

Coexistent dysembryoplastic neuroepithelial tumour and pilocytic astrocytoma

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ABSTRACT

Dysembryoplastic neuroepithelial tumour (DNET) is an uncommon mixed glioneuronal tumour. DNET is classified as Grade I neoplasm in revised World Health Organization classification of tumors of the nervous system. DNET is commonly seen in the temporal lobe of children and young adults with features of pharmaco-resistant complex partial seizures. Tumors arising in association with DNETs are rare. Only two cases of pilocytic astrocytoma (PA) arising in DNETs are reported. Surgical excision is the only successful management with favourable prognosis. The development of recurrence and malignancy after subtotal or even after complete excision challenges the premise of stability and highlights the importance of close clinical follow up. Here, a case of DNET with area of PA is described which helps in understanding the pathogenesis and biological behavior of DNET.

Key words: Dysembryoplastic neuroepithelial tumour, malignant transformation, pilocytic astrocytoma, seizure

Introduction

Dysembryoplastic neuroepithelial tumour (DNET) is a rare mixed glioneuronal tumour.^[1-4] In 1993, World Health Organization (WHO) classified the DNET as a Grade I tumour.^[2,4] Only two cases of pilocytic astrocytoma (PA) with DNETs are reported.^[1,2] To the best of our knowledge, this is the third reported case of coexistent DNET with PA. DNET have the potential for recurrence and malignant transformation.^[1,2,5-10] The identification of DNET by surgical pathologist has therapeutic and prognostic implications because surgical outcome and prognosis is much better and aggressive chemo-radiotherapy can be avoided.^[2,4,8,11,12] Here, we discuss a case of DNET with PA. We conclude that patients with unresected long standing DNET may develop secondary, histologically different neoplasm in DNET itself.

Case Report

A 14-year-old male presented with complain of headache,

vomiting and seizures. He had previous history of epilepsy before three years. Seizures were managed with carbamazepine without definitive diagnosis. There had been increased frequency of medically refractory seizures since 12 months. Neurological examination was unremarkable. Routine laboratory investigations were within normal limits. On magnetic resonance (MR) imaging, left temporal lobe revealed multinodular mass. It was hypointense on T1 and hyperintense on T2-weighted images without surrounding vasogenic edema. Post-contrast scans revealed only small focal enhancement. Little mass effect was seen [Figure 1]. Radiological diagnosis of DNET or low grade astrocytoma was made.

On left temporal craniotomy, the interface between the tumour and normal brain was well-defined. Total resection was achieved. Grossly multiple grayish white gelatinous friable tissue was evident. Histological evaluation disclosed two distinct morphologies with a sharp demarcation between tumour and normal cerebral cortex. The predominant component was complex form of DNET. It showed glioneuronal element composed of oligodendroglioma-like cells (OLCs), astrocytes and mature neurons. OLCs and astrocytes were arranged in trabecular pattern. OLCs contain uniform round dark nuclei with clear perinuclear halos. Floating neurons (ganglion cells) were seen in mucinous matrix [Figure 2]. Coexistent cortical dysplasia was not evident. Transitional zone between loose cystic area of DNET and more cellular area of PA was seen. The minor astrocytic component (approximately 15% of the total tumour bulk) showed fibrillated spindled Piloid cells with oval hyperchromatic, enlarged nuclei. Occasional Rosenthal fibers and granular bodies suggest PA. Mitotic activity was absent [Figure 3].

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Immunohistochemistry showed positivity for glial fibrillary acidic protein (GFAP) in the astrocytes but not in the OLCs and ganglion cells. OLCs are strongly immunoreactive with antibodies against S-100-Protein [Figure 4]. Pathological diagnosis of DNET with PA was made.

The patient recovered uneventfully. Clinical result of the surgery was excellent. No seizures or tumour recurrence have been observed during five years follow-up.

Discussion

In 1988 Dumas-Duport described the dysembryoplastic neuroepithelial tumour as a rare distinct benign cortical tumour

of neuroepithelial origin. They considered the DNET to be at least partially neoplastic and formed during embryonic development from secondary germinal layer.^[1,3,13] Malignant transformation and regrowth following subtotal resection supports the hypothesis of neoplastic origin.^[5,7,8,10] Till date only two cases of PA arising in association with DNETs are reported.^[1,2]

