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Morphological Manifestations of the Dandy-Walker Syndrome in Female Members of a Family

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ABSTRACT

The Dandy-Walker syndrome (DWS) is a hereditary disorder, appearing somewhat more frequently in women. The most important characteristics of the DWS are the lack of the cerebellar vermis, varying from a partial lack to a complete agenesis, and enlargement of the cerebrospinal spaces, especially in the fourth ventricle. The above mentioned morphological changes clinically manifest in ataxia, increased intracranial pressure and hydrocephalus. Here is presented a family with DWS, where the disease is contracted only by female members, in two generations, whereas no signs of DWS have been noticed in male family members. DWS is clinically manifested from early childhood to middle age, with the morphological changes varying from hypoplastic cerebellar vermis to widening of the brain ventricles and hydrocephalus and arachnoid cyst in the occipital part.

Key words: *Dandy-Walker, malformation, brain, women*

Introduction

Dandy-Walker syndrome (DWS) is a hereditary neurological disorder inherited autosomatically recessively[1,2], related to certain chromosomic abnormalities[3]. The most important DWS characteristics are the lack of cerebellar vermis, varying from hypoplasia to agenesis, and enlargement of the cerebrospinal spaces, especially the fourth ventricle[1–4]. These morphological changes are clinically manifested by ataxia, increased intracranial pressure and hydrocephalus[4]. Accompanying clinical signs of DWS are slower motor development of children, enlargement of the occipital part of the skull, arachnoid cysts, headache, vomiting, convulsions and eye vibration[5,6]. DWS is confirmed radiologically by ultrasound of the brain in newborns and by magnetic resonance (MRI) in adults[6,7]. DWS manifests in three forms: 1. DWS malformation: this is the most severe clinical form, represented by agenesis of the cerebellar vermis and dilatation of the fourth ventricle, often accompanied with hydrocephalus and spina bifida; 2. DWS cisterna magna: the lightest clinical form, alongside preserved vermis, there is present enlarged cisterna magna; 3. DWS variant: characterized by a wide scope of symptoms, from mild to very grave disorders with hypoplastic cerebellar vermis, the fourth ventricle and the posterior fossa being mildly enlarged[9–12]. Here we are presenting a family with DWS, where only female members of the family, in two generations, have contracted the disease.

Case report

In the presented family there are four daughters and one son. The son is of a fine overall status and has no disturbances or neurological disorders. One daughter, 42 years old, reports persistent, dull headache, and normal neurological findings. She has underwent magnetic resonance (MRI) of the brain. The MRI is made in the T1 an T2 sequences, showing a large cistern cerebromedullaris with hypoplastic cerebellum, and the ventricular system completely dilated (Figure 1).

The patient has one son, perfectly healthy, and a daughter who at the age of seven suffered from very intensive headache and epileptic attack of the grand-mal type. Her CT and MRI of the brain showed a large cistern cere-

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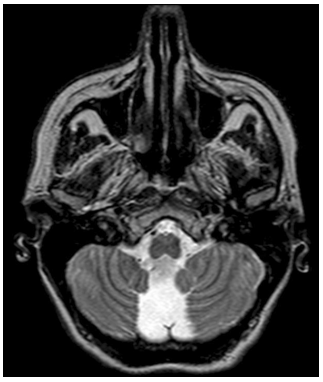

Fig. 1. Large cistern cerebromedullaris with hypoplastic cerebellum.

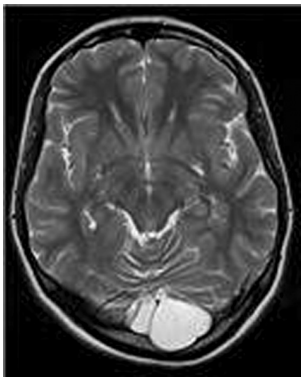

Fig. 3. Arachnoid cyst of the posterior fossa, sized 32 x 28 mm, producing no compression to the surrounding brain structures.

bromedullaris with hypoplastic cerebellum, especially the vermis, with the brain ventricular system dilated, which indicates a Dandy Walker variant (Figure 2). The patient underwent a surgery and is implanted ventriculoperitoneal drainage.

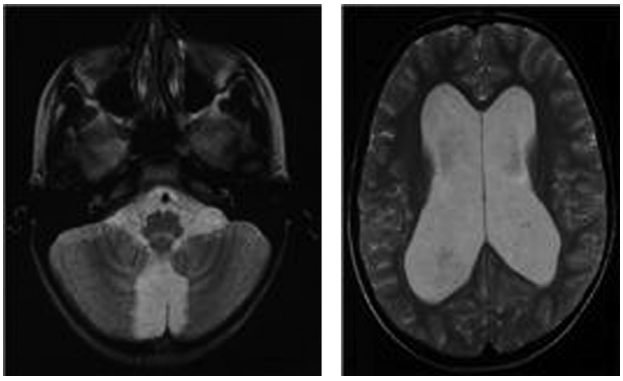

Fig. 2. Large cistern cerebromedullaris with hypoplastic cerebellum, especially the vermis (a). Brain ventricular system completely dilated (b).

The younger sister at the age of 37 reported intensive headaches. Her neurological findings are perfectly normal, but the brain CT and MRI showed arachnoidal cyst sized 88 x 46 mm (cysta arachnoidalis magna regionis occipitalis et fossae cranii posterioris). She underwent a neurosurgery.

The third, youngest, sister is 23, still not married and having no children. She has no discomforts and her clinical neurological findings are normal. Her brain MRI shows an arachnoid cyst of the posterior fossa, sized 32 x 28 mm, producing no compression to the surrounding brain structures (Figure 3).

