Desmoplastic Supratentorial Neuroepithelial Tumor in A 9-Month-Old Male Infant: A Case Report

9 Aylık Infantil Erkekte Desmoplastik Supratentoriyal Nöroepitelyal Tümör: Olgu Sunumu

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Abstract: Desmoplastic infantile neuroepithelial tumors (DINTs) are superficially located supratentorial neoplasms that include masses known as "desmoplastic infantile gangliomas" (DIGs) and "desmoplastic infantile astrocytomas" (DIAs). Apart from the presence of ganglion cells in DIGs, these tumors and DIAs share the same features. Traditionally, tumors have been designated as DIAs only when intensive histological examination has revealed no ganglion cells. Some DINTs show no ganglion cells on routine staining with hematoxylin and eosin (HE), but are positive for glial fibrillary acidic protein (GFAP), neuron-specific enolases (NSE), neurofilament protein (NF), and synaptophysine on immunohistochemical staining. Currently, it is generally agreed that DIGs and DIAs are variants of one type of tumor, and that both these forms of neoplasia should be labeled DINTs. We describe the case of a 9-month-old male infant who presented with progressive head enlargement. The baby had a cystic, 8 cm-diameter, space-occupying lesion in his left parietal lobe that was surrounded by edema. The mass was identified on cranial computerized tomography, and the patient underwent total tumor excision. Microscopic examination of the mass revealed extensive desmoplasia and focal aggregations of primitive cells. Sections stained with HE showed no ganglion cells; however, immunohistochemical staining revealed widespread GFAP positivity, and focal positivity for NSE and synaptophysine. The diagnosis was DINT. This report discusses the clinicopathologic features of the case, and compares our findings to those documented in previous reports of DIAand DIG attached to the dura.

Key Words: Desmoplasia, embryonal neuroepithelial tumors, infantile tumors

Özet: Desmoplastik İnfantil Nöroepitelyal Tümörler (DİNT), Desmoplastik İnfantil Gangliogliomalar 'DİG) ve Desmoplastik İnfantil Astrositomalar (DİA) olarakta bilinen yüzeyel yerleşimli supratentorial tümörlerdir. DİG'larda ganglion hücrelerinin bulunmasının dışında bu ikitip neoplazi aynı özellikleri taşır. Bu tömürler dikkatli histolojik incelemelere rağmen ganglion hücresi bulunamaz ise DİA olark isimlendirilir. Bazı DİNT'ler Hematoksilen Eozin (H.E) ile rutin boyamalarda ganglion hücresi göstermez fakat Glial fibriler Acidic Protein (GFAP), Nöron Spesifik Enolaz (NSE), Nöroflament Protein (NF) ve Synaptofizin ile immunohistokimyasal boyamalarda pozitiflik gösterirler. Genel olarak kabul edilen görüş, DİG ve DİA'nın bir tip tümörün varyantları olduğu ve bunların hepsinin DİNT terimi altında toplanması gerektiğidir.

Anahtar Kelimeler: astrositoma, desmoplastik, infantil ganglioglioma

INTRODUCTION

Desmoplastic infantile neuroepithelial tumor (DINT) is a rare neoplasm of infancy that is typically seen in the early months of life (0-18 months). DINTs are usually solitary and tend to be located in the supratentorial region, attached to the dura mater. Histopathologically, these masses are characterized by marked desmoplasia, and some also have a component of small, primitive, mitotically active cells. The latter feature makes it easy to confuse some DINTs with malignant neoplasms. Accurate diagnosis of DINT is essential because, although these tumors are rare and tend to be large, they take a benign course and this can greatly? influence treatment decisions.

CASE REPORT

A 9-month-old male infant had been under observation for pulmonary stenosis since birth at the Uludağ University School of Medicine pediatric clinic. The baby's head had become noticeably enlarged over a 1-month period, and the parents reported that he was vomiting and had developed a fever. On admission, a physical examination revealed purulent material the right ear, widespread maculopapular skin eruptions, and an ejection murmur (2/6) in the pulmonary valve region. A neurological examination showed somnolence, and increased muscle tone in both right limbs.

