·论 著·

6例胚胎发育不良性神经上皮肿瘤患者的临床病理学分析

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［摘要］ **背景与目的：**胚胎发育不良性神经上皮肿瘤（dysembryoplastic neuroepithelial tumor，DNT）是一种少见的良性混合性神经元-胶质肿瘤，探讨其临床病理学特征及鉴别要点。**方法：**回顾性分析苏州大学附属第一医院和苏州市立医院2009年3月—2021年1月经病理学检查确诊的6例DNT患者的资料，归纳总结其临床病理学特征、影像学特征及免疫表型，并进行随访。**结果：**患者以不同程度的肢体抽搐、癫痫样发作为主要症状。肿瘤位于颞叶4例，顶叶1例，额叶1例。磁共振成像（magnetic resonance imaging，MRI）主要表现为囊性病灶，其内可见分隔及“三角征”或T1低信号，T2高信号，周围水肿不明显。光镜下肿瘤由特征性的胶质神经元成分构成，间质黏液样变性，以少突胶质样细胞为主，可呈束状、巢状、微囊状分布，其间散在单个的神经元或增生的星形胶质细胞，局灶可见砂粒体样钙化。免疫组织化学检测显示，神经元NeuN（+）、Syn（+）、MAP2（+），少突胶质样细胞Olig-2（+）、S-100（+），增生的星形胶质细胞GFAP（+），P53野生型表达，Ki-67≤2%。6例患者均行手术治疗，术后未进行放疗或化疗。5例患者获得随访，其中1例于术后3年癫痫复发。**结论：**DNT是一种手术可治愈的肿瘤，联合临床表现、影像学检查及病理学检查可确诊，无需放疗和化疗。

［关键词］胚胎发育不良性神经上皮肿瘤；临床病理学特征；影像学特征；免疫表型

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A clinicopathological analysis of 6 cases with dysembryoplastic neuroepithelial tumor

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［**Abstract**］ **Background and purpose:** Dysembryoplastic neuroepithelial tumor (DNT) is a rare and benign mixed neuronal-glial tumor. This paper was to study the clinicopathological features and the key points of differential diagnosis of DNT. **Methods:** The data of 6 cases with DNT diagnosed by pathological examination in The First Affiliated Hospital of Soochow University and Suzhou Municipal Hospital from March 2009 to January 2021 were collected, the clinicopathological features, imaging characteristics and immunohistochemical phenotype were retrospectively analyzed, and the patients were followed up. **Results:** The main symptoms of the patients were limb convulsions and epilepsy. Four tumors were located in temporal lobe, 1 in parietal lobe, and 1 in frontal lobe. On magnetic resonance imaging (MRI), tumors mainly showed cystic lesions with septum and “triangle sign”, T1-hypointensity and T2-hyperintensity. Peripheral edema was inconspicuous. The histopathological hallmarks were so called specific glioneuronal element with myxoid matrix, floating neurons or proliferative astrocytes scattering among oligodendrocyte-like cells, which distributed in bundles, nests, microcysts with focal calcification. Immunohistochemistry showed that scattered neurons expressed Syn, NeuN and

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MAP2, oligodendrocyte-like cells expressed Olig-2 and S-100, and GFAP was expressed in proliferative astrocytes. The expression of P53 was wild-type. The index of Ki-67 was less than or equal to 2%. All patients received surgical treatment without radiotherapy or chemotherapy. Five patients were followed up, and one of them had recurrent epilepsy 3 years after operation. **Conclusion:** DNT can be cured by surgery, and it can be diagnosed by combination of clinical features, imaging examination and pathology without the need for radiation and chemotherapy.

［**Key words**］ Dysembryoplastic neuroepithelial tumor; Clinicopathological feature; Imaging characteristics; Immunophenotype

胚胎发育不良性神经上皮肿瘤（dysembryoplastic neuroepithelial tumor，DNT）是一种少见的良性神经上皮来源的肿瘤，在1993年世界卫生组织（World Health Organization，WHO）分类中被归入神经元和混合性神经元-胶质肿瘤中[1]，WHO Ⅰ级，主要发生于儿童和青少年，并可能出现药物难以控制的慢性癫痫[2]。对于这种特殊的实体瘤，主要以手术切除为主，无需放疗和化疗。为进一步加深对该肿瘤的认识，避免过度治疗，本研究回顾性分析6例DNT患者的临床病理学特征，查阅并总结相关文献，了解该疾病近年来的研究进展，以期为广大医务工作者提供参考。

