

A Dandy-Walker malformation associated with ganglioglioma

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To the Editor: The Dandy-Walker malformation (DWM) is a rare congenital malformation involving the posterior fossa. Diagnosis of the DWM is based on a series of characteristic neuroimaging findings, which include complete or partial agenesis of the cerebellar vermis, cystic dilatation of the fourth ventricle, and enlarged posterior fossa.^[1] Several malformation syndromes and cytogenetic abnormalities have been associated with the DWM. However, the co-existence of the DWM and neoplasms is rare.^[2] There are rare reports of the co-existence of the DWM and ganglioglioma.

A 6-year-old boy was admitted to the hospital with complaints of headache for 3 months. He was free from dizziness, nausea, vomiting, or limb weakness. He had normal vision, muscular strength and muscular ton. The laboratory examination of this case showed the increases of C-reactive protein (21.7 mg/L), blood glucose (7.6 mmol/L), and the decrease of albumin (39.6 g/L), blood potassium (3.5 mmol/L), sodium (136.5 mmol/L) and phosphorus (1.4 mmol/L). Cerebrospinal fluid (CSF) cytology was unremarkable. Computed tomography (CT) and magnetic resonance imaging (MRI) findings were compatible with variant DWM. At the same time, a round soft tissue mass was seen above the sellar region, with uneven internal density. The upper part of the lesion reached the interphalangeal cistern, the boundary of which was not clearly demarcated near the right parahippocampal gyrus [Figure 1A–1H]. He underwent a puncture of the hypothalamus and tissue samples were sent for pathological examination.

Histopathological examination revealed the presence of ganglioglioma which was composed of proliferated glial cells [Figure 1I], mature and immature ganglion cells [Figure 1J], in conjunction with vascular proliferation. The tumor cells were positive for glial fibrillary acidic protein (GFAP) [Figure 1K], Olig-2, neuronal nuclear antigen

(NeuN) and CD34 [Figure 1L], and negative for mutations in the v-raf murine sarcoma viral oncogenes homolog B1 (*BRAF*) *V600E*, p53, isocitrate dehydrogenase 1 (*IDH1*) *R132H* and Histone H3.3/H3.1 in the codon for lysine 27 (*H3K27M*). Antibodies were obtained from Beijing Zhongshan Golden Bridge Biotechnology Co., Ltd. (Beijing, China). Based on the radiological examination and pathological findings, the patient was diagnosed as DWM associated with ganglioglioma (World Health Organization grade I). Neurosurgeons recommended close observation and did not perform further tumor resection. Six months later, routine follow-up CT and MRI scans demonstrated that there was no significant change in the lesion. The headache symptom was successfully alleviated.

The DWM was first described by Dandy and Blackfan in 1914 and is the most common congenital malformation of the cerebellum, with an incidence of about one in 25,000 to 30,000 live births.^[3] DWM can be seen on CT and MRI by the presence of elevated venous sinuses and torcular, high tentorial attachment, and an enlarged cystic posterior fossa. Sometimes, DWM needs to be distinguished from other diseases, such as Joubert syndrome, mega cisterna magna (MCM), Blake pouch cyst, isolated vermian hypoplasia, arachnoid cyst, or cerebellar hypoplasia. Approximately, 70% to 90% of patients have supratentorial hydrocephalus, which represents the most common complication of this malformation. Associated neoplasms can be nephroblastoma, tongue hamartoma and intracranial cavernous angioma.^[4] However, the incidence of the DWM associated with central nervous system (CNS) glioma has not been reported. This case represents a rare report of ganglioglioma in a patient with the DWM.

The cause of DWM is unknown, but it is occasionally familial. The most convincing pathogenetic theory is a developmental arrest of the hindbrain before the third month. The etiology of DWM, including chromosomal

