Case Report

Desmoplastic Infantile Ganglioglioma with High Proliferation Index: Report of A Case

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Desmoplastic infantile ganglioglioma (DIG) is an uncommon neuroepithelial tumor associated with epilepsy, mostly occurring in the first 2 years of life. Most DIGs carry good prognosis after complete resection, even when a primitive cellular element is present. However, a few examples of DIG with histologic anaplasia have recently been reported, and one demonstrated an unusual aggressive behavior. The authors describe herein a DIG with high Ki-67 proliferation index (30%) in a 10-month-old male infant with epilepsy, but with an excellent prognosis after total tumor resection.

Keywords: *Desmoplastic infantile ganglioglioma, Anaplastic features, Epilepsy*

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Originally described separately, desmoplastic infantile ganglioglioma (DIG) and desmoplastic infantile astrocytoma (DIA) are now considered the same entity[1-3]. Both are circumscribed large solid cystic tumors that involve the superficial cerebral cortex and leptomeninges, often with dural attachment[1-4]. DIG/DIA corresponds histologically to WHO (World Health Organization) grade I, with a generally excellent prognosis following surgical resection; recurrence-free intervals of up to 14 years have been noted and spontaneous regression of residual tumors has also been described[3-5]. However, a few DIGs with anaplastic histology and aggressive clinical course have recently been reported[6,7]. A case of DIG with high proliferation index, but with an excellent outcome, is presented herein.

Case Report

A 10-month-old male infant presented with epilepsy and increased head circumference. Perinatal period was unremarkable except for mild jaundice, which was successfully controlled by phototherapy. There was no history of epilepsy or other illnesses noted in the family. Magnetic resonance imaging (MRI) study of the brain revealed an ill-defined solid-cystic mass, measuring 8.5 x 4.5 x 5.8 cm, in the right temporo-parieto-occipital lobe, associated with surrounding brain edema (Fig. 1). The lesion extended from right-sided tentorium cerebelli and right transverse sinus inferiorly to torcular helophili, straight sinus and superior sagittal sinus,

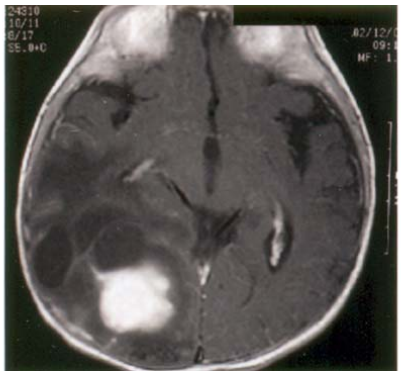

Fig. 1 MRI demonstrates a large solid-cystic tumor in the right temporo-parieto-occipital lobe

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posteromedially. Mass effect was evident by the falx-deviation to the left. The solid component was hyperintense to gray matter in T2-weighted images, hypointense in T1-weighted images, with intense enhancement post gadolinium administration. The patient underwent craniotomy with total gross removal of the tumor.

The specimen was fixed in 10% formalin, routinely processed and embedded in paraffin wax. Hematoxylin- and eosin-stained sections demonstrated a well-demarcated tumor (Fig. 2), consisting of spindle-shaped neoplastic cells with fascicular and storiform arrangements (Fig. 3). Tumor nuclei were moderately pleomorphic, and mitotic figures were easily recognized as 5-7 mitoses per 10 high power fields (Fig. 4). There was no endothelial proliferation or necrosis noted, nor was the primitive cellular element. Pericellular reticulum fibers were frequently observed (Fig. 5). The astrocytic nature of the lesion was verified by the strong immunoreactivity with glial fibrillary acidic protein (Fig. 6). There were occasional ganglion cells highlighted with neurofilament and NeuN immunohistochemistry (Fig. 7). In the most active region, 30% of the glial tumor nuclei were labeled with Ki-67 proliferation marker (Fig. 8). The pathological diagnosis of desmoplastic infantile ganglioglioma was rendered, with a worrisome comment on the high proliferation index.

The postoperative course was uneventful, and no adjuvant therapy was given. Postoperative MRI, 4 and 8 months after operation, showed no evidence of tumor recurrence. The patient had no epilepsy and was doing well on the two-year follow up visit.

