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CLASSIFICATION AND MANIFESTATION OF HYDROCEPHALUS

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Abstract:

Introduction: *Despite the absence of a precise definition, hydrocephalus usually means the presence of a disturbance of cerebrospinal fluid (CSF) physiology leading to an abnormal widening of the cerebral ventricles, classically linked with elevated intracranial pressure. Despite being surely linked, idiopathic normal pressure hydrocephalus leading to ventriculomegaly without intracranial hypertension and idiopathic intracranial hypertension (also known as pseudotumour cerebri) leading to intracranial hypertension without ventriculomegaly are not included in the scope of this manuscript,****Aim of work:*** *In this review the epidemiology, pathology, diagnosis, management and treatment, debates, and future research needed for pediatric hydrocephalus, which is surprisingly a neglected issue despite its high prevalence and economic burden.****Methodology:*** *We did a systematic search for Classification and manifestation of hydrocephalus in the emergency department using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.****Conclusions:*** *Hydrocephalus is a generally common condition that results from dysfunctions of the physiology of the CSF leading to an abnormal widening of the ventricles. Infants usually manifest with progressive macrocephaly while children older than two years typically manifest with symptoms and signs of intracranial hypertension. Treatment options of the disease include shunt approaches and endoscopic approaches, which must be individualized to each child. The chronic outcome for children that have received treatment for hydrocephalus varies. Advances in brain imaging, technology, and understanding of the pathophysiology should ultimately lead to improved treatment of the disorder.*

Key words: *Classification, symptoms, signs, management, procedures, hydrocephalus, children.*

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INTRODUCTION:

Despite the absence of a precise definition, hydrocephalus usually means the presence of a disturbance of cerebrospinal fluid (CSF) physiology leading to an abnormal widening of the cerebral ventricles, classically linked with elevated intracranial pressure. Despite being surely linked, idiopathic normal pressure hydrocephalus leading to ventriculomegaly without intracranial hypertension and idiopathic intracranial hypertension (also known as pseudotumour cerebri) leading to intracranial hypertension without ventriculomegaly are not included in the scope of this manuscript. Here we will review the epidemiology, pathology, diagnosis, management and treatment, debates, and future research needed for pediatric hydrocephalus, which is surprisingly a neglected issue despite its high prevalence and economic burden.

METHODOLOGY:

We did a systematic search for Classification and manifestation of hydrocephalus in the emergency department using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: Classification, symptoms, signs, management, procedures, hydrocephalus, and children.

Epidemiology:

Hydrocephalus is considered to be the commonest condition that is encountered by pediatrics neurosurgeons. It is responsible for about two billion dollars spent in healthcare in the US annually [1]. The incidence of hydrocephalus among infants is estimated to be about 1 case per 1000 live-births [2]. but this is likely to be higher in middle- and low-income countries. In For example, in the sub-Saharan Africa alone, the number of new cases of hydrocephalus in infants may be more than 200,000 annually, which is most likely because of the wide prevalence of neonatal infections [3]. On the other hand, the most common etiologies in developed countries include post-hemorrhagic hydrocephalus in premature infants, congenital aqueduct stenosis, myelomeningocele, and brain neompalsms [4].

Pathophysiology

Understanding the physiology of CSF is becoming more advanced but it is still not complete. In the traditional bulk flow model, CSF is normally secreted by the choroid plexus epithelium within the ventricles of the cerebrum. Then it flows into the subarachnoid spaces and enters the venous system of the cerebrum through the arachnoid granulations. In this model, hydrocephalus can be a result of the CSF flow obstruction in any area between the origin and most distal areas for absorption, with the presence of a few exceptions in which the CSF may be hypersecreted. Typically, CSF flow obstruction in ventricles is categorized as obstructive hydrocephalus or non-communicating hydrocephalus, while obstruction of the flow of CSF or absorption of it in the subarachnoid spaces is usually known as communicating hydrocephalus.

