaly, thereby fostering a deeper understanding of this rare disorder and facilitating early diagnosis and effective management.

Etiology and Clinical Manifestations

The etiology behind this condition is usually unknown. Different causes have been postulated. The researchers suggest that the most common mechanism may be due to ischemic stroke (infarction). Bilateral occlusion of the supraclinoid segments of the internal carotid artery (ICA) and, in some cases, the middle cerebral artery (MCA) can occur - usually between the 8th and 12th weeks of gestation. This may lead to the absence of structures perfused by the ICA/MCA while structures perfused by the posterior cerebral artery and the basilar artery are intact[3,5,7]. As such, hydranencephaly is categorized into a group of circulatory developmental encephalopathies. Another possible cause is infection. An intrauterine infection may cause necrotizing vasculitis and lead to hydranencephaly. Intrauterine infections such as toxoplasmosis and viral infections (enterovirus, adenovirus, parvovirus, cytomegalovirus, herpes simplex, Epstein-Barr, and respiratory syncytial viruses) may be responsible3,8. Other possible causes include hypoxia, syndromic/genetic, leukomalacia, toxic exposure, twin pregnancy, etc[3,7,9,10].

As the end of 2021, 7.9% (7.6% to 8.2%) of adults aged 15-49 years in Malawi were living with HIV. HIV prevalence among women was 10.4% (10.0% to 10.8%), twice as high as 5.1% (4.7% to 5.7%) among men[11]. Among the cases in this study, 8 mothers (38.46%) were HIV-positive. HIV infection, along with other related infections such as TORCH (note : serological testing for both mothers and infants was not conducted in this study due to limitations), may contribute to fetal malformations, including hydranencephaly. Most fetuses with hydranencephaly die before birth, while those who are born alive may initially appear normal, with primitive reflexes such as leg and arm movements, crying, and sucking and swallowing reflexes present. However, over time, these infants may exhibit progressively abnormal increases in head circumference due to hydrocephalus, with bulging or protrusion of the anterior fontanel, as well as corresponding symptoms of cerebral hypoplasia or agenesis, such as seizures, cerebral palsy, intellectual disability, developmental delay, lethargy, microcephaly, convulsions, and varying degrees of auditory and visual impairment. Most cases present with a combination of these clinical manifestations, as seen in all 22 infants in this study. The prognosis for infants with hydranencephaly is extremely poor, most of them would die from complications within one to two years. Some studies have reported median survival rates exceeding one to two years, but not reaching 7.5 years[12]. There are also reports of patients surviving for more than 32 years[7]. Four infants in this study underwent CSF shunt procedures, which resulted in varying degrees of relief from abnormal head enlargement but did not significantly improve other clinical symptoms unrelated to intracranial hypertension. Literature suggests that CSF shunt procedures do not improve the prognosis of hydranencephaly and is primarily performed to alleviate severe hydrocephalus[7,13,14]. Surgical intervention is generally not required if there is no significant increase in head circumference. Additionally, this study identified infants with concurrent conditions such as heart murmurs, testicular agenesis, and Dandy-Walker syndrome. The presence of these comorbidities indicates that hydranencephaly does not always occur as an isolated defect, and clinicians should be vigilant for the presence of other related malformations during diagnosis and treatment.

CT Imaging Manifestations

The majority of patients are diagnosed during pregnancy. Ultrasound examinations are performed between 21 and 23 weeks of gestation. Absence of cerebral hemispheres, replaced with homogeneous echoic material. Preservation of thalami, brainstem, and cerebellum. Although most commonly used during pregnancy, this test can be also used during the postnatal period to obtain a diagnosis[15]. Post-delivery, the gold standard for diagnosis encompasses CT scans and MRI examinations[3,7]. CT imaging reveals the complete or nearly complete absence of the cerebral hemispheres, replaced by a cystic area filled with CSF. Despite the severe damage to the cerebral hemispheres, minimal remnants of the frontal, occipital, temporal, and parietal lobes may persist. Infants with hydranencephaly exhibit, in addition to the absence of cerebral hemispheres, a generally intact tentorium cerebelli, thalamus, brainstem, and cerebellar hemispheres, with the cerebral falx present, albeit potentially incomplete or displaced. Pavone et al. proposed that, despite the undeveloped cerebral hemispheres, the choroid plexuses continue to produce CSF, which, if not adequately absorbed, may lead to increased intracranial pressure (ICP)[7]. In such cases, the authors contend that elevated pressure may cause rupture or displacement of the cerebral falx, serving as an ancillary indicator of ICP elevation. In this study, 10 infants exhibited signs and symptoms of intracranial hypertension. The majority of infants with hydranencephaly demonstrate complete destruction and absence of the bilateral lateral ventricles, while only a minority display relatively intact lateral ventricles. Within our case series, three infants exhibited nearly normal lateral ventricles. A literature review conducted by the authors between 1998 and 2023 collected data on 72 patients, all of whom underwent CT

