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PEDIATRIC HYDROCEPHALUS: CAUSES, SYMPTOMS AND TREATMENT MODALITIES

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Abstract

Depression is considered among the most prevalent of all mental health diagnoses. Besides pharmacotherapy and psychotherapy, extending the daily photoperiod with artificial bright light (bright light therapy – BLT) has been reported as being useful in treating mood disorders. The aim of this article is to analyze the available data in the literature and discuss the efficacy of BLT in both seasonal affective disorder (SAD) and non-seasonal major depressive disorder. We analyzed 20 studies covering the problems of efficacy of BLT versus placebo and antidepressants, its side-effects, predictive factors which suggest better therapeutic response, as well as unclarified questions. For SAD, data show well-established efficacy of BLT. Artificial light exposure consistently improves symptoms compared to placebo, with remission rates comparable to those seen for antidepressant medication. Regarding the predictive factors, morning treatment is shown to be superior to evening treatment, reflecting the hypothesis of phase-delayed circadian rhythms that underlie disordered mood. Also, atypical vegetative symptoms are shown to predict better therapeutic response. With high therapeutic benefits, and a favorable side-effect profile, it is considered as an appropriate alternative to antidepressants. On the other hand, data regarding the efficacy of BLT in non-seasonal depression show a high level of inconsistency. Although some studies confirm the therapeutic use of BLT in non-seasonal depression, meta-analyses express that the therapeutic benefits seem to be fleeting. Also, it is expressed that general quality of evidence seems to be poor, due to considerable methodological problems. To conclude, data from the literature support the efficacy of BLT in depression with seasonal pattern and recommend it as a first-line choice in this case. To evaluate BLT for non-seasonal depression more rigorous studies are necessary, with a focus on long-term-effects, larger groups, controlled group allocation, and adequate placebo treatment.

KEYWORDS: cerebrospinal fluid (CSF), endoscopic ventriculostomy, intracranial pressure, neurosurgery, pediatric hydrocephalus, ventriculoatrial shunt, ventriculoperitoneal shunt

INTRODUCTION

Hydrocephalus can be defined as an abnormal increase in the amount of cerebrospinal fluid (CSF) within the ventricles of the brain.[1] It involves dilatation of the cerebral ventricular system as well as corresponding compressive effects on the parenchyma.[2] It can be divided into two main types – obstructive and communicating. If the main cause is the obstruction of the outflow of CSF, usually in the cerebral aqueduct (also known as aqueduct of Sylvius) or foramina Luschka and Magendie (where CSF can exit from the brain ventricles to the subarachnoid space), it is called obstructive hydrocephalus. Communicating (non-obstructive) hydrocephalus can occur due to impaired CSF reabsorption which can be caused by functional impairment of arachnoid Pacchioni's granulations, but impaired reabsorption usually emerges due to meningitis or subarachnoid hemorrhage.[3]

CLINICAL PRESENTATION OF HYDROCEPHALUS

Clinical features of hydrocephalus depend on the patient's age, causes of hydrocephalus, rapidity of onset, and site of obstruction if the type is obstructive hydrocephalus. The usual physical manifestation in infants is head enlargement because of the excess CSF and enlarged ventricles. Head enlargement is defined as a head circumference above the 98th percentile for the infant's age. The patient usually presents