Fig. 2 DIG is clearly separate from the adjacent brain (Hematoxylin-eosin stain, original magnification x 20)

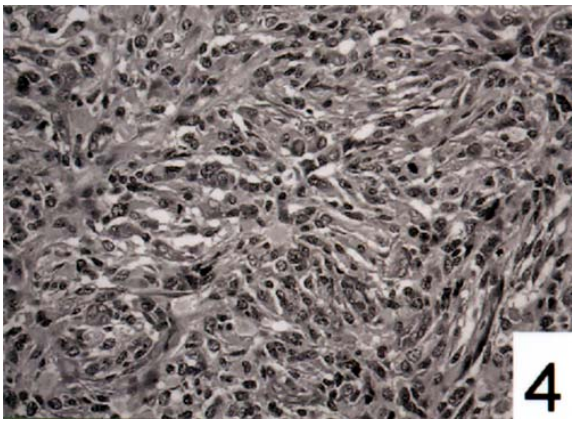

Fig. 4 Nuclear pleomorphism and mitoses are shown (Hematoxylin-eosin stain, original magnification x 200)

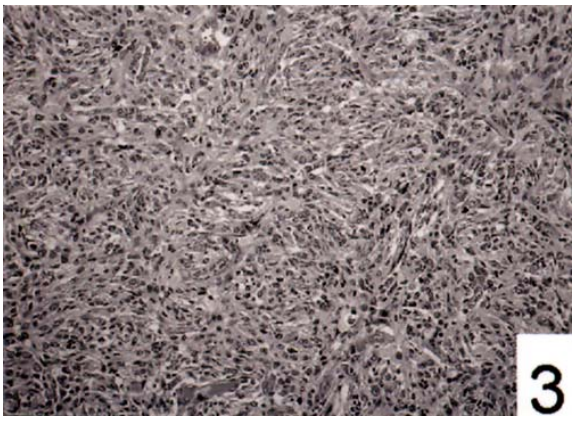

Fig. 3 Spindle-shaped tumor cells form fascicular and storiform patterns (Hematoxylin-eosin stain, original magnification x 100)

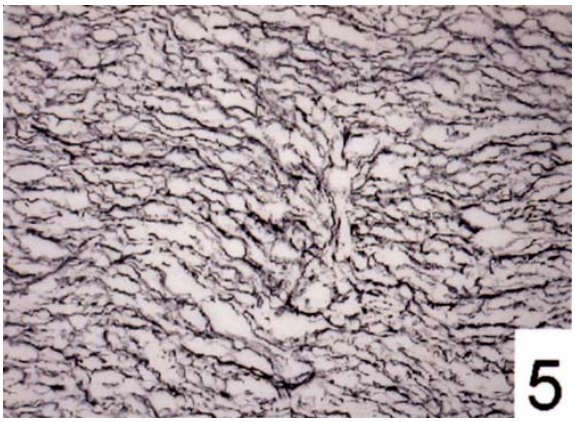

Fig. 5 Individual tumor cells are wrapped by pericellular reticulum fibers (Reticulin stain, original magnification x 100)

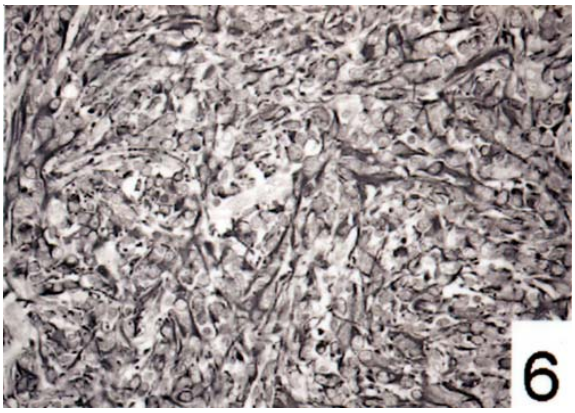

Fig. 6 Tumor cells strongly express glial fibrillary acidic protein (GFAP stain, original magnification x 200)

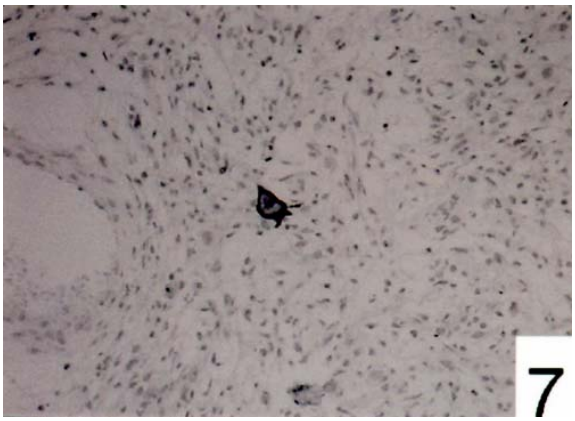

Fig. 7 A neuronal cell is highlighted with NeuN immunostain (NeuN stain, original magnification x 100)