 https://dx.doi.org/10.4314/mmj.v36i5.4

imaging that described the status of their lateral ventricles. Among these, only one case showed nearly normal lateral ventricles, seven cases presented with enlarged, deformed, or residual lateral ventricles, and 64 cases demonstrated destruction and disappearance of the lateral ventricles. The third ventricle was visible, either partially or fully, in infants with hydranencephaly, while the fourth ventricle generally appeared normal.

Differential Diagnosis

The differential diagnosis primarily revolves around severe-extreme forms of hydrocephalus. The distinction between severe-extreme hydrocephalus and hydranencephaly, though challenging, is critical to prognosis and treatment response. Sutton and colleagues conducted a follow-up study on five infants with hydranencephaly and five with severe hydrocephalus over a period ranging from 4 to 23 months[16]. Despite aggressive surgical interventions and SCF shunting, the five infants with hydranencephaly showed no neurological or radiological improvements, whereas the five infants with severe hydrocephalus demonstrated moderate clinical improvements. The primary distinction lies in the presence of intact, albeit compressed and marginalized, parenchymal tissue in cases of hydrocephalus. When hydrocephalus arises from obstruction of the mesencephalic aqueduct, the dilated third ventricle may serve as a pivotal factor in differential diagnosis. Additionally, infants with hydrocephalus present with abnormal head circumference at birth, bulging fontanels, and normal cerebrovascular imaging findings, which can also serve as distinguishing points.

Other differential diagnoses include holoprosencephaly (alobar), schizencephaly (severe open), and anencephaly[3,7,17]. Holoprosencephaly (alobar) is the most severe form of holoprosencephaly. It is a condition that occurs due to a congenital cerebral anomaly that results due to the absence or incomplete division of the forebrain. In this form of holoprosencephaly, there is a partial fusion of the thalami, while the falx is missing. Patients often present with facial anomalies and small head circumference. Schizencephaly (severe open) occurs due to an abnormality in the migration of neurons, leaving clefts lined with abnormal gray matter, described as polymicrogyria. The cortical mantle may appear thinned, in hydranencephaly the cortical mantle tends to be completely absent. Anencephaly is caused by a neural tube obstruction disorder and the classical finding will be defects in the skull as well as in the brain parenchyma.

Conclusion

In summary, this retrospective analysis revealed a higher incidence of HIV infection among mothers of infants with hydranencephaly, despite mothers denying risky behaviors and relevant family histories. The infants primarily exhibited preserved primitive reflexes, progressive abnormal increase in head circumference, bulging or dilated anterior fontanel, epilepsy, cerebral palsy, intellectual disability, developmental delay, lethargy, microcephaly, convulsions, and varying degrees of auditory and visual impairments. They may also present with other intracranial malformations or bodily abnormalities. On CT imaging, the primary manifestations include the absence of cerebral hemispheres, replaced by CSF; the disappearance of bilateral lateral ventricles,; the presence of the cerebral falx, which may be incomplete or displaced; and the thalamus, brainstem, and cerebellum are generally intact.

Acknowledgements

This work was supported by the Natural Science Foundation of Shaanxi Province (No. 2023-JC-QN-0979).

Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical approval

This study was approved by Mzuzu University Research Ethics Committee (MZUNIREC/DOR/24/137).

Data availability statement

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

References

1. Hino-Fukuyo N, Togashi N, Takahashi R, Saito J, Inui T, Endo W et al. Neuroepidemiology of Porencephaly, Schizencephaly, and Hydranencephaly in Miyagi Prefecture, Japan. Pediatr Neurol. 2016 Jan;54:39-42.e1. doi: 10.1016/j.pediatrneurol.2015.08.016.

