A rare embryological malformation of brain – Dandy-Walker syndrome – and its association with Kallmann's syndrome

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Abstract

BACKGROUND & AIM: Dandy-Walker malformation, a rare congenital brain malformation, is described as a triad of cystic dilatation of the fourth ventricle, complete or partial agenesis of the cerebellar vermis, and an enlarged posterior fossa with elevated tentorium. We aimed to report an association of Kallmann's syndrome and Dandy-Walker malformation.

CASE: A fifteen years old boy was referred to endocrinology department due to delayed puberty. Stages of male genital development according to Marshall and Tanner, was stage G1 and P1 respectively. In the LHRH test, peak LH level was 40th min.:15.3 IU/ml. Peak growth hormone with insulin tolerance test was 14.5 μg/L. Olfactory test revealed light anosmia. With these findings the patient was accepted as isolated gonadotropin deficiency (Kalmann's syndrome). In computed tomography of the brain, cerebellar vermis was found to be hypoplastic and 4th ventricle was large and in posterior fossa broad hypodens area with cerebrospinal fluid density were seen (Dandy-Walker malformation).

CONCLUSION: We reported an association of Kallmann's syndrome and Dandy-Walker malformation. This is second reported case probably.

INTRODUCTION

The normal structures in the back of the brain include the cerebellum which lies on top of the brain stem and encloses a space referred to as the fourth ventricle. This space connects the ventricles of the upper brain (the cerebrum) through a narrow canal called the aqueduct of Sylvius. Normally, cerebrospinal fluid (CSF) flows from the interior of the cerebrum through this canal through the fourth ventricle to bathe the outside of the brain and the spinal cord.

The Dandy-Walker malformation is a rare developmental abnormality of the central nervous system characterized by hypoplasia or plasia of the cerebellar vermis, cystic dilation of the posterior fossa, an

CASE REPORT

enlarged fourth ventricle and usually hydrocephalus. Dandy-Walker syndrome (DWS) is a rare congenital brain malformation (occurs in approximately one in 25,000 babies) [2]. It accounts for approximately 1–4% of cases of hydrocephalus and is seen more frequently in females than in males. The classic Dandy-Walker malformation is described as a triad of cystic dilatation of the fourth ventricle, complete or partial agenesis of the cerebellar vermis, and an enlarged posterior fossa with elevated tentorium [3]. It is characterized by: cystic dilatation of the fourth ventricle due usually to absence of the foramina, dilatation of the third and lateral ventricles – but to a lesser extent than the fourth, enlargement of the posterior fossa with a high tentorium cerebelli and transverse sinuses, wide separation of the cerebellar hemispheres with a small vermis, displaced laterally and various other developmental abnormalities in 65% of patients [2]. A large head is the main physical sign of DWS [7]. Numerous brain abnormalities accompany the Dandy-Walker malformation; among them are agenesis of the corpus callosum agenesis, polymicrogyria, agyria, grey matter heterotopias, aqueductal stenosis, Klippel-Feil syndrome, microcephaly, posterior fossa lymphomas, hamartomas of the infundibulum, and syringomyelia [1]. The pathogenesis of the DWM has always been considered controversial. Maldevelopment of the anterior zone of the roof of the IV ventricular associated with lack of patency of the foramina of Luschka and M agendie was suggested as the cause of the enlargement of the IV ventricle and the developmental failure of the cerebellum in earlier studies [6].

The majority of patients with the classic Dandy-Walker malformation are usually diagnosed within the first year of life. Diagnosis can be confirmed by computed tomography (CT) or ultrasound, be observing superior displacement of the lateral sinus groove on plain x-rays, or by transillumination of the posterior fossa [9]. MR scanning best demonstrates the characteristic pattern of hydrocephalus and cystic enlargement of the fourth ventricle [1]. Treatment for individuals with DWS generally consists of treating the associated anomalies, if needed. Also, a ventriculoperitoneal shunt may be inserted to control the hydrocephalus. The prognosis for patients with DWS is only moderately favorable, even when the hydrocephalus is treated early and correctly. Prognosis for normal intellectual development is variable depending on the severity of the syndrome and associated malformations.

