Dandy-Walker syndrome- A rare case description

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ABSTRACT

Dandy-Walker syndrome is a congenital developmental disorder of the central nervous system with characteristic pathological changes in the area of the lower cranial fossa. The syndrome encompasses hypoplasia of the cerebellar vermis, cystic enlargement of the IV chamber, dislocation of lateral venous sinuses and tentorium cerebelli. Clinical symptoms depend on the multitude of defects in the central nervous system. The multitude of variants of the co-occurrence of changes proves the complex etiology of this syndrome. Proper diagnosis and therapeutic treatment requires cooperation of specialists in the field of neurology, psychiatry and rehabilitation. In our study, we discuss a case of a 34-year-old man with a randomly detected Dandy-Walker syndrome, leading a normal life.

Key words: Dandy- Walker syndrome, neurophysiology, congenital defects, hydrocephalus, vermis hypoplasia.

INTRODUCTION

Dandy's Walker syndrome (Dandy-Walker malformation) is a congenital developmental defect of the central nervous system with characteristic pathological changes within the posterior cranial fossa that include: dilation of the lateral ventricles and the third chamber (less intensified than the expansion of the fourth chamber); widely separated, hypoplastic hemispheres of the cerebellum with a small hypoplastic Vermis displaced by the cephalopod; enlarging the posterior cranial fossa with a high position of the tentorium orium of the cerebellum and transverse sinuses; cystic widening of the fourth chamber usually associated with congenital lack of Luschka and Magendi foramina (Aldinger et al., 2013; Forzano et al., 2007; McClelland et al., 2015; Mytilinaios et al., 2010; Udayakumaran, 2013).

There are numerous coexistences of the above types of defects, in the absence of some (Hart et al., 1972; Jha et al., 2012; Parisi and Dobyns, 2003; Shankar et al., 2016). In approximately 50% of cases, the lateral and third chambers communicate through a thin, transparent membrane containing cells lining and sporadically of the cerebellum tissue. Hydrocephalus is often an accompanying symptom in this disease entity, affecting 90% of cases. Clinically, hydrocephalus is often the only symptom; however, it is not included in the diagnostic criteria of Dandy's Walker syndrome and often only coincides with additional abnormalities. According to literature and statistical information available to authors, approximately 50% of patients diagnosed with Dandy's Walker syndrome suffer from mental retardation, the rest does not show significant deviations (Forzano et al., 2007; Jha et al., 2012; McClelland et al., 2015).

Historical view

The first reports on the pathology of the central nervous system in the form of hydrocephalus, posterior cranial cyst and cerebellar vermis hypoplasia appeared in 1887 (Sutton, 1887). In 1914, Dandy and Blackfan (1914) classified the above triad of symptoms as a syndrome formed as a result of the closing of Luschka and Mangendi foramina, connecting the fourth chamber with the subarachnoid cavity. Taggart and Walker (1942) confirmed previous achievements regarding cerebrospinal fluid flow disorders. In 1954, Benda (1954) introduced the term "Dandy-Walker's Syndrome". Later, Benda linked the disease to the
family history of numerous brain defects, rejecting the hypothesis that Luschka and Magendi had no foramina as a factor causing this pathology, or which was definitely coexisting with it. Hart et al. (1972) delineated a triad of symptoms of Dandy-Walker’s syndrome. These include:

1) Hydrocephalus;
2) Partial hypoplasia or complete aplasia of the cerebellar vermis;
3) Cyst of the posterior cranial fossa connected to the IV chamber.

The precise etiology of Dandy-Walker’s syndrome is still undetermined. Murray et al. (1985) in 1985 emphasized the heterogeneity of etiology, stating that this syndrome may co-exist with other genetic syndromes. These include Walker-Warburg syndrome (brain-free cortex type 2, hydrocephalus, muscular dystrophy, visceral defects, posterior cranial malformations), as well as lethal Meckel-Gruber syndrome (polycystic kidney disease, CNS defects, polydactyly, liver and lung defects).