with increased irritability, vomiting, and poor feeding. They can also have headaches due to skull rigidity. If we were to perform a physical examination, we would be able to palpate disjunction of the skull sutures and we would be able to see dilated and prominent scalp veins. The patient will also present with a bulging and tense anterior fontanelle on the top of the head. Due to increased intracranial pressure (ICP), the eyes will deviate downward and the infant will present with persistent downward gaze, the upper eyelids can be retracted and upward gaze is completely paralyzed – this is called a setting-sun sign and it is an ophthalmologic sign of hydrocephalus, but it can also be benign in healthy infants and represent immaturity of the reflex systems that control eye movements. Hydrocephalus can easily stretch the periventricular pyramidal tract fibers and cause spasticity of the lower limbs.
In children, if the ICP is increased due to hydrocephalus, a very dangerous physical manifestation may be papilledema, optic disc swelling secondary to elevated ICP, which often presents as blurry vision. If papilledema is not treated well it can lead to optic atrophy and vision loss, so it is a medical emergency. Like infants, children may also experience a sun-setting phenomenon or failure of the upward gaze. It appears secondary to high pressure on the tectal plate through the suprapineal recess. One more clinical sign that is important in diagnosing hydrocephalus is called the Macewen sign and it is usually described as a „cracked pot" sound due to percussion of the head near the junction of the frontal, temporal and parietal bone. If the test is positive, it indicates separated sutures which is a common finding in hydrocephalus. Patients may present with an unsteady gait which is related to lower limb spasticity. Children's heads will be unusually large, but with closed sutures, unlike infants. If ICP is chronically elevated, it can lead to progressive macrocephaly and, secondary to increased ICP, unilateral or bilateral sixth cranial nerve palsy may occur and it usually presents as double vision (diplopia). Some additional symptoms in children are stunted growth and sexual maturation because of the third ventricle dilation and it can lead to precocious puberty or obesity. Dilation of the third ventricle may also lead to Parinaud syndrome which manifests as an inability to move eyes upwards and downwards. If a patient suffers from neck pain, it can be a sign of a tonsillar herniation. Similarly to children, adults suffering from hydrocephalus may present with papilledema, the inabililty to move the eyeballs upwards and impaired eye accommodation, truncal and limb ataxia, an enlarged head which is very common, and palsy of the sixth cranial nerve may occur and present with horizontal diplopia. NPH, or normal pressure hydrocephalus, has diverse symptoms and often occurs in the elderly, which means that we can rarely see NPH in patients younger than 60 years old. The triad of symptoms, also known as Hakim's triad, is defined by incontinence, gait apraxia which gets worse with time, and dementia. Parkinsonism and personality changes may also occur.[1,3] Another, albeit rare, complication of hydrocephalus is sensorineural hearing loss. Jamshidi et al. have reported a case of a 10-month old infant presenting with a bilateral sensorineural hearing loss of moderate severity, diagnosed after failing newborn hearing screening. Subsequent imaging demonstrated obstructive hydrocephalus, which was treated by inserting a ventriculoperitoneal (VP) shunt. Afterwards, the patient had immediate improvement of her hearing, which indicates hydrocephalus was the cause of this condition.[4]

ETIOLOGY OF HYDROCEPHALUS

Hydrocephalus can be congenital (recognized at birth) or acquired during the lifetime. The incidence of congenital hydrocephalus is about 0.2–0.5/1000 live births, with a higher incidence reported in elderly primiparous mothers.[2] One of the important congenital causes of hydrocephalus in children is a type of brainstem malformation, aqueductal stenosis (stenosis of mesencephalic aqueduct of Sylvius), which is responsible for about 10 % of cases in newborns. Some other congenital syndromes that may lead to hydrocephalus are Dandy-Walker malformation and Arnold-Chiari malformation type 1 and type 2. Dandy-Walker malformation is primarily described as cerebellar hypoplasia, dilatation of the fourth ventricle and enlarged posterior fossa where macrocephaly is the most frequent manifestation. Arnold-Chiari malformation is a developmental defect that usually involves the cerebellum. Type I is defined as the protrusion of the cerebellum into the foramen magnum, while type II (classic Chiari malformation) is often combined with spina bifida in newborns and consists of a protrusion of the cerebellum and part of the brain stem through the foramen magnum. Agenesis of the foramen Monroi, which is a communication between lateral ventricles of the brain can lead to congenital hydrocephalus because CSF cannot circulate through the ventricles as it normally does.