Investigators have then created a more advanced hydrodynamic model that deals with hydrocephalus as a condition related to intracranial pulsations [5]. Within this model, waves of the arterial systolic pressure that enter the brain are typically dissipated by the subarachnoid spaces, capacitance veins, and intraventricular pulsations that are transmitted by the choroid plexus. These intraventricular pulsations are later absorbed through the outlet foramina of ventricles. Based on this new model, an abnormality in these pulsation absorbers contributes to dysregulated high amplitudes of pulsations which lead to the widening of the ventricles. Abnormal pulsations could have varying effects according to the presence of age-related alterations in the compliance of the brain, leading to a continuum of dysfunctions in the physiology of CSF (eg, idiopathic infantile hydrocephalus, idiopathic adolescents intracranial hypertension, and normal pressure hydrocephalus in the elderly population) [6].

Causes

Regardless of the used model to explain hydrocephalus, obstruction of the ventricles or the subarachnoid space along with elevated cerebral venous pressures can all cause hydrocephalus, with multiple possible etiologies for every mechanism.

Possible genetic origins:

Recent advances have discovered some of the genetic etiologies behind the development of congenital inherited hydrocephalus. Genetic etiologies are significant contributors to both syndromic and non-syndromic types of hydrocephalus.[7] Population-based studies demonstrate familial aggregation of congenital hydrocephalus cases, with higher recurrence ratios for same-sex twins, first-degree relatives and second-degree relatives [8]. More than half mutant genes or loci have been found to be associated with non-syndromic congenital hydrocephalus in some animals, but only three of these mutations have been found to be associated with non-syndromic congenital hydrocephalus in

humans. Most individuals who developd non-syndromic congenital hydrocephalus have significant aqueduct stenosis. Of these, X-linked hydrocephalus is the commonest form to be inherited, being responsible for more than ten percent of hydrocephalus cases in males [9].

Mutations that develop in the L1CAM gene, which is responsible for encoding the L1 cell adhesion molecule, are the commonest causes of developing hydrocephalus. Investigators have demonstrated two more genetic mutations in severe autosomal-recessive cases: truncating mutations in the MPDZI gene which encodes MUPP-1, 16 and mutations in the CCDC88C gene that encodes encoding DAPLE [10].

Primary ciliopathies conditions like Joubert's syndrome and Meckel-Gruber syndrome are usually linked with the development of congenital hydrocephalus in humans. Most recent studies suggest that polarization of ependymal cell, that is responsible for the CSF flow and ciliary beating orientation, when it is disrupted, causes hydrocephalus along with developmental anomalies [11]. In mice models, 8 of twelve novel genes that lead to the development of autosomal-recessive congenital hydrocephalus 24 code for proteins related to the cilia [12].

Both, humans molecular genetic data and animal molecular genetic data indicate that many genes of hydrocephalus are responsible for encoding growth factors, receptors, cell-surface molecules (like cilia), and related intracellular signaling molecules that usually regulate both the growth and development of the brain.

When these genes are mutated, they perturb the fate, survival, and proliferation of the neuroglial cells, leading to the creation of structural (anatomical) or functional impediments to the pulsatility or circulation of the CSF (or both sometimes).

The commonest pediatric neoplasms of the posterior brain fossa are cerebellar astrocytomas, medulloblastomas, and ependymomas, which usually manifest with hydrocephalus from obstruction of the fourth ventricle.

Inflammatory processes

Inflammation of the ventricles or the presence of meningitis from an infection or hemorrhages can usually cause hydrocephalus by impairing the circulation and absorption of CSF or disrupting the arterial pulsations normal dampening. Intraventricular hemorrhages associated with prematurity are considered to be among the commonest etiologies in high-income countries, 6 while neonatal ventricular inflammations with a cyclical incidence pattern that was found to be associated with climate changes has been recently observed as the main etiology in Uganda and possibly other sub-Saharan African areas.[13] Ventricular inflammations could stimulate scarring of ependymal tissue, obstruction of the ventricles, and the development of a multi-compartment hydrocephalus. Some congenital hydrocephalus cases could be the results of ventricular inflammations in the fetus that block the development and functions of ependymal ciliary, or from the impact of blood-borne lysophosphatidic acid on the adhesion and localization of neural progenitor cell [14].

Vascular dysfunction

Decreased compliance of veins might be an essential etiology of the development of communicating hydrocephalus. For example, communicating hydrocephalus cases have been attributed to idiopathic venous outflow resistance and collapse of venous sinus as well as to venous thrombosis and venous outlet stenosis linked to craniofacial dysostoses. Cases of idiopathic infantile hydrocephalus have also been linked to cerebral hyperaemia [15].