Kallmann's syndrome (KS) is the most common form of isolated gonadotropin deficiency. Gonadotropin deficiency in these patients is associated with hypoplasia or aplasia of the olfactory lobes and hyposmia and anosmia; remarkably, they may not notice that they have no sense of smell, though olfactory testing will reveal it [8].

We aimed to report an association of KS and Dandy-Walker malformation. This is an interesting case because we could find only one patient KS associated with Dandy-Walker malformation in medical literature [10].

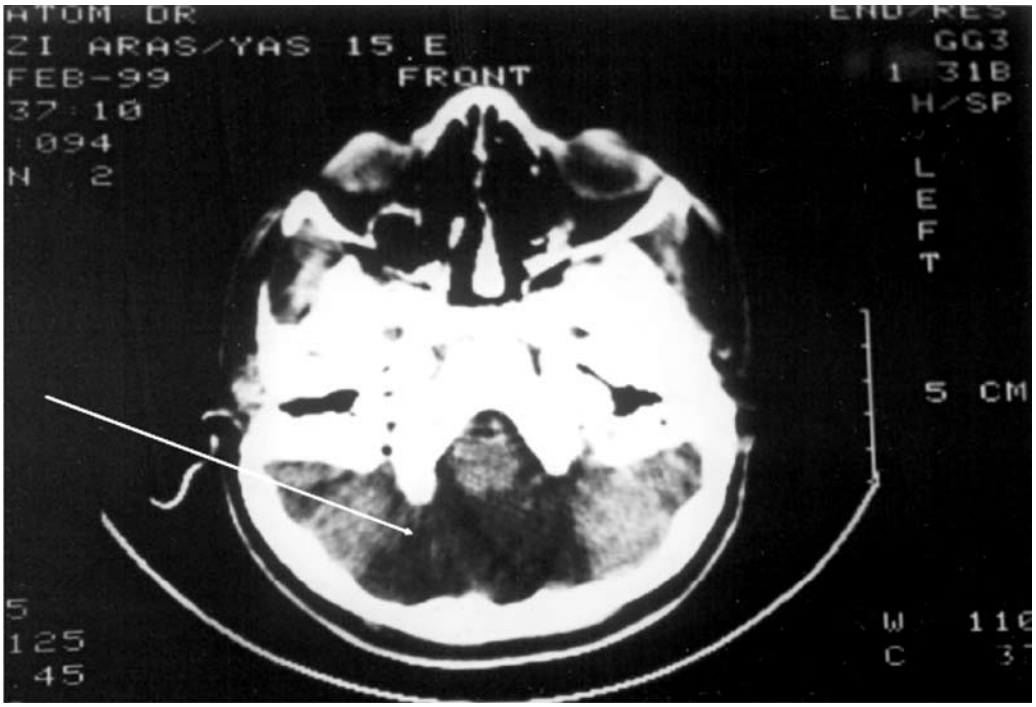

Figure 1. Cerebellar vermis was hypoplastic and 4th ventricle was large.

CASE

RA, 21 yr old male patient. The patient was referred to endocrinology department because of delayed puberty. Body weight: 62 kg, height: 176 cm, pubis to floor height: 85 cm, crown-pubis height:71 cm, head circumference 54,5 cm. Stages of male genital development and pubic hair development, according to Marshall and Tanner were stage G1-2 and P1-2 respectively [4]. Biochemistry: fasting blood glucose: 86 mg/dL, BUN: 18 mg/dL, creatinine: 0.9 mg/dL, SGOT: 21 mIU/DL, SGPT: 26 mIU/DL, total cholesterol: 180 mg/dL, HDL-cholesterol: 51 mg/dL, triglyceride: 155 mg/dL, LDL-cholesterol: 98 mg/dL. Hormonal evaluation: FSH: 2.16 IU/ml,