On the other hand, hydrocephalus can develop after birth and then it is defined as acquired. It can develop due to overproduction, poor absorption, or obstruction of the outflow of CSF. Choroid plexus papillomas and carcinomas can secrete excess CSF and rarely lead to hydrocephalus due to CSF overproduction. The most common reasons for obstruction in the brain ventricles or between ventricles and subarachnoid space are brain tumors (such as ependymomas that are located in the ventricles and develop from the ependymal tissue or medulloblastomas), hematomas, or intraventricular hemorrhage that can occur in prematurely born babies or due to vascular malformations in the brain that lead to a predisposition to bleed heavily. Subarachnoid hemorrhage (SAH) can block reabsorption of CSF in the subarachnoid space leading to excess CSF in the brain ventricles. SAH is a very common reason for hydrocephalus in adults, including tumors and head injury.1 Intramedullary tumors commonly present as hydrocephalus and other nonspecific symptoms, which can lead to a delayed diagnosis in children. Although rare, hydrocephalus may be an initial manifestation of spinal cord tumors.[5]

Infections, especially bacterial meningitis, can induce development of hydrocephalus. Also, hypervitaminosis A can be an iatrogenic cause because it increases production of cerebrospinal fluid and it can also increase the permeability of the blood-brain barrier and in that way lead to hydrocephalus. It can also lead to increased ICP.[1]

IMAGING TECHNIQUES IN DIAGNOSING HYDROCEPHALUS

The most commonly used imaging techniques for diagnosis of hydrocephalus are CT and MRI.[1] CT (computerized tomography) is a form of X-ray examination where a higher

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radiation dose is received than with some other conventional X-ray techniques.[6] It is very useful for measuring the size of the ventricles of the brain and planning the surgery. When CT with contrast is used, tumors or infections that cause obstruction can easily be visualized.[1] MRI (magnetic resonance imaging) is one of the diagnostic imaging techniques whose major advantage over CT is the lack of X-rays which reduces exposure to ionizing radiation and reduces the risk of overexposure to radiation.[6] MRI is very useful for evaluating Chiari malformation or cerebellar tumors and it provides better imaging of the posterior cranial fossa than CT. In general, a CT scan is used to visualize bone injuries, to diagnose lung diseases and to detect tumor masses, while an MRI is suited for examining soft tissues (tendons and ligaments), brain tumors or spinal cord injuries. An MRI is an examination that takes more time than a CT scan which is usually done in only 5 minutes, so a CT is used more often in an Emergency Room. An MRI, on the other hand, can take up to half an hour. Also, CT will give us more details in bony structures, while MRI gives higher detail in soft tissue. Another advantage of MRI is its ability to change the imaging plane without moving the patient. If we have to detect a tumor mass, MRI would be a superior choice, but CT is faster, less expensive and the person is rarely sedated during scanning.[7] Some of the CT/MRI criteria for acute hydrocephalus include some of these findings: upward bowing of the corpus callosum which we are able to see on sagittal MRI and it is an indicator of acute hydrocephalus, ballooning of the frontal horns of the lateral ventricles and ballooning of the third ventricle (often called "Mickey mouse" ventricle) – it may indicate aqueductal stenosis. Normally, temporal horns of the lateral ventricles are barely visible, but in case of hydrocephalus, they are clearly visible and usually bigger than 2 mm. CT/MRI criteria for evaluating chronic hydrocephalus include; atrophy of the corpus callosum between two brain hemispheres, erosion of the sella turcica, sometimes herniation of the third ventricle in the sella turcica, and the temporal horns of the lateral ventricles may be visible but are less prominent than in acute phase. Also, macrocrania is one of the findings in the chronic phase.1
Another imaging method that is used for diagnostics in infants is ultrasonography through the anterior fontanelle for evaluating intraventricular or subependymal hemorrhage. Neonatal cranial ultrasound is used in neonatal intensive care units. One of the novel imaging techniques is DTI – diffusion tensor imaging, which allows recognition of some microstructural defects in the periventricular white matter which is edematous in the acute phase (edema may be present as a histological finding).[1]
Cerebral angiography is not often used, except in cases of major venous anomalies or vein of Galen malformations. Cerebral arteries are visualized as hyperplastic, occluded and elongated on angiograms.[2]
If a seizure occurs, the patient may be sent for an EEG to check the electrical activity of the brain. No specific blood tests are needed to diagnose hydrocephalus. Sometimes, CSF evaluation is helpful in posthemorrhagic and postmeningitic hydrocephalus and lumbar puncture (LP) can be used for measuring intracranial pressure. If X-linked hydrocephalus is considered as a potential diagnosis, genetic testing is recommended. It develops when there is a mutation in the gene for neural cell adhesion molecule L1 and it is inherited recessively.[1,3]