The only abnormal laboratory finding was a white blood cell (WBC) count of 15,000/μL. Cranial magnetic resonance imaging (MRI) revealed a large cystic mass with septae and peripheral edema. The lesion was located in the left temporoparietal cortex and measured 8 cm in diameter (Figure 1). It was compressing the left lateral ventricle, resulting in a displacement of midline structures to the right and causing hydrocephalus.

Based on clinical and MRI findings, and a tentative diagnosis of brain abscess, we performed an emergency burr hole aspiration with a 3 mm diameter brain cannula for the diagnosis and decompressive effect, was taken approximately 40 ml cloudy, hemmorhagic, odorless fluid. Since the material did not match that expected with an abscess, 5 days later we placed the patient under general anesthesia and performed surgery through a left fronto-temporal surgial approach. On opening the dura in this region, we found a firm mass attached. The neoplasm was easily separated from the surrounding brain tissue and was totally excised.

Examination of HE-stained sections of the tumor showed a storiform pattern of desmoplasia predominating throughout the mass (Figure 2). The desmoplastic fusiform cells stained strongly for reticulin. We also noted smaller numbers of primitive

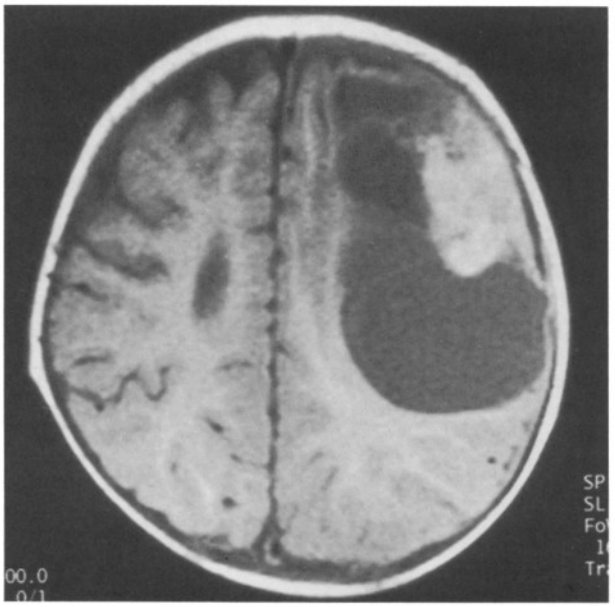

Figure 1: MRI shows a large cystic mass containing septae.

round cells with hyperchromatic nuclei and scant cytoplasm (Figure 3). Reactive islands of glial tissue were also present within the desmoplastic areas (Figure 4). No mature ganglion cells were observed. Application of glial fibrillary acidic protein (GFAP), neuron-specific enolases (NSE), Neurofilament protein (NF) and synaptophysine immunohistochemical stains revealed strong diffuse positivity for GFAP in the desmoplastic regions (Figure 5), whereas comparatively few primitive cells stained for GFAP. In contrast, the small undifferentiated cells were strongly positive for NSE and synaptophysine, whereas this staining was rarely observed in the desmoplastic cells and, when seen, was confined to the cytoplasm (Figure 6). On the basis

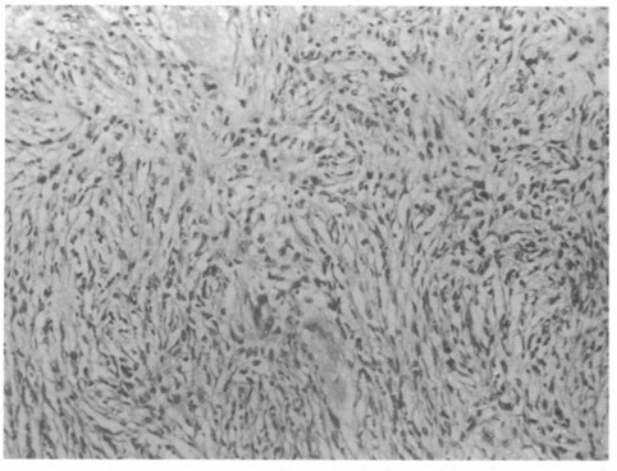

Figure 2: Desmoplasia predominates in the tumor tissue. (HE x100)