The fourth sister suffers from no neurological disorders or morphological changes, as proven by brain MRI. She has two children: a son of 5 years with no discomforts, and a daughter of 3 months, where ultrasound diagnostics established dilated liquor spaces with hydrocephalus.

The family tree (Figure 4) shows spreading of the disease in the family through generations, among the female family members.

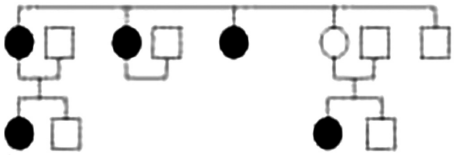

Fig. 4. Family tree. Key: ● sick female, ○ healthy female, □ healthy male.

Discussion

Dandy-Walker syndrome (DWS) is a rare neurological hereditary disorder[1,2]. The main features of DWS are hypoplasia or agenesis of the cerebellar vermis and enlargement of the fourth brain ventricle[1,2]. The sydrom was mentioned for the first time by Dandy in 1914 and Walker in 1942, the term Dandy-Walker syndrom to have been introduced by Bend in 1954[3–5]. The disease incidence is very low, between 1/25,000 and 1/35,000 of newborns, prevailing in females. DWS is a heterogeneous hereditary disorder[6]. Researches have shown that the persons suffering from DWS have deletions at the 3q chromosome. The cause is deemed to be in changes of the ZIC1 and ZIC2 gens, on the 3q24 and 3q25 chromosomes[7]. Another research showed that DWS was related to the 3, 9, 13 and 18 chromosome abnormalities[8]. DWS is inherited autosomatically recessively[9,10]. DWS prevails in childen of blood related parents[10,17], cases or the disease repeated in subsequent pregnancies being recorded as well[11]. Literature reports family cases with prevailing occurrence in female children, but there are recorded also cases where male children became ill as well[9,10]. DWS has numerous clinical features, besides the cerebellar vermis hypoplasia or agenesis and the enlarged fourth ventricle. The enlarged ventricles cause signs of high intracranial pressure, such as headache, nausea, vomiting and hydroceph-

alus[12,21]. Hydrocephalus is among the most frequent DWS complications and features. The disorder in the cerebellum development causes also ataxia[12]. There may also occur bulging of the occipital skull and cysts in the posterior fossa[13,14]. In children are found cases of slower motor development, and about a half of all patients have a form of mental retardation[12,15]. There are also extracranial malformations, such as cardiovascular defects, polycystic kidneys and palate development disorders[1].

DWS manifests in three forms[16]: 1. DWS malformation (DWM)[17]: this is the most severe clinical form, represented by agenesis of the cerebellar vermis and dilatation of the fourth ventricle, often accompanied with hydrocephalus and spina bifida; 2. DWS cisterna magna (MCM)[18]: the lightest clinical form, alongside preserved vermis, there is present enlarged cisterna magna (space between medulla oblongata and cerebellum); 3. DW variant (DWV)[19]: characterized by a wide scope of symptoms, from mild to very grave disorders with hypoplastic cerebellar vermis, the fourth ventricle and the posterior fossa being mildly enlarged.

DWS is proven radiologically, firstly by ultrasound of brain in small children[20], and by CT and/or MRI in adults[2,21]. In fetuses, the cerebellum agenesis can be proven after 18 weeks of gestation[1]. In fetuses and newborns it can be proven by dilated ventricles and hydrocephalus[20]. DWS rarely appears in adulthood, because symptoms normally appear in childhood and adolescent period. Adults suffer from long lasting symptoms such as headache, nistagmus, but the decease can also be completely asymptomatic, where only radiological examination shows intracranial changes consistent with DWS[21]. Therapy is symptomatic, such as liquor drainage due to the increased intracranial pressure and/or hydrocephalus, and possibly physical therapy due to the slower motor development[22].

We have presented the case of an family of four sisters and one brother, where three sisters suffer from DWS, whereas the brother and one sister show no clinical or radiological signs of the disease. Clinically and radiologically, conclusion can be made this is a case of a Dandy-Walker variant[19], a form of the disease varying in symptoms, and characterized by hypoplastic cerebellar vermis and increased fourth ventricle. Some of their children have enlarged ventricles, and one girl has clear signs of DWS, wherefore she underwent a neurosurgery and implemented ventriculoperitoneal drainage. Our presentation supports the thesis that DWS is more frequent in female population, and in particular families in their female members. This requires further research, aimed to establishing what factors case larger prevalence of DWS in female family members.

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MORFOLOŠKE MANIFESTACIJE DANDY-WALKER SINDROMA MEĐU ŽENSKIM ČLANOVIMA JEDNE OBITELJI

S A Ž E T A K

Dandy-Walker sindrom (DWS) je nasljedni neurološki poremećaj koji se javlja nešto češće u žena. Najvažnije karakteristike DWS-a su nedostatak cerebelarnog vermisa, koji varira od djelomičnog nedostatka do potpune ageneze, i povećanje cerebrospinalnih prostora, poglavito 4. ventrikularne komore. Navedene morfološke promjene klinički se manifestiraju ataksijom, povećanjem intrakranijskog tlaka i hidrocefalusom. Prikazujemo obitelj sa DWS u kojoj su oboljeli samo ženski članovi obitelji u dvije generacije. DWS se klinički manifestirao od ranog djetinjstva do srednje životne dobi, sa morfološkim promjenama koje variraju od hipoplastičnog vermisa cerebelluma do proširenja moždanih komora i hidrocefalusa i arahnoidalne ciste okcipitalnog dijela.