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Case Report

Desmoplastic Infantile Astrocytoma in a 47-day Old Male Infant with Four-year Follow-up: A Rare Case Report and Literature Review

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Abstract

Desmoplastic infantile astrocytoma/ganglioglioma (DIA/DIG) is a rare mixed neuronal-glial solid cystic brain tumor found in infantile cerebral hemispheres. The main presentation of the tumor is the rapidly enlarging of the head circumference with hydrocephalus and seizure. DIA is classified as a WHO Grade 1 brain tumor but, due to the rarity of the tumor, few studies are available on tumor survival and prognosis. Herein, we report a 47-day-old male infant diagnosed with DIA and the four-year follow-up.

Keywords: brain neoplasm, astrocytoma, pediatric neurosurgery, oncology, desmoplastic cerebral astrocytoma of infancy, desmoplastic infantile ganglioglioma

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1. Introduction

Desmoplastic infantile astrocytoma (DIA) and desmoplastic infantile ganglioneuroma (DIG) were described in 1982 and 1987, respectively [1, 2]. Both have solid and cystic components with similar imaging and clinical presentations; therefore, in 2016, the WHO categorized them as Grade 1 brain tumors as DIA/DIG [3]. Usually, DIA/DIG presents with a single large supratentorial mass with solid-cystic elements, especially in the superficial area of frontoparietal and temporal lobes. Leptomeningeal attachments are common [4]. The occipital lobe, brain stem, and thalamus have been reported as infrequent sites of involvement. Infants and children less than two years old are mostly involved, especially in the first six months of birth. However, the involvement of older children and adolescents has been mentioned [3, 4]. Male to female ratio is 1.5–2 to 1 [2,

5]. Most patients initially present with signs and symptoms of increased intracranial pressure, including increased frontoparietal circumference resulting from hydrocephaly, fontanelle protrusion, blurred vision, projectile vomiting, and severe headaches. Tumor mass effect may also cause focal neurological deficits such as ataxia, paresis, and progressive weakness [6, 7]. In brain magnetic resonance imaging (MRI), the solid component enhances despite the cystic segment. DIA can be diagnosed with its characteristic clinical and imaging manifestations in children; however, histopathological assessments are mandatory to confirm the diagnosis. It contains spindled neoplastic astrocytes with a neuroepithelial origin. Undifferentiated neuroepithelial cells display a hypercellular pattern without desmoplasia. Signs of necrosis, mitoses, and vascular tissue might be detected [4, 6]. Complete surgical removal of the tumoral mass as the definitive treatment has shown promising outcomes. Multifocal involvement and rapid tumor expansion imply a poor prognosis regardless of surgery. DIA seems to behave as a benign lesion; however, current data about survival and prognosis are insufficient due to its rarity. Therefore, we report a four-year follow-up of a male child diagnosed with DIA in the first 1.5 months of his infantile period.

2. Case Report

2.1. History and examination

In February 2017, an infant boy recently passing his neonatal period showed a head circumference expansion to 41.5 cm in his regular physical examination in a local hospital. So, he was referred to our neurosurgery clinic. In March 2017, when first encountered, he was 47 days old. His chief complaint was the abnormal enlargement of the head circumference that was too large for his age (51 cm, $>97^{th}$ percentile). The baby was born by cesarean section to a gravida Π, para Π woman at 38 wk of gestation and weighed 3800 gr at birth. His parents noted gradual asymmetric enlargement of their son's head accompanied by agitation and sleepiness. Nevertheless, he had neither vomiting nor seizure. Physical examination showed sunset eyes and indurated left frontoparietal bulging with cystic-solid consistency in palpation. In brain spiral computed tomography (CT) scan without contrast, a large subdural effusion in the left temporoparietal region was detected that had a pressure effect on the left ventricle and shifted midline structures to the right side. CT scan also revealed pneumocephalus in the left frontal region and dilation of the right lateral and third ventricles. Brain MRI on axial T1-Weighted (T1W), T2W1, sagittal, and coronal T2W sequences showed a large area of

signal abnormality. An inhomogeneous space-occupying lesion (SOL) had replaced the left temporal lobe measuring 40 × 38 mm. A complicated subdural effusion containing some septations was also reported. Two hemorrhagic masses in septum pellucidum measuring 22 × 15 and 21 × 8 mm, respectively, were visible (Figure 1). At first, emergent ventriculoperitoneal shunt placement provided relief from hydrocephalus. After that, subtotal tumor removal was carried out by left temporoparietal craniotomy.