Barkovich et al. (1989) suggested the existence of correlation of several defects of the posterior cranial fossa that complicate the defects of the cerebellum. It was called the Dandy-Walker Complex (DMC). The DMC includes the hypoplasia or aplasia of the cerebellar vermis, cystic enlargement of the IV chamber, dislocation of the lateral venous sinuses and the cerebellum tentorium. The extensive genetic mapping performed by Grinberg et al. (2004) on animal models and seven human models showed the coexistence of DWS characteristic features with deletion within the arm of the long chromosome 3, and the presence of defects within the ZIC-1 and ZIC-4 genes.

Pathogenesis

It has been proven that the problems of overall prenatal development reach as early as 4 months of age when, as a result of possible infection or disturbances of the circulatory system, structural disturbances might take place. The authors deliberately use the word "possible" because there is still not enough evidence in the literature to prove that. However, numerous anomalies in the craniofacial area, heart, cardiovascular system and limb structure accompanied with Dandy Walker syndrome indicate the formation of multiple complex and multiorgan defects between 6th and 7th week of fetal life. The variety of pathological changes indicates the diversity of etiological factors that may affect the formation of the discussed syndrome. The literature available to authors indicates the role of environmental and genetic factors in the pathogenesis of this syndrome, including existence of an additional locus on the X chromosome, the cases of deletion and the presence of ZIC genes mentioned above (Aldinger et al., 2009; Barkovich et al., 2009; Basson and Wingate, 2013; Dhupar et al., 2012; Ferraris et al., 2013; Forzano et al., 2007; Grinberg et al., 2004; Imataka et al., 2007; Murray et al., 1985; Pawlaczyk and Borysewicz-Szumigala, 2005; Tohyama et al., 2011; Zanni et al., 2011). However, in the vast majority of cases, the cause of the syndrome is unknown, although family history has been described, autosomal recessive inherited (Chitayat et al., 1994).

Occurrence

The incidence of Dandy-Walker syndrome is 1 case in 25,000 - 30,000 live-born children (McClelland et al., 2015). Studies of many centers give different results of analyses as for the occurrence of the disease. Some specify a similar probability of disease in women, as in men; others indicate more frequent occurrence in women. DWS is usually detected during pregnancy, in children, symptoms of the syndrome in adulthood appear very rarely (Chitayat et al., 1994).

Diagnostics

Dandy- Walker syndrome can be diagnosed ultrasonographically during pregnancy between 12 and 14 weeks after conception; however, the sensitivity of prenatal ultrasound is significantly higher in subsequent weeks of fetal life. Studies show that ultrasound examination performed at 18 weeks after fertilization allows confirmation of the diagnosis and also to determine other malformations from the central nervous system. In addition, amniocentesis (Chitayat et al., 1994; Klein et al., 2016; Lufti and Smirniotopoulos, 2015) is often used in prenatal diagnosis. After birth, the diagnostic tests are computed tomography (CT) and magnetic resonance imaging (MRI) - also functional MRI.

Morphological changes detected by imaging examinations cover the range from very subtle changes in the structure of the cerebellar vermis to the giant cysts of the fourth chamber, the enlarged posterior cranial fossa, and the loss of brain tissue (Lufti and Smirniotopoulos, 2015; Mytilinaios et al., 2010).