1 材料和方法

1.1 一般资料

收集苏州大学附属第一医院和苏州市立医院2009年3月—2021年1月经病理学检查确诊的6例DNT病例，其中1例为外院会诊病例，整理所有患者的临床资料并进行随访（表1）。

表 1 6例DNT患者的临床资料

Tab. 1 Clinical data of 6 patients with DNT

Case number	Gender	Age/year	Tumor location	Symptom	Imaging	Follow-up
1	Male	23	Right temporal lobe	Sudden syncope for more than a week, followed by limb convulsions lasting 1 min	MRI: cystic lesion with internal compartments, wedge-shaped and no edema around the lesion	2 years, no recurrence
2	Female	27	Right temporal lobe	Daze for more than 10 years, lasting 2-3 min	MRI: cystic lesion with internal compartments. The lesion was connected to the brain surface with a broad base, no surrounding edema, no obvious enhancement	Half a month, no recurrence
3	Male	16	Left temporal lobe	Intermittent headache with aggravation for more than 2 years	MRI: multiple cystic structures and septations were seen in the lesion. The lesion was connected to the brain surface with a broad base, T2-hyperintense, without surrounding edema	4 years, recurrence
4	Female	8	Right parietal lobe	Limb convulsions accompanied by numbness for more than 10 d	MRI: circular abnormal signal, T1-hypointensity and T2-hyperintense, no obvious enhancement	Loss to follow-up
5	Female	57	Right temporal lobe	Paroxysmal limb convulsions for over 33 years	MRI: round mass, T1-hypointensity and T2-hyperintense, spot enhancement, mainly diffuse low signal, surrounding edema was not obvious	15 months, no recurrence
6	Female	22	Left frontal lobe	Limb convulsions for 16 years, aggravated for 1 month	CT: irregular morphology of mixed density focus, mainly showed low density, surrounding edema was not obvious, compression absorption can be seen close to the skull	12 years, no recurrence

MRI: Magnetic resonance imaging; CT: Computed tomography

1.2 方法

6例手术切除标本均经过4%甲醛溶液固定，依次进行常规脱水、石蜡包埋、切片、H-E染色和免疫组织化学染色。免疫组织化学检测采用EnVision法。

1.3 试剂

所用抗体Syn、Olig-2、S-100、GFAP、NeuN、MAP2、P53、Ki-67均购自基因科技（上海）股份有限公司。

2 结　果

2.1 影像所见

6例患者的病灶均位于幕上，颞叶4例，顶叶1例，额叶1例。磁共振成像（magnetic resonance imaging，MRI）显示，3例为囊性病灶，内部可见分隔，病灶与脑表面宽基底相连，整体形态呈楔形，病灶周围无水肿（图1A、1B）；2例示T1低信号，T2高信号，其中1例增强后可见斑点状强化；1例计算机体层成像（computed tomography，CT）可见形态欠规则混杂密度灶，以低密度为主，周围水肿带不明显，邻近颅骨见压迫性吸收。

2.2 大体所见

6例患者中，3例送检为灰白碎组织，2例送检为灰白灰红组织，1例送检为灰白灰红胶冻样结节1枚。

2.3 镜下所见

肿瘤在大脑皮质内呈结节状分布，间质疏松黏液样（图2A）。肿瘤由数量不等的神经元、少突胶质样细胞和星形胶质细胞构成。可见特征性的胶质神经元成分：少突胶质样细胞沿着轴突束排列，其间散在分布正常形态的神经元（图2B）；可见微囊结构（图2C），黏液背景中可见散在的神经元漂浮其中（图2D）；少突胶质样细胞可形成巢状（图2E）、条索状，可见薄壁血管（图2F），类似少突胶质细胞瘤，其间可见增生的星形胶质细胞（图2I），1例肿瘤组织边缘可见砂粒体样钙化。所有病例核分裂象少或不见，未见坏死和微血管增生。

2.4 免疫组织化学

散在分布的神经元NeuN（+）、Syn（+）、MAP2（+），少突胶质样细胞Olig-2（+）、S-100（+），增生的星形胶质细胞GFAP（+），肿瘤细胞P53野生型表达，Ki-67≤2%，其中1例复发者Ki-67约为5%（图2G、2H）。