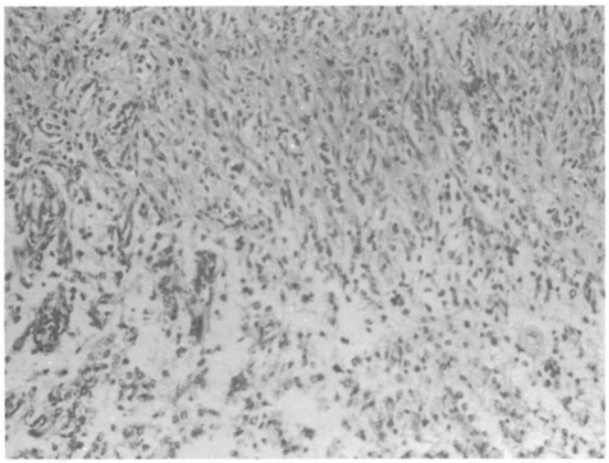

Figure 3: Some primitive round cells with hyperchromatic nuclei and scant cytoplasm are seen, in addition to the marked desmoplasia. (HE x100)

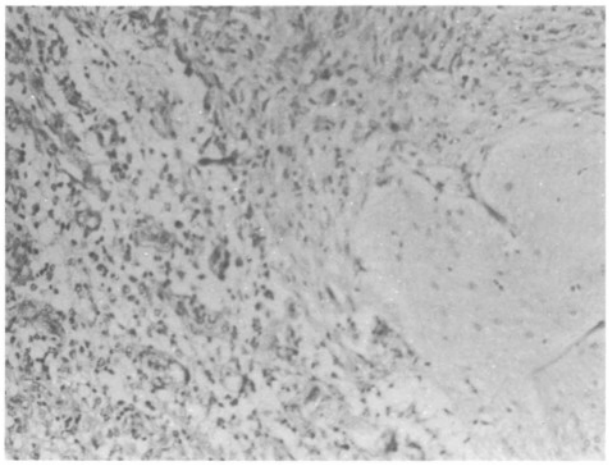

Figure 4: Reactive glial tissue islands within the desmoplastic regions. (HE x100)

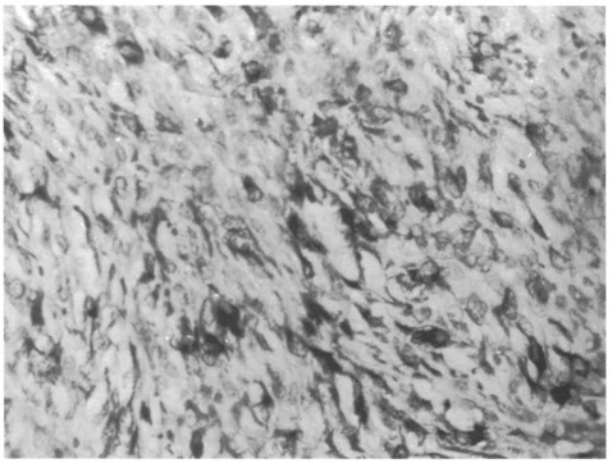

Figure 5: A diffuse, strongly positive reaction for GFAP in the desmoplastic areas. (GFAP x200)

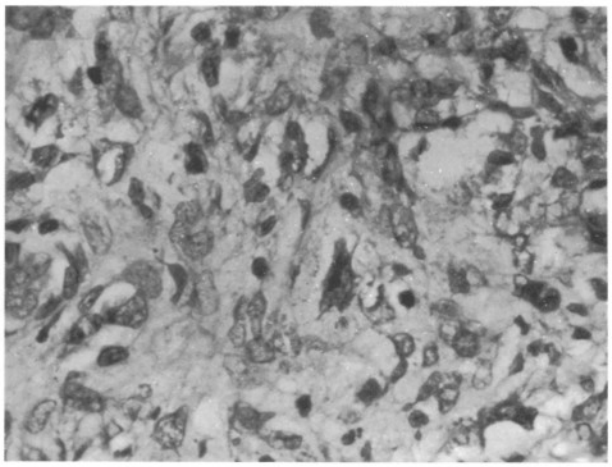

Figure 6: The cytoplasm of occasional cells in the desmoplastic regions also stained positive for NSE. (NSE x400)

of these features, we diagnosed the mass as a DINT lacking mature ganglion cells but showing immunohistochemical evidence of neuronal differentiation.