Dysregulated ion and water transport

The choroid plexus usually have highest rates of water and ions transport more than any epithelial tissue in the human body and this procedure occurs by specialized enzymes and molecules for ion transportation like carbonic anhydrase, bumetanide-sensitive Na-K-2Cl cotransporter [16] and aquaporin water channels, which are also important in the ventricular ependymal cells. These transportation procedures have been found to be associated with the pathophysiology and targeted therapies of hydrocephalus [17]. For example, AQP4 is present within glia and ependymocytes, and a subset of AQP4-knockout mice have been found to develop and obstruction of the aqueduct. On the other hand, ependymal AQP4 is usually upregulated in the late stages of developing hydrocephalus, which suggests a role of compensation to recover homoeostasis of fluids. A para-vascular system that facilitates mobility and transportation of water and solutes from the subarachnoid CSF into the brain interstitial fluid and out through the deep draining veins, also known as the glymphatic system, has been found to contain para-vascular channels that are normally bounded by astrocytic end-feet that contain AQP4 [18]. Dysfunctions of this system may lead to hydrocephalus. Hypersecretion of CSF that occurs

secondary to the development of hyperplasia of the choroid plexus or non-obstructive neoplasms of the choroid plexus has also been found to cause hydrocephalus.

Other outcomes of hydrocephalus like mechanical disruption, ischemia, inflammation, increased intra-ventricular pressure and ventriculomegaly could all lead to the development of secondary neurovascular damage and inflammations, leading to the formation a crescendo of tissue damage that further worsens the development of the brain [19].

Acute ventriculomegaly can lead to the compression and stretching of periventricular tissues (like axons, myelin, and micro-vessels) leading to the ischemia, hypoxia, inflammation, and higher pulsatility of CSF. Chronic ventriculomegaly stimulates gliosis and chronic inflammation, demyelination, degeneration of axons, edema of the periventricular area, metabolic dysfunctions, and alterations to the permeability of the blood brain barrier. Hydrocephalus can also be associated with ependymal denudation, which further worsens hydrocephalus and exposes the sensitive subventricular zone to toxic material that will negatively affect neurogenesis. Considerable compensation also potentially happens as a response to hydrocephalus, including glymphatic CSD absorption [20].

Clinical presentation

Clinical manifestations of hydrocephalus can vary among different ages. Performing prenatal ultrasound can help detect fetal ventriculomegaly, as early as eighteen weeks of gestation in some cases. This detection will usually be followed with further evaluations, that include a level two ultrasound, a fetal MRI imaging, TORCH infections screening, and/or amniocentesis.56 In mothers who are known to be carriers of L1CAM gene mutation, chorionic villus sampling or amniocentesis could also be used to achieve prenatal diagnosis of X-linked hydrocephalus [21].

In infants, the presence of hydrocephalus usually leads to the development of an abnormally enlarging circumference of the head, irritability, vomiting, anterior fontanel bulging, or cranial sutures splaying. True hydrocephalus should be distinguished from what is known as benign external hydrocephalus or benign subarachnoid space enlargement, that does not any treatment and is characterized by enlargement of the subarachnoid spaces, with only mild or even absent ventriculomegaly, and a clinically healthy child.[22] After infancy, hydrocephalus will classically present with a constellation of clinical findings that can include a combination of headaches, vomiting, delayed developmental milestones, diplopia (typically a result of VI cranial nerve palsy), and/or papilledema.

Imaging of the brain is considered to be an essential investigation during the work-up of hydrocephalus. For example, an infant who has an open fontanel can be checked for ventriculomegaly by performing cranial ultrasonography, while an MRI image (preferred over CT because MRI prevents exposure to radiation and gives more data) is classically used to understand the anatomy and cause.

CSF shunts:

Previously, the treatment of hydrocephalus was mainly dependent on the bulk flow model of CSF physiology that we mentioned above in details. In the early twentieth century, there have been attempts to bypass the obstructions within CSF pathways by performing open craniotomy or decreasing the production of CSF using crude endoscopic methods. These measurements were found to be mildly successful but had significantly high rates of morbidity and mortality. With the advent of silastic tubing and early valve mechanisms, focus was brought toward mechanical conduits for the diversion of CSF, and, more than sixty years after its invention, CSF shunting is still the standard best treatment.