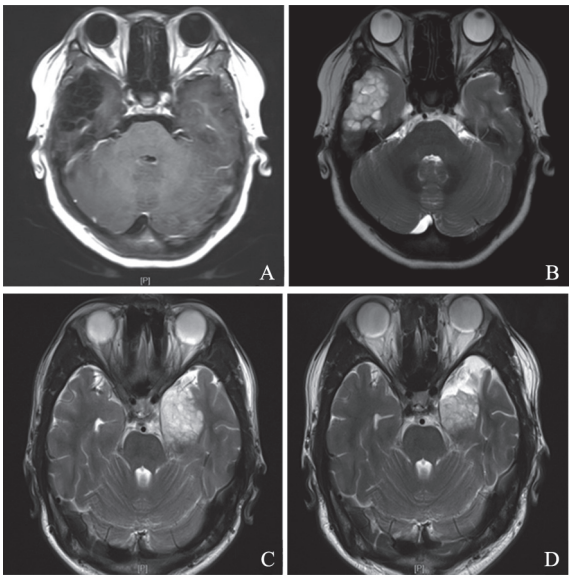

图 1 DNT典型的MRI表现

Fig. 1 The representative MRI presentation of DNT

A, B: Cystic abnormal signal in the right temporal lobe, cord-like partition can be seen inside. The lesion is connected to the brain surface in a wide base, with T1-hypointensity and T2-hyperintense, no obvious edema around. C, D: Recurrence epilepsy case, with left temporal lobe space occupying lesion. Compared the first data (C) to the second before operation (D), the lesion was not completely removed during the first operation. Postoperative follow-up showed no significant changes in the size, shape and signal of residual lesions.