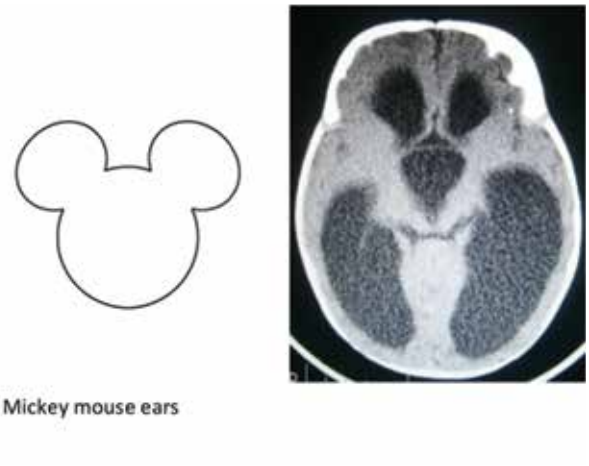

Figure 1. Mickey mouse sign seen on a CT scan, ballooning of the frontal horns of the lateral ventricles and dilatation of the third ventricle. *Source: Mohamed M.A. Zaitoun. Diagnostic Imaging of Hydrocephalus & Pneumocephalus [PowerPoint Presentation]. https://www.slideshare.net/meshmesh2013/diagnostic-imaging-of-hydrocephalus-pneumocephalus. Published December 29, 2015. Accessed August 4, 2017.*

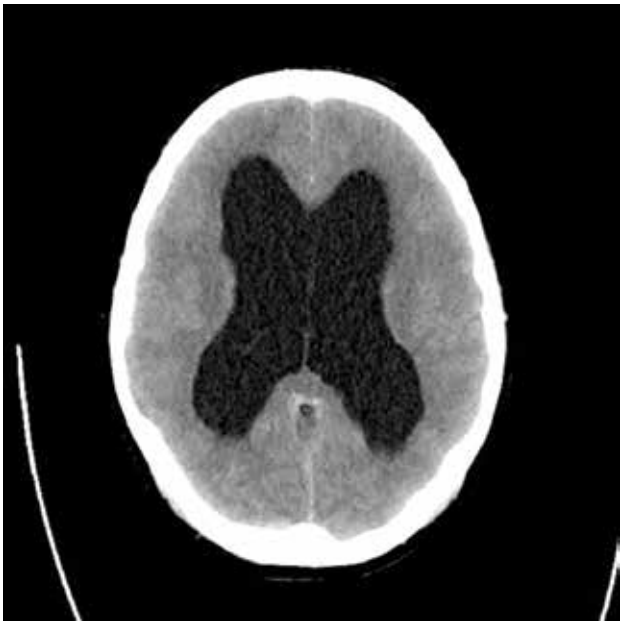

Figure 2. Obstructive hydrocephalus seen on a CT scan, dilation of the lateral ventricles. Obstructive hydrocephalus. *Case courtesy of Dr. Paul Simkin, rID 30453, Radiopaedia.org.*