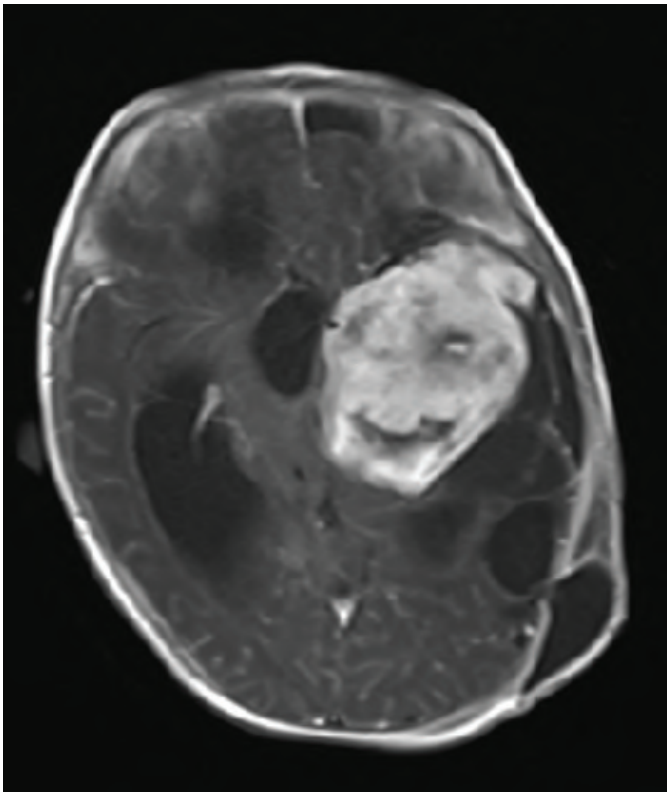


Figure 1: Initial brain MRI. Axial contrast-enhanced T1-weight imaging showed a large area of signal abnormality with an inhomogeneous space-occupying lesion which replaced the left temporal lobe.

2.2. Gross description

In terms of gross pathology, the specimen measured 60 × 55 mm; it consisted of multiple pieces of grayish colored tissues with a soft consistency and hemorrhagic areas.

2.3. Microscopic description

In the microscopic examination, the tumoral lesion was composed of neuroepithelial cells within a desmoplastic spindled stroma. The neoplastic cells were arranged in fascicles with a storiform pattern. The spindle stromal cells had a fibroblast-like feature.

Round to oval shape nuclei, primitive features, and conspicuous mitotic figures were noted in some of the neuroepithelial cells (Figure 2).

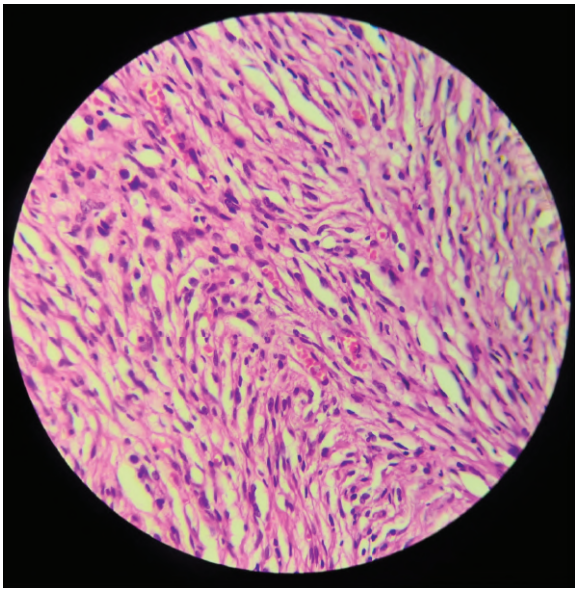


Figure 2: The neoplastic cells are arranged in fascicles with a storiform pattern. The spindle stromal cells have a fibroblast-like feature. Round to oval shape nuclei, primitive features, and conspicuous mitotic figures are noted in some of the neuroepithelial cells (H&E staining, ×400).

2.4. Differential diagnoses and follow-up:

The primary differential diagnoses were infantile desmoplastic astrocytoma, fibroblastic meningioma, and less likely ganglioglioma. Immunohistochemical studies revealed positive reactivity for GFAP (glial fibrillary acidic protein), Vimentin, NSE (neuron-specific enolase), and S-100. Neoplastic cells had negative immunostaining for EMA (epithelial membrane antigen) (Figure 3A & 3B). Therefore, the pathology results were compatible with DIA. One month later, the residual tumoral mass was excised in the second surgery.