DNETs are most commonly seen in temporal lobe of cerebral cortex.^[1-4,14] Occasionally DNET has been found in caudate nucleus, septum pellucidum, brainstem and cerebellum.^[2,4] Occasional multifocal DNETs are associated with neurofibromatosis, XXY syndrome and intradural spinal lipoma.^[11] DNET usually occur in 6-20 years of age range. Males are affected more frequently than females.^[4] Review of literature suggest that development of pilocytic astrocytoma, recurrence and malignant transformation occurs mainly in childhood and young age with predilection to temporal and frontal cortex.^[1,2,5,7-10] Intracranial hypertension and neurologic deficits are not common with DNETs.^[4,14] The signs of raised intracranial pressure suggest malignant

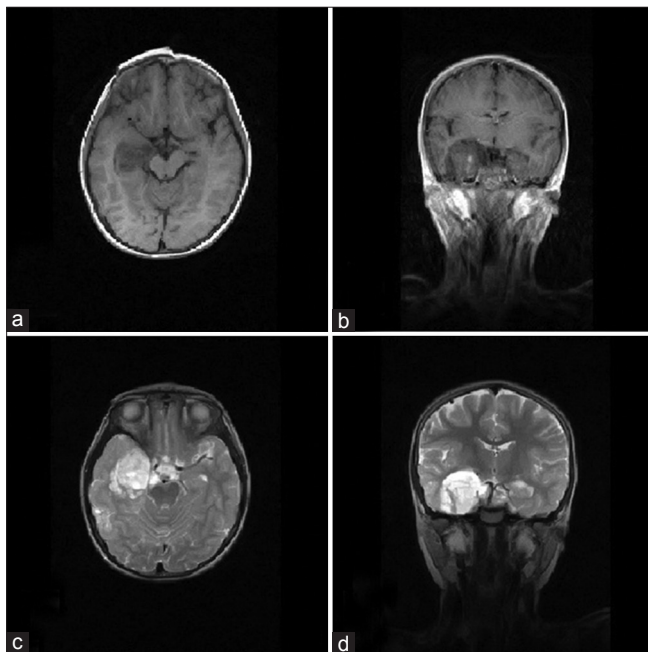


Figure 1: Dysembryoplastic neuroepithelial tumour: (a) Axial T1-weighted MR image shows a hypointense mass in left temporal lobe; (b) Contrast-enhanced coronal T1-weighted MR image shows focal contrast enhancement in the tumour; (c) Axial T2-weighted MR image shows high signal intensity within the mass with lobulated margins; (d) The lesion is of high signal intensity with sharp boundaries on an axial T2-weighted MR image, with little mass effect

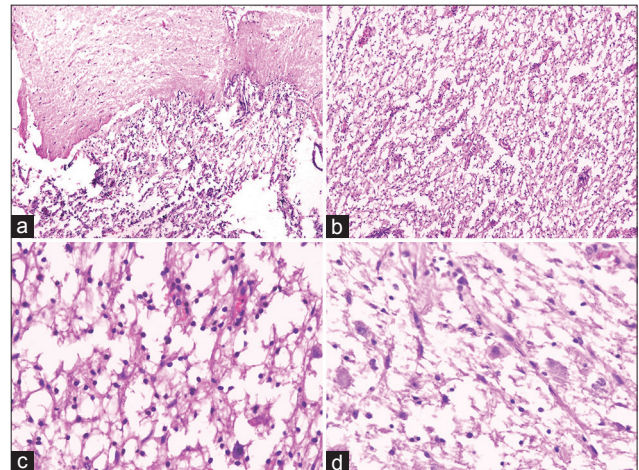


Figure 2: Dysembryoplastic neuroepithelial tumour: (a) Sharp demarcation between tumour (lower) and normal cerebral cortex (upper) is seen (H and E, $\times 10$); (b) Glioneuronal element in a partially microcystic background (H and E, $\times 10$); (c) Oligodendrocyte-like tumour cells (OLCs) and astrocytes are arranged in trabecular pattern. OLCs contain uniform round dark nuclei with clear perinuclear halos. (H and E, $\times 40$); (d) Mature neurons (ganglion cells) floating in a mucinous matrix (H and E, $\times 40$)

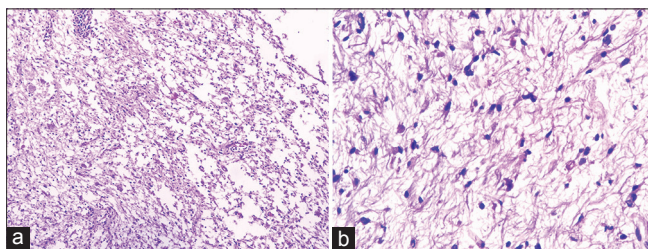


Figure 3: Dysembryoplastic neuroepithelial tumour with pilocytic astrocytoma: (a) Transitional zone between loose cystic area of DNET (upper-right) and more cellular area of PA (lower-left) is seen (H and E, $\times 10$); (b) The astrocytic component showed fibrillated spindled Piloid cells with oval hyperchromatic, enlarged nuclei with occasional Rosenthal fibers and granular bodies (H and E, $\times 40$)