TREATMENT MODALITIES OF HYDROCEPHALUS

Hydrocephalus can be treated either with medications or surgery. Most patients are treated surgically and shunts are performed. A shunt provides an alternative CSF pathway as a bypass between the brain and a drainage cavity. In that way, CSF can bypass the obstruction in the brain ventricles. A shunt usually serves as a communication between brain ventricles (or spinal canal) and a drainage cavity such as the peritoneum, pleura, right cardiac atrium etc. The most commonly used shunt is ventriculoperitoneal shunt (VP) where CSF from the lateral brain ventricle as a

proximal location is drained in the peritoneum as a distal location and the abdomen should be able to absorb the excess CSF.[1] A VP shunt is the gold standard of treatment.[2] Patients who are unable to have distal abdominal catheters because of big abdominal surgeries, malabsorptive peritoneal cavity, abdominal pseudocyst, obesity, peritonitis, undergo the ventriculoatrial shunting, which is also called vascular shunting. The catheter is located in the brain ventricle and carries excess CSF through the jugular vein to the superior vena cava and into the right atrium which represents the drainage cavity in this case. Fluoroscopic guidance is needed in this procedure to prevent cardiac arrhythmias (long distal catheter used) and catheter thrombosis (short distal catheter used). The procedure has some side effects and it is not really harmless. Every shunting procedure carries risks of infections. Some serious complications are renal failure and vein thrombosis. Aside from the most commonly used VP and ventriculoatrial shunts, the lumboperitoneal shunt is also performed in case of communicating non-obstructive hydrocephalus. The Torkildsen shunt (also named internal shunt) is rarely performed because it is valid only in the case of acquired obstructive hydrocephalus and it shunts CSF from the brain ventricles to the cisternal place. One more possible drainage cavity is the pleura, hence one more potential shunt is the ventriculopleural shunt which is performed when other shunts are contraindicated. Shunts function on the mechanism of valves which act as on-off switches. If the pressure between the valves is increased, then the flow is also increased, so, the pressure difference across the valve is the valve's opening pressure.[1,6]

One more procedure other than shunting that may be done is called endoscopic third ventriculostomy (ETV), which is often used as an alternative to shunting.[1,8] It is performed in cases of obstructive hydrocephalus. An opening is made on the floor of the third ventricle (more precisely, the tuber cinereum) that allows the excess CSF to flow to the basal cistern, thus bypassing the obstruction in the brain. The major advantage of ETV over cerebral shunting is decreased risk for infections since it avoids the use of a foreign body.[8] Hoshide et al. have recently reported a 16.6 % incidence of injuries to neural structures during ETV in North America. A robot-assisted endoscopic third ventriculostomy system (ROSA system) was introduced to improve the trajectories of the endoscope stereotactically, thereby reducing the risk for injuries and providing stabilization for the endoscope.9 Possible complications of the ETV procedure are hemorrhages from the basilar artery if it ruptures and damage to some brain structures such as the hypothalamus, pituitary gland etc.10 A single-institution experience from Great Ormond Street Hospital for Children in London included 286 pediatric cases of intraventricular endoscopic procedures. ETV was performed in 159 cases, and endoscopic fenestration in 64 patients. Some of the complications included: postoperative seizures, CSF leakage, CSF infection and intracranial hemorrhage, while no perioperative deaths were reported. Intraventricular endoscopy was concluded to be a safe procedure in the pediatric population, although it was associated with increased shunt rates, especially in infants. Higher failure rates are expected in younger infants.11 Nishiyama et al. reported that the success rate for ETV in shunt malfunction is really high, around 80%, and therefore patients with hydrocephalus who were not successfully treated using shunts are candidates for ETV. They also report how endoscopic aqueductoplasty (EAP) is an alternative to ETV because it can avoid severe arterial hemorrhage, but it is also considered a riskier procedure due to the risk of destroying some midbrain structures and leading to neurologic deficits such as oculomotor nerve palsy.[12] If rapid-onset hydrocephalus with increased intracranial pressure occurs, it is a medical emergency. Open ventricular drainage can be done, the ventricular tap is used in infants and sometimes VP or ventriculoatrial (VA) shunts are performed.[1]