Symptoms

The clinical picture largely depends on the size of the abnormalities, but this is not the rule. The occurring symptoms also depend on the total accompanying disorders or the age at which the defect was detected. Generally, the syndrome diagnosed in fetal life or early in life after pregnancy is worse. Symptoms usually appear as early as in the first year of life - 70%, at the latest up to the age of 3 - this applies to 80% of patients. The classical Dandy-Walker syndrome in 90% of cases is accompanied...
by hydrocephalus that may not occur at birth; however, up to 3 months of age, 75% of patients appear. In children up to 1 year of age, an increase in intracranial pressure, enlarged head circumference, and sporadically microcephaly are common. In some patients, there is a prominent bulging of the occiput, the dividing of the skull. After the age of 12 months, psychomotor disorders, seizures, older children, chronic headaches and walking disorder usually appear. In 90% of patients, in additional tests, there are numerous other defects, such as corpus callosum agenesis, encephalocoele, hearing and visual impairment. In the authors’ literature, it is suggested that in 50% of patients, mental retardation is caused by anomalies present in the central nervous system, not by the hypoplasia of the cerebellar vermis itself or the enlargement of the fourth chamber. The long-lasting pharmacological treatment and the mentioned hearing and vision disorders are quite an important factor causing the mental impairment of patients. In the 2008 study, other systemic disorders co-occurring in the syndrome were analyzed, from which it follows that 41.7% are heart anomalies, that is, Fallot tetralogy, atrial septal defect, persistenteontorium oval hole; neurological disorders - 33.3%; gastrointestinal tract malformations - 20.8%; abnormalities of the skeletal system, that is, polydactyly, syndactyly, vertebral column disorders - 12.5%; and disorders of the genitourinary system - 12.5%. Craniofacial abnormalities, present in 80%, relate to cleft palate, hemangiomas, low ear pinna, hypertelorism (Forzano et al., 2007; Graf et al., 2013; Hart et al., 1972 Jha et al., 2012; McClelland et al., 2015; Zhang et al., 2013).

Coexistence

Dandy-Walker syndrome often coexists with Klippel-Feil, Coffin-Siris, Meckel-Gruber-Warburg, osteogenesis imperfecta, orofacialdigital and trisomy 8, 13, 18. pair of chromosomes (Basson and Wingate, 2013; Forzano et al., 2007; Hart et al., 1972; Jha et al., 2012). Patients with Dandy-Walker syndrome, due to the disorders discussed by the authors, require interdisciplinary medical care, often long-term. Due to hydrocephalus, the patients, especially the younger ones, undergo intraventricular valve implantation to remove excess cerebrospinal fluid. Not infrequently complicated by this surgical intervention may be the so-called "Rehabilitation syndrome" whose clinical picture is often confused with symptoms of increased intracranial pressure. Hence the need for performing advanced imaging examinations. Single cases of early surgical intervention have been described in the literature, which enabled the proper intellectual development of patients. Mortality in Dandy-Walker syndrome reaches up to 50%. According to the collected and available literature, the authors of this study emphasize that the survival rate depends on the speed and accuracy of the diagnosis, the use of possible treatment, the presence of coexisting pathologies, as well as the applied rehabilitation and care of a multidisciplinary clinical syndrome.

A case report

A 34-year-old patient first reported to the psychiatry department due to the incapacitation of affect and completely non-characteristic, severe behavioral disorders. He was never hospitalized until he was admitted. He was brought to the hospital by the Medical Rescue Team assisted by the family police officers. The police were notified by their sister in connection with another domestic problem and in this case sudden and intense aggression of the patient. The patient was threatening to commit suicide, however, brought to the hospital and quite quickly calmed down. The psychiatric examination described full and logical verbal contact, fully preserved allo- and autopsychic orientation. The patient consented to hospitalization and was admitted to the ward to observe the mental state. During hospitalization, he quickly adapted to the regulations of the ward and adapted to other patients with whom he made proper contact. Generally, the behavior of the patient in the ward did not indicate any pathology in any way.

The results of laboratory and psychological tests (IQ and WISKAD) also did not show any disturbing deviations, as well as the way the patient moved or any other features of the neurological condition. After additional neurological consultation, no symptoms of focal brain damage or the presence of meningitis were found. The neurologist suggested that paroxysmal behavioral disorders may be associated with possible convulsive seizures. In the search for pathology, head CT was ordered urgently and MRI examination of the head in planned mode, was planned after completion of hospitalization. In the meantime, it was planned to perform an EEG, but the CT images of the brain showed the real essence and scope of the developmental anomalies probably underlying the affective disorders (Figures 1 to 6).