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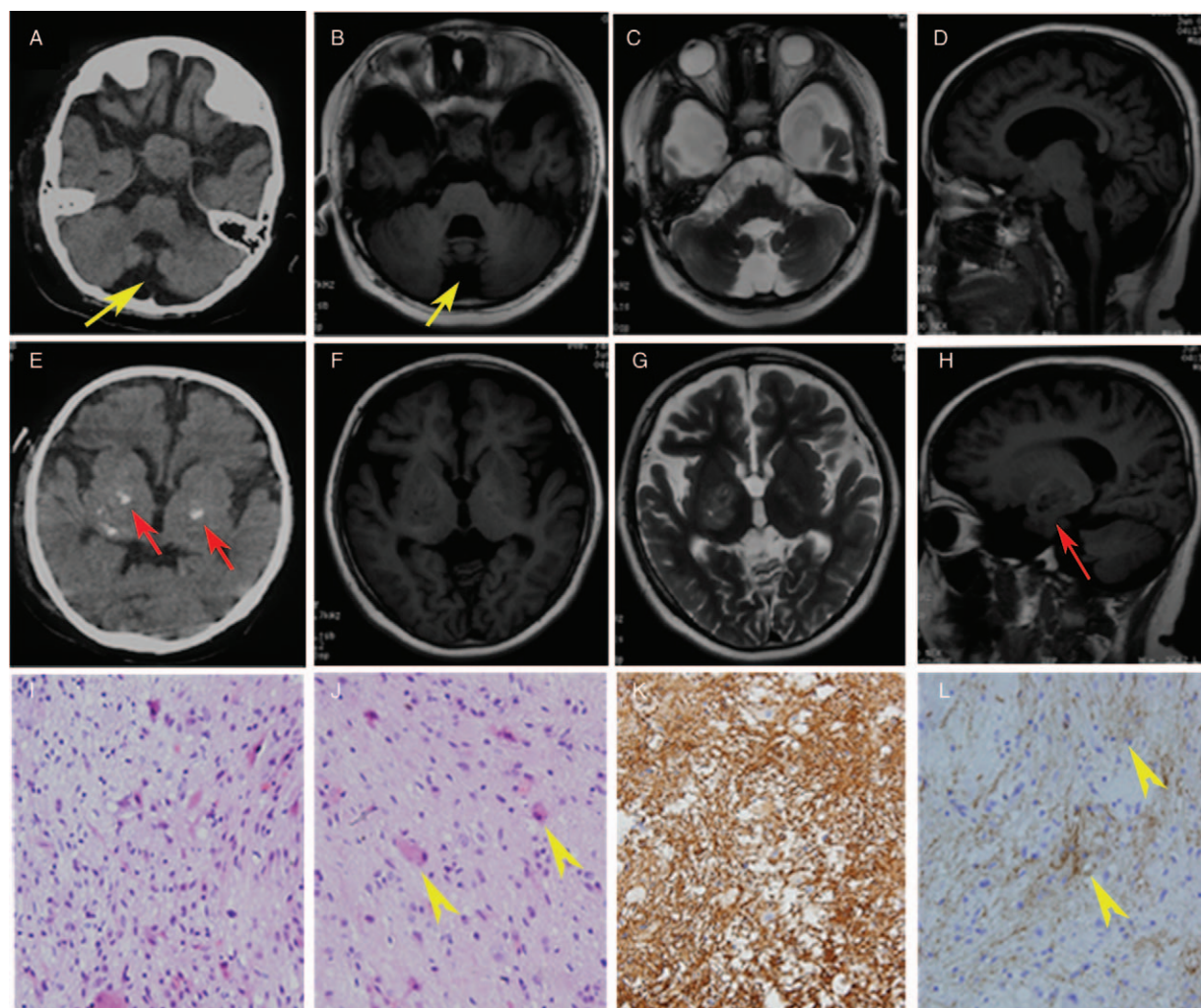


Figure 1: Radiological and pathological features of the patient with Dandy-Walker malformation and Ganglioglioma. Radiological findings of CT scan (A) and MRI axial T1WI (B), T2WI (C) and sagittal T1WI (D) showed an atrophy of the cerebellar hemispheres, hypoplasia of the vermis, and an enlargement of the fourth ventricle, which communicated with the occipital cistern forming a posterior cerebellar cyst (yellow arrows). At the same time, the upper part of the lesions with calcification on CT scan (E, red arrows), reached the interphalangeal cistern, which of the boundary near the right parahippocampal gyrus was not clearly demarcated on MRI axial T1WI (F) and T2WI (G). Moreover, a round soft tissue density masse was seen above the sellar region, with uneven internal density on MRI sagittal T1WI (H, red arrow). Pathological findings revealed the proliferation glial cells and vascular (I; H&E, original magnification $\times 400$), with immature ganglion cells (J; H&E, original magnification $\times 400$, yellow arrow heads). Tumor cells of ganglioglioma were immunoreactive for GFAP (K; immunohistochemical, original magnification $\times 400$). Tumor cells of ganglioglioma were prominent cytoplasmic and membranous staining for CD34 (L; immunohistochemical, original magnification $\times 400$, yellow arrow heads). CT: Computed tomography; GFAP: Glial fibrillary acidic protein; H&E: Hematoxylin and eosin; MRI: Magnetic resonance imaging.

abnormalities and single-gene disorders, is also heterogeneous. Mutations of the sonic hedgehog (*Shh*) signaling pathway genes, zinc finger protein 1 (*ZIC1*) and *ZIC4*, as well as fibroblast growth factor genes (*FGF*) 8 and *FGF17* have been implicated in DWM.^[5] In our present case, no other pathological molecular alterations, including *BRAF V600E*, were found by next generation sequencing.

Various treatment options are available for children with DWM, such as shunt placement, either ventriculoperitoneal, cystoperitoneal, or combined ventriculoperitoneal and cystoperitoneal shunt, membrane excision, and endoscopic procedures. Cystoperitoneal shunts are currently favored by many neurosurgeons. A prognosis, which is only moderately favorable, is difficult to formulate even when hydrocephalus is treated early and correctly. Some people have variant Dandy-Walker without showing any symptoms in their entire lives. However, some infants may have it

in association with other syndromes, resulting in severe complications or death. The presence of comorbidities may heavily affect the prognosis and quality of patients' life. Although the patient in our case was diagnosed with ganglioglioma, neurosurgeons recommended close observation and did not perform further tumor resection or adjuvant therapy. He is under regular follow-up and no progression of the lesions has been observed. The identification of such associations highlights the correlation of pathogenesis of both the DWM and ganglioglioma, which suggests a novel and yet unexplored mechanism of disease that could be the basis for future study.

Declaration of patient consent

The authors certify that they have obtained the appropriate patient consent form. In the form, the parents of the patient have given their consent for his images and other clinical information to be reported in the journal. The parents of

the patient understand that his name and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

None.

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