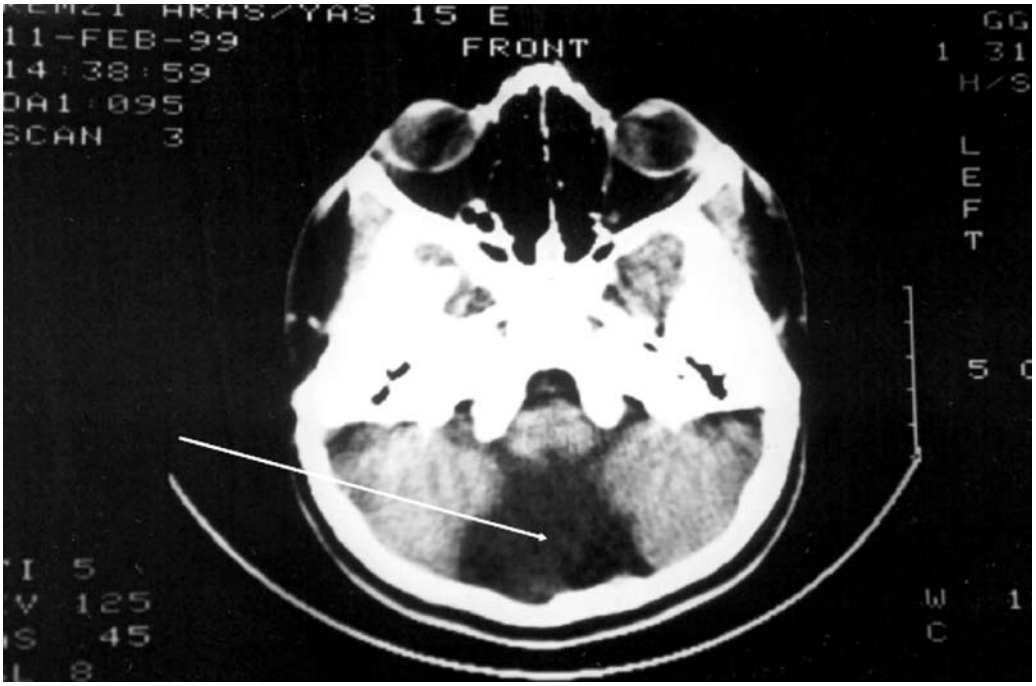

Figure 2. In the posterior fossa, broad hypodens area with cerebrospinal fluid (CSF) density.