Head CT description: Native and contrast enhanced CT scan of the patient’s brain was performed. For both slice, thickness was 2.5 mm for infratentorialimural structures and 5 mm for supratentorialimural ones. Posterior cranial fossa structures presented type I Chiari malformation with hypoplastic cerebellum, dilated pericerebellar subarachnoid space and cerebellar tonsills protruding into foramen magnum (Figures 1 and 2). The ventricular system was also slightly dilated with Evans ratio of 0.32, suggesting mild hydrocephalus (Figure 3). The third was 14.5 mm wide (Figure 4) and the fourth ventricle was 20.7 × 13.7 mm (Figure 5). Cavum septi pellicudi was 4.5 mm wide (Figure 3). Posterior cerebello-medullary cistern was 28 × 11 mm (Figure 4). Pontine cistern was 83 × 31 mm (Figure 6). In contrast enhanced CT vascular system presented no
abnormalities with symmetrical internal carotid and vertebral arteries and well developed circle of Willis. No focal lesions, ischemic changes or intracranial bleeding were found within the brain. Mild calcifications were present in choroid plexuses, pineal gland and falx cerebri.

The results of imaging examinations are additionally surprising because the patient by the profession is a welder and coordinates body movements in a way that does not give rise to anxiety. Despite several years of work in the agricultural equipment factory, he still remains in the position, which gives grounds for assumptions that he is doing well. From the supplementary interview from the patient's family, it is known that for 4 years he learned to ride a bike and finally he learned this skill (he commutes to work daily using his bicycle). In principle, apart from a short stay in childhood, he did not stay in any hospital ward for more than a few hours. The patient is a person functioning in a fairly simple and uncomplicated way. It can be assumed that he stays only in a hospital located several kilometers from his place of residence. Analyzing the history of medical assistance provided to the patient within the framework of broadly understood healthcare, there are frequent trauma and numerous stays at the Hospital Emergency Department. The verified data cover the period...
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Figure 5: Axial section of the patient’s brain at the level of the fourth ventricle and posterior cerebello-medullary cistern.

Figure 6: Axial section of the patient’s brain at the level of the pontine cistern.

from 2011 (full and central computerization of the hospital) until 2018, reported to the A&E eight times, each time it was a stay caused by a trauma to one of the limbs, most often a bruise.

After leaving the psychiatry ward, the patient never went on further diagnosis in any direction (even EEG), nor did he go for the planned MRI. He was discharged from a psychiatry ward on small doses of perazine and valproic acid, which resulted in the expected improvement. Since then, he regularly comes to the Clinic for further doses of medicines. He still remains very reluctant to take any other treatment and obtaining further diagnosis. Physiologically, the most puzzling would be the degree of adaptation of neuronal connections. The patient is able to function normally, perform his profession and lead a family life, with shortages of brain structures visible as in the CT examination. Despite the technical possibilities (MRI, fMRI) to better understand the functioning of the brain structures of the patient, with his reluctance and lack of consent for these tests, it is impossible to perform them.

Conclusions

Dandy-Walker syndrome is a rare pathological condition. Its complex etiology and physio-pathological aspects are still unknown. Dandy-Walker syndrome is characterized by a high variability of phenotypic expression, which often confuses diagnosing clinicians. Occurring in the vast majority of macrocephaly cases in conjunction with any other neurological or psychological symptoms, it imposes detailed diagnostics of the central nervous system on the diagnostics. Each detected pathology is associated with a detailed examination and clinical description of the patient and further treatment to detect other pathologies in the organic and mental aspects. Most cases of Dandy-Walker syndrome occur sporadically in patients with families without current genetic strain in this respect. However, this does not absolve you from the obligation to conduct a detailed family interview. We believe that the case described by the authors proves that the overall clinical picture and prognosis regarding the possibility of adapting to everyday functioning in people with Dandy-Walker syndrome are difficult to determine and depend on the multitude of congenital defects affecting the central nervous system. People diagnosed with Dandy-Walker syndrome require multidisciplinary and specialist neurological, psychological and rehabilitation care.

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