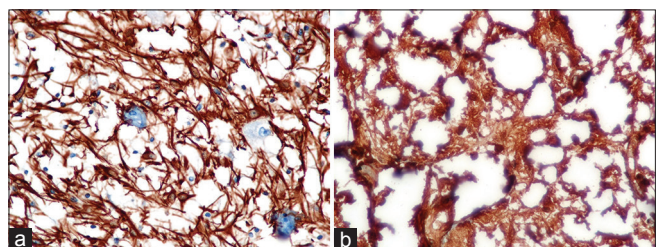


Figure 4: Dysembryoplastic neuroepithelial tumour: (a) Immunostain for GFAP highlights the astrocytes but not the oligodendrocyte-like cells and ganglion cells (Immunostain, $\times 40$); (b) Small oligodendrocyte-like tumour cells are strongly immunoreactive with antibodies against S-100-Protein (Immunostain, $\times 40$)

transformation.^[1] On computed tomography DNETs are typically well-demarcated, hypodense cortical lesions. MR images often show a solid and cystic mass. The solid components often appear multinodular, hypointense on T1-weighted MR images, hyperintense on T2-weighted MR images, and occasionally weakly enhancing.^[1,2,11,13] In our case, the clinical and radiological features were not entirely specific to DNET; dilemma occurs between DNET and low grade astrocytoma.

Histologically DNET divided into a simple, complex and non-specific form. The simple form consists of only glioneuronal elements without multinodular architecture. The complex form consists of glioneuronal elements, multinodular architecture, and associated cortical dysplasia. The nonspecific form has neither glioneuronal elements nor the multinodular architecture. It resembles a low-grade astrocytoma but has clinical and radiological features more consistent with a DNET.^[4,13-15] Occasional DNET may show presence of increased cellularity, pleomorphism, cytological atypia, microvascular proliferation, calcification, necrosis, high MIB-1 labeling indices and extensive involvement of surrounding structures.^[1,3,4,10,11,13,15] Theoretically, overgrowth of any components of DNET may result in an independent tumour.^[1] However, commonly associated secondary neoplasm with DNETs are PA, anaplastic astrocytoma and glioblastoma suggesting that astrocytic component has more proliferative potential than other component of DNET.^[1,2,7,8,13] DNET with unresected, incompletely resected or even completely removed tumour can show development of pilocytic astrocytoma, recurrence or malignant transformation over a period of 3-11 years.^[1,2,5-9] The combined mutagenic effects of radiotherapy and chemotherapy may cause or accelerate the malignant transformation.^[8] In all cases of DNET with PA, recurrence and malignant transformation common factor is subtotal excision of tumor and it is probably the major risk factor for the unstable behaviour of DNET in such cases. These might serve as a warning for considering this entity as totally benign.^[1,2,5-9] In our case we think that unresected long standing DNET made suitable condition for overgrowth of astrocytic component within the DNET itself.

DNET must be differentiated from low grade gliomas especially oligodendrogliomas, mixed oligo-astrocytomas or astrocytomas in order to avoid unnecessary post surgical radiotherapy or chemotherapy.^[3,4]

Natural history of DNET is not yet completely defined.^[2,13] DNET appear to be remarkably stable in terms of biologic behavior.^[13] Complete surgical resection without any adjuvant radiotherapy or chemotherapy is recommended treatment as it gives excellent control of seizures.^[2,4,8,11-13] However, long term follow-up is required because majority of recurrence and malignant transformation occurs after 3 years.^[1,2,5-9] Our patient had neither undergone previous surgery nor received any adjuvant therapy and hence this case is a de novo development of PA in a DNET.

Conclusion

DNET is a rare mixed neuroepithelial tumour of younger patients who present with refractory seizures. The early recognition of DNET is important as it has an excellent prognosis on complete surgical excision without use of adjunct therapies. Unresected or incompletely removed DNET and secondary radio-chemotherapy may give rise to recurrence and malignancy. Most common secondary neoplasm is astrocytic in origin. The development of the secondary neoplasm challenges the stability in terms of biological behaviour and highlights the importance of complete surgical excision and close follow up.

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