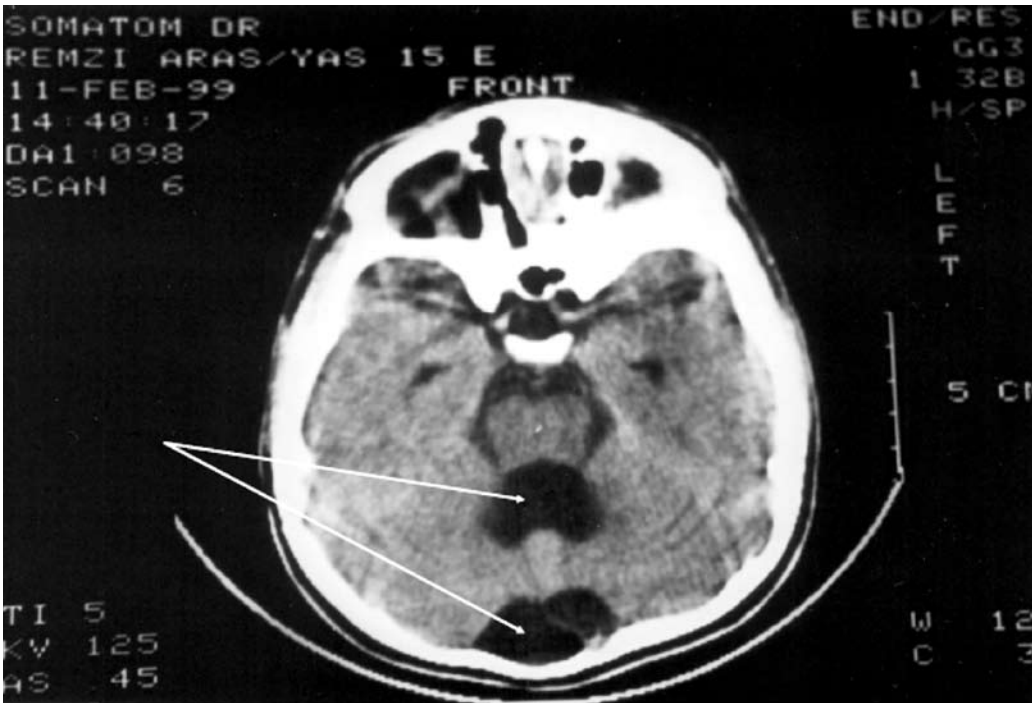

Figure 3. Moderately large third and lateral ventricles with normal situation.

LH: 0.14 IU/ml total testosterone: 2.17 ng/dL, free testosterone: 0.62 ng/L, androstenedione:0.62 ng/ml, DHEA-S: 214 μg/dL, estradiol: 8.63 pg/mL, TSH: 3.11 μIU/mL, Free T4: 1.71 ng/dL, Free T3: 0.34 ng/dL, cortisol: 13.8 μg/dL, prolactin: 11.7 ng/mL. We performed LHRH and insulin tolerance test. In the LHRH test, LH levels were baseline: 0.21 IU/ml, 20th min.: 3.67 IU/ml, 40th min.: 15.3 IU/ml and 60th min.: 8.47 IU/ml respectively. Peak growth hormone with insulin tolerance test was 14.5 μg/L, IGF-1 and IGFBP-3 were 421 μg/L and 3.12 ng/ml. Olfactory test revealed light anosmia. With these findings the patient was accepted as isolated gonadotropin deficiency (Kallmann's syndrome). In CT of the brain, cerebellar vermis was found to be hypoplastic and 4th ventricle was large (Figure 1). In the posterior fossa broad hypodens area with CSF density were seen (Figure 2). Third and lateral ventricles were normal situation, but those were moderately large (Figure 3). Cerebral grey and white matter and basal ganglia and capsular formations are normal appearance. After the IV contrast material injection, pathological contrast was not developed. With these findings the patient was accepted as Dandy-Walker malformation.

DISCUSSION

DWS is uncommon, and this malformation occurs in approximately one in 25,000 babies [2]. It accounts for approximately 1–4% of cases of hydrocephalus and is seen more frequently in females than in males [5]. Our patient was classic Dandy-Walker malformation, and diagnosis was confirmed by CT. Because in CT of the brain of the patient, cerebellar vermis was found to be hypoplastic and 4th ventricle was large. In the posterior fossa, broad hypodens area with CSF density. The symptoms tend to be related to hydrocephalus and increased intracranial pressure. The baby may have weak neck muscles along with poor head control and spasticity. In older children symptoms of increased intracranial pressure such as irritability, vomiting and convulsions, and/or signs of cerebellar dysfunction such as ataxia and nystagmus may occur. Delay in intellectual development is a common feature of the Dandy-Walker malformation. Seizures may occur in 20–30% of these patients. The syndrome can appear dramatically or be totally asymptomatic. Other symptoms include increased head circumference, bulging occiput, cranial nerve dysfunction, and abnormal breathing patterns. Of importance is the high association of DWS with other central nervous system structural anomalies including agenesis of the corpus callosum and malformations of the face, limbs, digits and heart. Familial forms of DWS have been described with autosomal recessive inheritance. The familial cases are associated either with polycystic kidneys or with cataracts, retinal dysgenesis, and choroid coloboma [1].

KS is the most common form of isolated gonadotropin deficiency. Gonadotropin deficiency in these patients is associated with hypoplasia or aplasia of the olfactory lobes and hyposmia and anosmia; remarkably, they may not notic that they have no sense of smell, though olfactory testing will reveal it [8]. This is an interesting case because we could find only one patient KS associated with Dandy-Walker malformation in medical literature [10].

CONCLUSIONS

We reported an association of KS and Dandy-Walker malformation. This is second reported case probably.

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