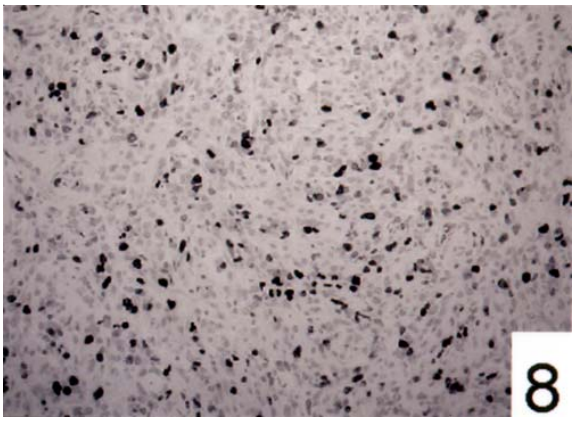

Fig. 8 High Ki-67 proliferation index in DIG with anaplastic features (Ki-67 stain, original magnification x 100)

Discussion

Desmoplastic infantile ganglioglioma (DIG) is an uncommon neuroepithelial tumor, presumably derived from the subpial astrocyte[1-3]. Although the age range of patients is typically between 1-24 months, a few non-infantile cases have been reported[8,9]. In addition to increasing head circumference, tense and bulging fontanel, and forced downward ocular deviation; the affected infants may experience paresis, seizures, increased muscle tone with hyper-reflexia and, rarely, palsy of the 6th and 7th cranial nerves[3]. A recent study has indicated that genetic alterations in DIG differ from those commonly encountered in ordinary astrocytomas[10].

Most DIGs carry good prognosis after gross total resection, even when a primitive cellular component is observed[3,6]. Although adjuvant chemo-and/or radiotherapy is generally applied after incomplete removal, benefit of such treatments has been questioned[11]. However, a few examples of DIG with histologic anaplasia (presence of high mitotic activity, high Ki-67 labeling index, endothelial proliferation and necrosis) have been reported, and an example of DIG with metastasis at presentation has also been described[6, 7]. Though exceedingly rare, these exceptional cases indicate a spectrum among DIGs.

The amount or degree of anaplasia has been suggested to bear some indications toward the biological behavior of DIG[6]. In most cases with long-term survival, the primitive-appearing cells demonstrated a low mitotic rate and Ki-67 labeling index (LI) (0.5-5%); necrosis and endothelial proliferation were not uniformly present[3,6]. A case with highly aggressive behavior was characterized by the extremely high mitotic activity and Ki-67 LI (45%), with obvious necrosis and endothelial proliferation[6]. Postoperative chemotherapy was given to this patient. On the other hand, another 2 DIGs with high mitotic rate and Ki-67 LI (20%) have been noted to follow a benign course after macroscopically complete resection[6]. The present DIG behaved more toward the last 2 examples (with no recurrence), but focally demonstrated a very high Ki-67 LI (30%).

To summarize, although designated WHO grade I neoplasm, some DIGs can demonstrate histological anaplasia and few behave aggressively. Even though surgery remains the principle management, more cases of DIG with atypical histologic features need to be documented, in order to define the minimal histologic criteria to predict biological behavior and to select cases for adjuvant therapeutic interventions.

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เนื้องอก Desmoplastic infantile ganglioglioma ที่มีดัชนีการเจริญเติบโตสูง: รายงานผู้ป่วย 1 ราย

พฐู ตัณฑไพโรจน์, อนพัช สรรพาวัตร, กฤษณพันธ์ บุญยะรัตเวช, ทายาท ดีสุดจิต, ชนพ โชติช่วง

Desmoplastic infantile ganglioglioma (DIG) เป็นเนื้องอกระบบประสาทที่มีความสัมพันธ์กับการชักที่พบได้น้อย โดยมักพบในช่วงอายุ 2 ปีแรก ผู้ป่วยส่วนใหญ่มีการพยากรณ์โรคที่ดีหลังการผ่าตัดแม้ว่าจะพบส่วนประกอบที่เป็นเซลล์ตัวอ่อน (primitive cellular element) ร่วมด้วย อย่างไรก็ตาม ได้เคยมีรายงานเนื้องอกชนิดนี้จำนวนหนึ่งที่มีลักษณะผิดปกติทางจุลพยาธิ (histologic anaplasia) ซึ่งหนึ่งรายในจำนวนนั้นมีการดำเนินโรคที่ไม่ดี คณะผู้เขียนได้รายงานเนื้องอก DIG ที่มีค่าดัชนีการเจริญเติบโตเคไอ-67 (Ki-67 proliferation index) สูงถึงร้อยละ 30 ในผู้ป่วยเด็กชายไทยอายุ 10 เดือนที่มีอาการลมชัก แต่การพยากรณ์โรคของผู้ป่วยรายนี้ดีมากหลังจากที่ได้รับการรักษาโดยการผ่าตัดเนื้องอกออกทั้งหมด