Nevertheless, currently, the patient is alive, dealing with cancer and treatment complications. The patient is examined periodically. Examinations include measuring the mobility of the upper and lower limbs, as well as improving brain function, such as communication with others and obedience. Examination of the patient's memory included visual memory and utterance. He did not meet the expected developmental milestones for his age and has not been able to voluntarily control urine and feces and uses diapers (four-year follow-up details is shown in Table 1). The MRI and CT scans were also used to inform the progression or regression of the tumor (Figure 4). Fortunately, the child has not shown any signs of tumor recurrence during our four-year follow-up. At first, the patient could not hold his head up steadily on the neck due to its weight. Gradually,

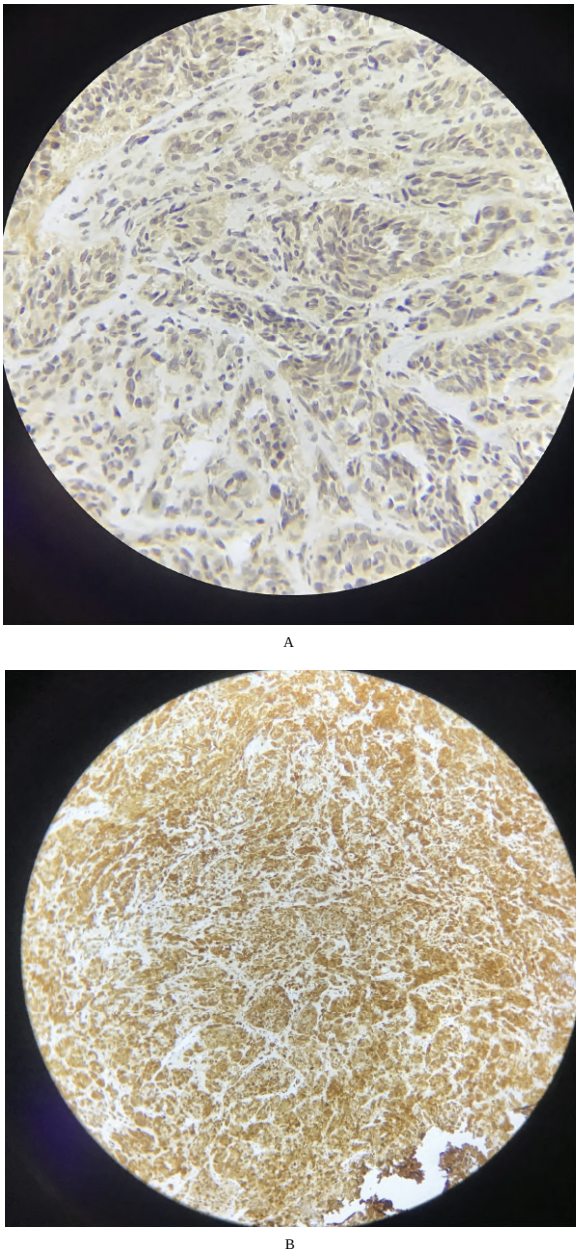


Figure 3: (A) Positive reaction of neoplastic cells for GFAP. (B) Positive reaction pattern of neoplastic cells for vimentin (IHC staining, ×200).

as he became older, he acquired complete head control due to the accelerated truncal growth rate (Figure 5).

2.5. Chemotherapy and side effects

The patient received eight cycles of chemotherapy regimens of CCNU (75 mg/m^2 PO, day 1), Vincristine (1.5 mg/m^2 IV, days 1, 8, 14), and Cisplatin (75 mg/m^2 IV, day 1 over 6 hr) at 6-wk intervals (day 1 to day 1). Regarding the chemotherapy common side

Table 1: Four-year follow-up table of a 47-day old male infant with desmoplastic infantile astrocytoma (available data relating to head circumference, physical and cognitive development and received medication are presented).

Age	Head circumferen	Physical development	Cognitive development	Right proximal and distal limbs forces	Medication
Neonate	41.5	–	–	–	–
47 days	51	–	–	–	–
10 months	55	–	He knows his mother and father perfectly	–	Chemotherapy plus Phenytoin)continued due to changes in the electroencephalogram*(
26 months	–	Could sit in scooter without parents' assistance	–	4/5	Chemotherapy is discontinued, only Phenytoin continued
3 years	–	–	He knows people around him, including his brothers, grandmothers and aunts	4/5	Chemotherapy port removed, Phenytoin discontinued
4 years	–	Sit without personal help, disability in the right limbs hinders his motor development, has not been able to voluntarily control urine and feces and uses diapers	Says short sentences and memory acceptable, visual memory excellent	Right hand force 4/5	–