DISCUSSION

First described by Taratuto et al. in 1984 (6), DIAs are large cystic tumors that induce a leptomeningeal reaction and are usually encountered in infants. DIGs were initially described by Vandenberg et al. in 1987, and exhibit all the features of DIA in addition to populations of neuronal cells. It has yet to be established whether DIAs and DIGs are truly separate entities (4). In their study of 11 cases, Vandenberg and co-workers postulated that the two may be slightly different forms of the same tumor, and predicted that their variant features would be observed in future cases. They also suggested that the apparent absence of ganglion cells in DIA cases might reflect insufficient sampling (4).

Paulus et al. reported two cases that had both DIG and DIA features. They were the first authors to propose the general label of "infantile desmoplastic supratentorial neuroepithelial tumor," to encompass both these neoplastic forms. After they found no neurons in sections stained with routine HE preparation, Paulus et al. used immunohistochemical staining to confirm that the masses featured neuronal differentiation (3).

There is intriguing speculation that DINTs originate from foci of neurogenesis in the subpial

granular layer of the cerebral hemispheres. In humans, this cell layer starts to disappear at 8 months of gestation, but remnants of it have been found in the frontal lobes even at 6 months after birth. Due to their large size, their pre-perinatal development, and their undifferentiated nature, DINTs are considered embryonal tumors (3,4). Unlike other poorly differentiated embryonal tumors of the central nervous system, the behavior of this tumor is not aggressive, and DINTs are generally seen in the first 18 months of life. Grossly, the masses have a multiple cystic structure and are firm in consistency. Their significant microscopic features are the presence of populations of neuroepithelial cells and desmoplasia (1,2,3,4).

In addition to immature neuronal cells, some reports on DIG have noted the presence of mature ganglion cells. As Vandenburg et al. proposed, the lack of neuronal differentiation in other cases may be due to insufficient sampling and the paucity of neoplastic neuronal components (2,4). However, another opinion is that the undifferentiated cells' potential for transformation may stop at the astrocytic line. This fits with the hypothesis that the neoplastic change may begin in the fetal stages. If there is enough undifferentiated cellular material, this may lead to diffuse proliferation of desmoplastic cells and spread of the tumor to the leptomeninges. Spread to the leptomeninges is seen in almost all patients, and is an important feature. As well, it is a trait common to other desmoplastic tumors. The extensive fibrous tissue may specifically originate from meningeal fibroblasts, and may reflect the neoplasm's invasion of the leptomeninges.

A different theory concerning the origin of this neoplasm is that aberrant metaplasia in the neoplastic glial cells may trigger the development of the fibrous tissue. However, to date it has not been proven that extracellular matrix material is produced in central neuroepithelial tumors such as DIGs (1,2,3,4). Further study is needed in this regard.

The key issue in cases of DINT is accurate diagnosis. These tumors must be distinguished from malignant neoplasms. In the past, DINTs have been erroneously diagnosed as gliosarcoma, anaplastic astrocytoma, malignant meningioma, and leptomeningeal fibrosarcoma (4). Information on patient age, radiological features, histological findings of marked desmoplastic and primitive cell components, and immunohistochemical staining traits for GFAP, NSE, NF, and synaptophysine should be assessed as a whole when attempting to differentiate DINTs from malignant neoplasms.

In general, DINT carries a good prognosis. However, the tumor's considerable bulk relative to the small size of the infant brain can make surgical intervention difficult, and this is the basis for the considerable mortality risk (2,4). Apart from surgical complications, the patient may develop serious problems with hydrocephalus, or brain edema and herniation. If the mass can be totally excised, radiation and chemotherapy are not indicated. Postoperative disease-free survival of 14 years has been reported in excision cases (4).

CONCLUSION

DINT is a benign embryonal tumor that is suspiciously large and often appears malignant on histopathological examination. Accurate diagnosis of DINT is crucial in terms of treatment and prognosis, as these neoplasms can be easily confused with malignancies. This case marks the first diagnosis of this type of tumor in our pathology department. We view this description as a significant contribution to the current literature on the basis of the rarity of DINTs and the need for further information on their clinical, radiological, and histopathological features.

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