The commonest type of shunt acts by diverting CSF from the ventricles to the peritoneal cavity (this is called ventriculo-peritoneal shunt), although other sites like the right atrium of the heart and the pleural cavity can also be used. Shunts typically include silastic tubing that runs subcutaneously between the head and the abdomen, with a valve that is present between the ventricular and distal catheters. Differential pressure or flow-regulating valve mechanisms are usually paired with anti-siphon or gravitational gadgets to avoid over-drainage of CSF from posture-associated siphoning. However, despite the advances and technological developments, valve designs still seem to have little effects on the shunt efficacy or failure rates [23].

Endoscopic third ventriculostomy and choroid plexus cauterization:

During the 1990s, endoscopic third ventriculostomy (ETV) was introduced as a possible alternative for the treatment of patients with hydrocephalus, especially in patients who have non-communicating hydrocephalus. It is now routinely used at most important pediatric neurosurgical centers in developed countries. The process incudes passing an endoscope to the frontal horn of the lateral ventricle,

then through the foramen of Monro, and into the third ventricle. An opening is later made within the third ventricle floor, making it possible to achieve direct communication into the prepontine cistern.

Although the use of ETV has been found to be successful in many patients with hydrocephalus, there is still a high rate of early procedure failure, especially among infants. Starting from the early 2000s, however, choroid plexus cauterization was added to ETV procedure to enhance efficacy of ETV among infants [24].

During the early 20th century results from small studies in which CPC was used alone to manage patients with hydrocephalus demonstrated some success in cases of communicating hydrocephalus, but with the use of available techniques, mortality and morbidity rates were still significant, and any long-term collateral effects of CPC were still unknown. The more recent use of CPC has mostly been in combination with ETV, especially in countries of the sub-Saharan Africa.

Shunt complications

Children who have treated hydrocephalus can have many possible chronic complications and morbidities, usually associated with the treatment. Shunt failure, often as a result of mechanical obstruction, requiring some intervention can potentially occur in up to forty percent of children during the first two years following the original placement of the shunt with continuous risk of failure present later. Failure of shunt is typically diagnosed using imaging modalities that show increased size of the ventricle when compared to the baseline with symptoms like headache, vomiting, restlessness, reduced levels of consciousness, and, in infants, bulging fontanel and increased head growth. Randomized trials results indicate that the shunt valve type that was used has no impact on the failure rates [25]. The obstruction of the shunt is managed and treated with urgently performed surgery to detect and replace the obstruction. In cases where symptoms are subtler, monitoring of the intracranial pressure could sometimes be beneficial to confirm the presence of shunt obstruction. Peri-operative mortality rates following shunt surgery is rare (less than one percent) [26].

The rate of shunt infections is about nine percent and is most likely to occur within the first three months following the surgery. It presents with fever, restlessness, wound erythema, or other symptoms of shunt dysfunction. Diagnosis can be confirmed using positive microbiological culture from CSF that can be obtained from the shunt tap. The most common organisms responsible for the condition include cutaneous commensal organisms, like coagulase-negative Staphylococcus, Staphylococcus aureus, and, less often, Propionibacterium spp [27].

CONCLUSIONS:

Hydrocephalus is a generally common condition that results from dysfunctions of the physiology of the CSF leading to an abnormal widening of the ventricles. Infants usually manifest with progressive macrocephaly while children older than two years typically manifest with symptoms and signs of intracranial hypertension. The typical conception of hydrocephalus as the result of obstruction to bulk flow of CSF is evolving to models that integrate dysfunctional cerebral pulsations, brain compliance, and newly characterized water-transport mechanisms. Hydrocephalus can have many causes. Congenital hydrocephalus, most commonly occurs in the aqueduct stenosis, has been found to be associated with genes that regulate the growth and development of the brain. Hydrocephalus can also be acquired in some cases, mostly from pathophysiological processes that usually affect ventricular outflow, subarachnoid space function, or the compliance of the cerebral veins. Treatment options of the disease include shunt approaches and endoscopic approaches, which must be individualized to each child. The chronic outcome for children that have received treatment for hydrocephalus varies. Advances in brain imaging, technology, and understanding of the pathophysiology should ultimately lead to improved treatment of the disorder.

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