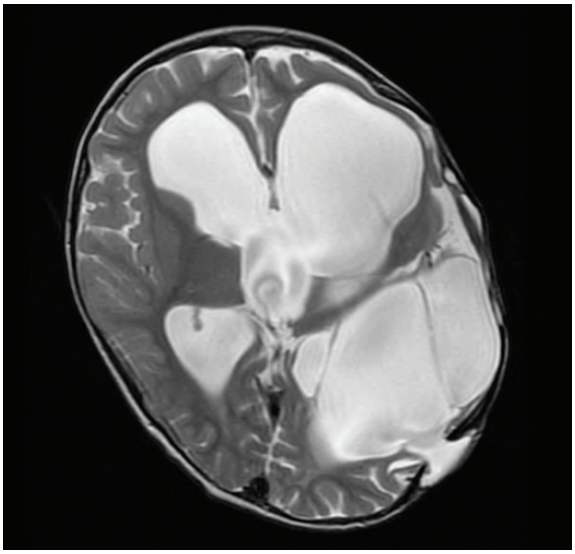
*Although Levetiracetam is the preferred medication for postoperative prophylaxis in patients with brain tumors, Phenytoin was recommended for him four years ago due to its scarcity and high cost in Iran.

effects, this patient did not demonstrate CCNU-induced neutropenia, Cisplatin-induced nephrotoxicity, ototoxicity, and severe nausea and vomiting. Also, peripheral neuropathy as the well-known side effect of Vincristine was not experienced by the patient.

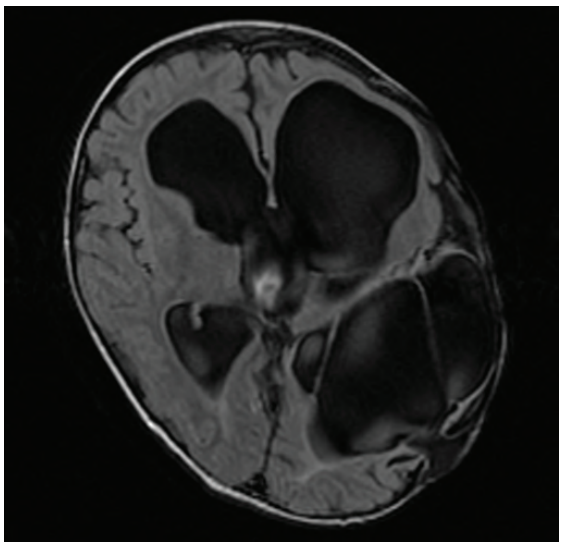
3. Discussion

Consisting only 0.1% of pediatric neurological malignancies, DIA is often seen in male children younger than two years old [3, 4]. Similarly, our case was 47 days old when he first presented.

In 1987, the first case was described by Taratuto *et al.*, and three years later, Vandenberg *et al.* presented the DIG for the first time. Considering their cytopathological similarities, they fit into the category of desmoplastic infantile gliomas. The DIA and



A



B

Figure 4: Four-year follow-up brain MRI**.** (A) Axial T2-weight imaging and (B) FLAIR imaging demonstrating a big cystic lesion of left middle cranial fossa, diffuse severe dilation of third and lateral ventricles, and also a small subcutaneous fluid collection in left temporoparietal region with connection to left lateral ventricle, representative of postoperative changes and noncommunicating hydrocephalus.

DIG belong to the WHO grade 1 tumor classification due to their benign nature [3]. However, synchronous or metachronous multifocal lesions with high recurrence have been reported in some patients, which may arouse controversy regarding their benign nature. Almost all patients, as observed in this patient's left frontoparietal bulging, have demonstrated a sign or symptom of an increase in intracranial pressure, especially bulgy fontanelle and substantial expansion of the parietooccipital circumference [6, 7].

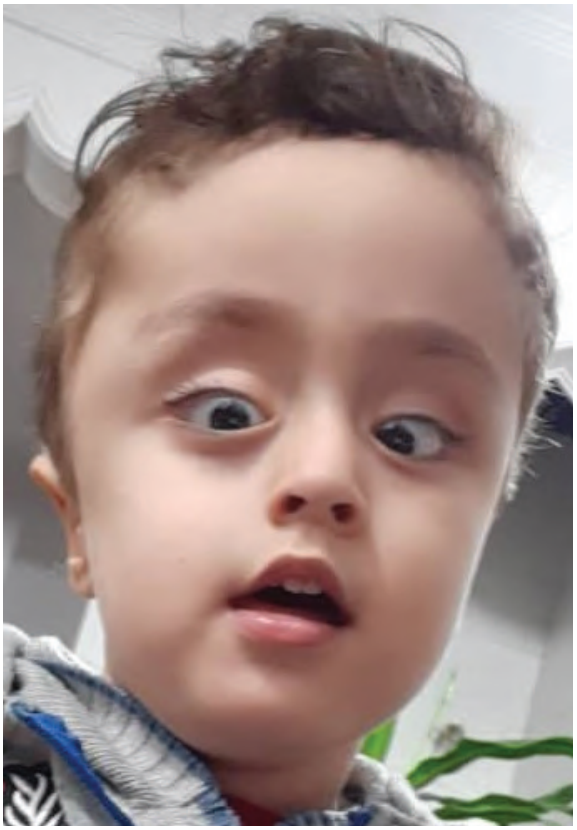


Figure 5: Patient after four years of initial diagnosis.