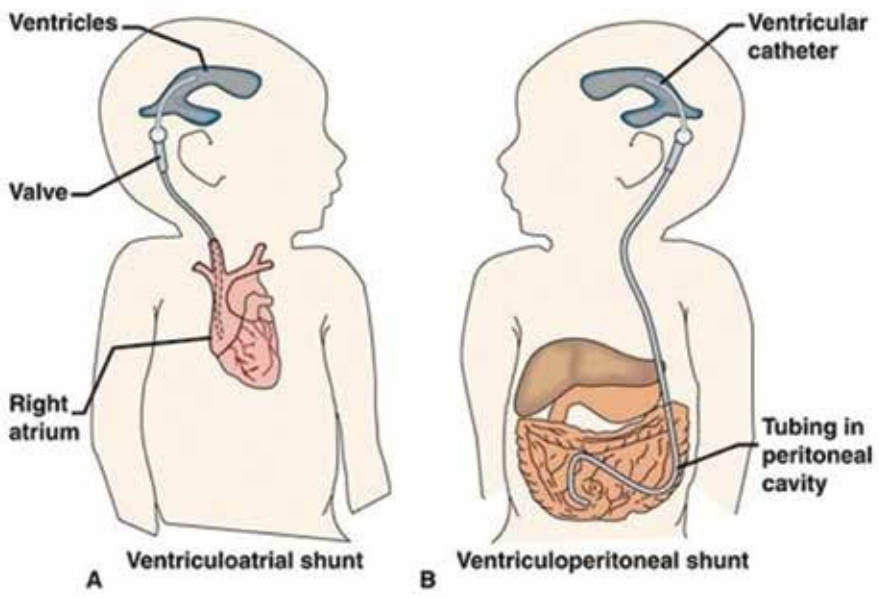

Figure 3. Ventriculoatrial (VA) shunting (on the left) and most commonly performed, ventriculoperitoneal (VP) shunting (on the right).
Source: Where do cerebral shunts drain cerebrospinal fluid (CSF) to, and what happens to CSF once drained? - Quora.
https://www.quora.com/Where-do-cerebral-shunts-drain-cerebrospinal-fluid-CSF-to-and-what-happens-to-CSF-once-drained.
Published May 12, 2014. Accessed August 4, 2017.

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Rarely, some medications can be used to treat hydrocephalus and to delay surgical treatment. It is used in premature infants in cases of posthemorrhagic hydrocephalus, but it is never considered as a long-term therapy in the chronic phase of hydrocephalus. Diuretics can decrease the production of CSF by the choroid plexus, such as acetazolamide (carboanhydrase inhibitor) and furosemide (loop diuretic). Isosorbide can increase CSF reabsorption, but its effectiveness is still questionable.[1]

HYDROCEPHALUS IN CLINICAL AND GENETIC SYNDROMES

Many clinical and genetic syndromes are accompanied by hydrocephalus. Tully and Dobyns report that the vast majority of patients with neural tube defects present with hydrocephalus. Intracranial arachnoid cysts are also a cause of hydrocephalus where those simple cysts obstruct CSF outflow. Progressive hydrocephalus can also occur due to skeletal dysplasias and FGFR – associated craniosynostosis syndromes because mutations in FGFR genes cause cranial changes which can lead to the obstruction of CSF outflow and reduction of CSF absorption. FGFR mutation can also enlarge the brain itself. Mutations in the RAS pathway (also called RASopathies) can lead to multifactorial hydrocephalus. One of the RASopathies called Costello syndrome is defined by cerebellar overgrowth and structural heart disease which can lead to increased venous pressure and that may create a pressure gradient that impedes absorption of CSF into the systemic circulation. Some additional syndromes that are associated with hydrocephalus are Gorlin syndrome, primary ciliary dyskinesia, and mucopolysaccharidoses.[13]