2. Gezmu AM, Shifa JZ, Kgwarae C, Siamisang A. Hydranencephaly in a Neonate: A Literature Review. Neurol India. 2020 Jan-Feb;68(1):199-201. doi: 10.4103/0028-3886.279698.

3. Pant S, Kaur G, De JK. Hydranencephaly. Kathmandu Univ Med J (KUMJ). 2010 Jan-Mar;8(29):83-6. doi: 10.3126/kumj.v8i1.3227.

4. Greene ND, Copp AJ. Neural tube defects. Annu Rev Neurosci. 2014;37:221-42. doi: 10.1146/annurev-neuro-062012-170354.

5. Khalid M, Khalid S, Zaheer S, Redhu N, Ekramullah. Hydranencephaly: a rare cause of an enlarging head size in an infant. N Am J Med Sci. 2012 Oct;4(10):520-2. doi: 10.4103/1947-2714.102015.

6. Husain T, Langlois PH, Sever LE, Gambello MJ. Descriptive epidemiologic features shared by birth defects thought to be related to vascular disruption in Texas, 1996-2002. Birth Defects Res A Clin Mol Teratol. 2008 Jun;82(6):435-40. doi: 10.1002/bdra.20449.

7. Pavone P, Praticò AD, Vitaliti G, Ruggieri M, Rizzo R, Parano E, Pavone L, Pero G, Falsaperla R. Hydranencephaly: cerebral spinal fluid instead of cerebral mantles. Ital J Pediatr. 2014 Oct 18;40:79. doi: 10.1186/s13052-014-0079-1.

8. Malik AM, Ahmad M, Khan A, Ullah E. Hydranencephaly: a rare cause of delayed developmental milestones. BMJ Case Rep. 2013 Apr 30;2013:bcr2013009589. doi: 10.1136/bcr-2013-009589.

9. Meuwissen ME, de Vries LS, Verbeek HA, Lequin MH, Govaert PP, Schot R et al. Sporadic COL4A1 mutations with extensive prenatal porencephaly resembling hydranencephaly. Neurology. 2011 Mar 1;76(9):844-6. doi: 10.1212/WNL.0b013e31820e7751.

10. Sen K, Kaur S, Stockton DW, Nyhuis M, Roberson J. Biallelic Variants in LAMB1 Causing Hydranencephaly: A Severe Phenotype of a Rare Malformative Encephalopathy. AJP Rep. 2021 Jan;11(1):e26-e28. doi: 10.1055/s-0040-1722728.

11. Wolock TM, Flaxman S, Chimpandule T, Mbiriyawanda S, Jahn A, Nyirenda R, Eaton JW. Subnational HIV incidence trends in Malawi: large, heterogeneous declines across space. medRxiv [Preprint]. 2023 Feb 4:2023.02.02.23285334. doi: 10.1101/2023.02.02.23285334.

12. Omar AT 2nd, Manalo MKA, Zuniega RRA, Reyes JCB, Brillante EMB, Khu KJO. Hydranencephaly: Clinical Features and Survivorship in a Retrospective Cohort. World Neurosurg. 2020 Dec;144:e589-e596. doi: 10.1016/j.wneu.2020.09.029.

13. Adeloye A. Hydranencephaly in Malawian children. East Afr Med J. 2000 Jun;77(6):316-8. doi: 10.4314/eamj.v77i6.46641.

14. Thiong'o GM, Ferson SS, Albright AL. Hydranencephaly treatments: retrospective case series and review of the literature. J Neurosurg Pediatr. 2020 May 15;26(3):228-231. doi: 10.3171/2020.3.PEDS19596.

15. Sepulveda W, Cortes-Yepes H, Wong AE, Dezerega V, Corral E, Malinger G. Prenatal sonography in hydranencephaly: findings during the early stages of disease. J Ultrasound Med. 2012 May;31(5):799-804. doi: 10.7863/jum.2012.31.5.799.

16. Sutton LN, Bruce DA, Schut L. Hydranencephaly versus maximal hydrocephalus: an important clinical distinction. Neurosurgery. 1980 Jan;6(1):34-8.

17. Omoto T, Takahashi T, Fujimori K, Kin S. Prenatal diagnosis of fetal microhydranencephaly: a case report and literature review. BMC Pregnancy Childbirth. 2020 Nov 11;20(1):688. doi: 10.1186/s12884-020-03400-1.