This child had a delay in the expected developmental milestones, but he did not have vomiting or a seizure. Projectile and recurrent vomiting, seizure, visual problems, focal neurological deficits, dysphoria, and developmental retardations are other described clinical findings. Clinical manifestations occur within three to six months after tumor formation as a result of its large size [8, 9]. Untypical findings like headaches are not enough to suspect this disease and may postpone the diagnosis too late in childhood or adolescence.

DIA often has a supratentorial origin, especially in superficial areas of frontoparietal and temporal lobes [10]. In some cases, the occipital lobe, brain stem, thalamus, and suprasellar parts of the brain can be affected. Multilobes involvement is a common finding due to its large size [3]. Solid components are closer to the brain surface and often engage the cortex and leptomeninges; compared to cystic elements [4–6]. Narayan *et al.* reported a multifocal DIA case with parenchymal and cisternal lesions [11]. The infratentorial involvements caused serious obstructive hydrocephalus. Two theories consider the origin of multifocal cases with spinal tumors. Since neoplastic cells have been found on CSF analysis, the spinal lesion is assumed to be the result of metastasis

from brain DIA. On the other hand, in some cases, DIAs were detected simultaneously on the brain and spinal cord, which favors genetic mutations as a probable etiology.

MRI is the imaging modality of choice for DIA diagnosis. The tumor's solid component has a mural nodule and enhancing feature, which exhibits isointense signal to brain parenchyma on T1 and T2 sequences. Nevertheless, the cystic portion and the desmoplastic part of the mass appears as a hypointense lesion on the T1 sequence [7]. In some cases, it may be mistaken for a low-grade tumor named ganglioglioma; since it also has a mixed structure. However, its solid part is hyperintense and the cystic component may have variable intensity, which is dependent on the amount of protein and vascular tissue.

On gross pathology, DIA is a massive mixed tumor. The solid component is a gray-to-white firm mass along with simple or complex cysts that are filled with yellowish fluid. Since DIA originates from neuronal and glial cells, the neoplastic cells have positive immunoreactivity for GFAP, Vimentin, S-100, synaptophysin, and NSE; and negative reaction pattern for AE1/AE3 and EMA. The tumor is composed of desmoplastic spindled stromal cells arranged in storiform and fascicular pattern with neuroepithelial cells admixture. It has a low proliferative labeling index (MIB1) [4, 6]. In some patients, immature small cells with round to oval shape nuclei are identified. Significant diversity among neoplastic cells in phases of cell cycle and size is observed. Also, eosinophilic granular bodies and infiltrated lymphocytes around blood vessels are recognizable in the desmoplastic stroma.

Total resection of the tumoral mass is challenging since it is massive and consists of deeper cystic components. However, total resection of the tumor is the gold standard of DIA treatment [11]. In some single masses like this case, the tumor is excised with two or more surgeries. However, multifocal DIA is inoperable and surgical intervention is reserved for lesions causing complications, including seizure. Adjuvant chemotherapy and radiotherapy are indicated in these patients to provide symptomatic relief. Samkari *et al.* reported 18 months-old child with DIA who underwent subtotal resection, and after 18 months of follow-up the patient passed away. However, our patient is still alive and has improved learning skills without tumor recurrence [10].

DIA is a rare tumor in children under two years of age, abnormal enlargement of the head circumference could be the early sign of this type of brain tumor with compressive effects on the surrounding tissues. If completely resected, it will have a low recurrence rate, however, due to the large size of the tumor and the extensive surgery that must be performed, in the future, the child will have developmental and learning disorders.

4. Acknowledgements

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5. Ethical Considerations

This study is approved by Shahid Sadoughi University of Medical Science ethnics commission (code: IR.SSU.MEDICINE.REC.1400.182). A written and signed informed consent from guardians for publishing the patient's photograph and case report was obtained.

6. Competing Interests

The authors declare that there is no conflict of interest in the publication of this paper.

7. Availability of Data and Material

Authors confirm that all relevant data are included in the article and/or its supplementary information files.

8. Funding

None.

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