CSF SHUNTS

Hydrocephalus is still a very common condition treated by pediatric neurosurgeons and many advances have been made in shunt and adjuvant technology. Krystal L. Tomei has reported that neurosurgeons have an array of valve options that facilitate improved customization of CSF diversion, depending on the patient's needs. Today, neurosurgeons have both fixed-pressure and programmable valves available. Fixed-pressure valves may include antisiphon components to prevent overdrainage. On the other hand, programmable valves that are adjustable by magnets and safe for MRI up to 3 Tesla are also available. Both types of valves have several advantages and disadvantages, as Krystal L. Tomei reports. Programmable valves may be beneficial in younger patients, while fixed-pressure valves can be used in patients where MRI is necessary. Siphon-guard options that are available help to prevent overdrainage, but cannot be used in patients with low pressure hydrocephalus. Nonprogrammable valves have a 5-year survival rate in children which is higher than programmable ones. In addition to that, programmable valves may have a higher intrinsic failure rate. One of the earliest programmable valves is the Codman-Medos-Hakim valve which is used in neonates. However, there are also studies that support the use of programmable valves where it is determined that programmable valves carry a reduced risk of proximal failure and prevention of the formation of the ependymal adhesions along the proximal catheter. In adult patients, there is lower risk for revision when using programmable valves than fixed-pressure valves, while there is no significant difference in pediatric population.[14]

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PEDIJATRIJSKI HIDROCEFALUS: UZROCI, SIMPTOMI I MODALITETI LIJEČENJA

Sažetak

Hidrocefalus se može definirati kao nagomilavanje cerebrospinalne tekućine u moždanim komorama. Može se podijeliti na opstruktivni i komunicirajući hidrocefalus ili se etiološki klasificirati u kongenitalni i stečeni. Pacijent se uglavnom prezentira s makrocefalijom, povećanom iritabilnosti, glavoboljom, znakom zalazećeg sunca, spastičnošću donjih udova, pozitivnim Macewen znakom te znakovima povećanja intrakranijalnog tlaka poput papiledema. Najčešći uzroci kongenitalnog hidrocefalusa su određene malformacije moždanoga debla kao akveduktalna stenoza, Dandy-Walker malformacija, Arnold-Chiari malformacija tip 1 i 2, ageneza foramena Monroi. Česti razlozi za razvoj opstruktivnog hidrocefalusa su tumori mozga (medulobastom), intraventrikularno krvarenje i subarahnoidalno krvarenje. Općenito, hidrocefalus se može razviti zbog opstrukcije protoka cerebrospinalne tekućine, njezine povećane proizvodnje, ili pak slabe reapsorpcije. CT i MR su dobro poznate slikovne tehnike koje se koriste za dijagnosticiranje hidrocefalusa, uključujući i ultrazvuk kroz prednju fontanelu i rijetko korištenu cerebralnu angiografiju. Ponekad, ako se sumnja na X-vezani hidrocefalus, radi se genetičko testiranje, a EEG se koristi samo u slučaju epileptičnih napadaja. Većina pacijenata se liječi kirurškim putem. Lijekovi, poput diuretika acetazolamida i furosemida, koriste se samo kako bi malo odgodili operaciju. Najčešće izvođena operacija je izvođenje „šanta“ čija je svrha stvaranje komunikacije između moždanih komora i neke tjelesne šupljine za drenažu kao što su pleura, peritoneum ili desna pretklijetka. Najčešće izvođeni su ventrikuloperitonelani (VP) i ventrikuloatrijski (VA) šant. Alternativa šantu je endoskopska ventrikulostomija treće komore, čija je glavna prednost u odnosu na šant smanjeni rizik od infekcija.

KLJUČNE RIJEČI: cerebrospinalni likvor, endoskopska ventrikulostomija, intrakranijalni tlak, neurokirurgija, pedijatrijski hidrocefalus, ventrikuloatrijski šant, ventrikuloperitonealni šant

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