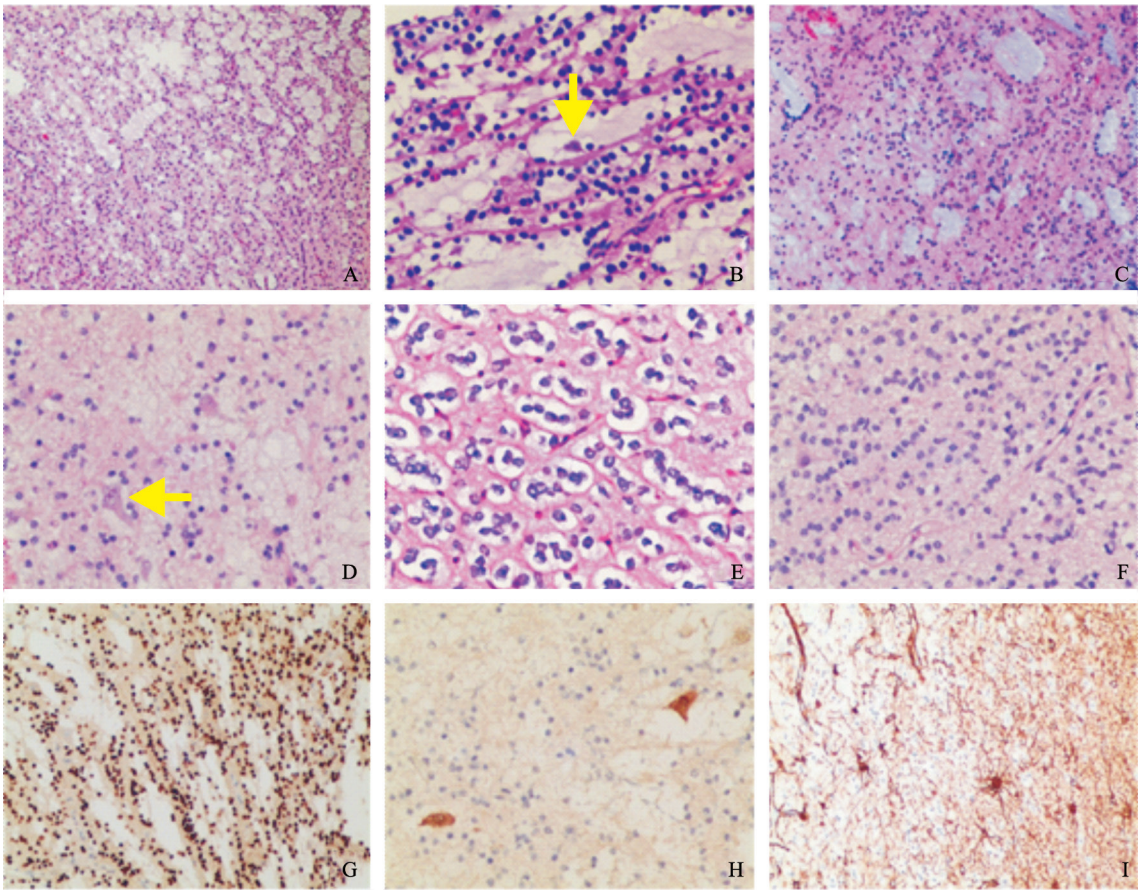

图 2　DNT的组织学形态和免疫表型

Fig. 2　The histological and immunophenotyping presentation of DNT

A: Myxoid matrix (×40); B: Oligodendroglia-like cells were arranged along the axon bundles with scattered neurons (yellow arrow) (×200); C: Microcapsule area (×100); D: Scattered neurons in the myxoid matrix (yellow arrow) (×200); E: The oligodendroglia-like cells were arranged in nests (×200); F: Thin-walled blood vessels (×200); G: Oligodendroglia-like cells Olig-2 (+) (×100); H: Scatter-distributed neurons NeuN (+) (×200); I: Proliferated astrocytes GFAP (+) (×100)

3　讨　　论

DNT是一种良性的神经元和混合神经元-胶质肿瘤，主要发生于幕上脑皮质，以颞叶和顶叶为主，也可发生于透明隔、尾状核、丘脑、小脑、脑干和脑室[3]。在神经上皮肿瘤中，其发病率20岁以下为1.2%，20岁以上为0.2%[1]。主要表现为难治性癫痫。本组6例患者病灶均位于幕上，4例位于颞叶，1例位于顶叶，1例位于额叶，发病年龄8~24岁，男性2例，女性4例，主要表现为肢体抽搐、愣神、间断性头痛，抗癫痫药物治疗效果欠佳。

随着影像学技术的不断进步，MRI和CT对DNT具有重要诊断价值，尤其是MRI，表现为皮质或皮质下单发或多发囊性信号，其内可见分隔样改变[4]，部分可见典型的“三角征”。T1加权成像（T1-weighted imaging，T1WI）呈低信号，T2加权成像（T2-weighted imaging，T2WI）呈高信号，增强后强化不明显。液体抑制反转恢复序列（fluid attenuated inversion recovery，FLAIR）上有典型的“环状征”[4]。CT扫描呈低密度或囊状，部分可出现钙化，占位效应不明显和病灶周围水肿少见[5]，这些特点有助于与其他类型的胶质瘤鉴别。本研究的6例患者中，3例可见典型的囊性信号、内部分隔影及“三角征”，瘤周无明显水肿，1例患者于术后3年癫痫发作，术后其组织学形态与原发肿瘤相似，我们回顾性分析其影像学资料发现第1次手术时未完全切除病灶，在癫痫复发时残余病变大小、形态和信号无明显变化（图1C、1D），推测其复发

可能与其周围脑皮质发育不良有关。

该肿瘤有独特的组织学特点，光镜下可见病变呈单灶或多灶分布，间质黏液样变，典型特征为少突胶质样细胞沿着轴突束排列，其间散在单个的神经元；少突胶质样细胞可形成微囊状结构，其间可见漂浮的神经元；神经胶质结节由少突胶质样细胞和星形胶质细胞组成，其间伴或不伴有神经元。少突胶质样细胞可形成类似少突胶质细胞瘤样区域，部分可伴有微血管增生，无肿瘤性坏死。DNT的组织学亚型分为3种，即单纯型、复杂型和非特异型。本研究的6例患者均为复杂型DNT。非特异型DNT一直备受争议，由于其缺乏典型的DNT病理学特征，组织学上与胶质瘤难以鉴别。

鉴别这种特殊肿瘤的重要性在于它是一种手术可治愈且预后良好的肿瘤，术后不需要放疗和化疗。DNT需要与以下疾病鉴别：① 节细胞胶质瘤，发病年龄广，颞叶多见，常表现为囊实性占位性病变，其内无分隔，肿瘤实性成分多强化，钙化常见[4]，该肿瘤也是一种混合性神经元-胶质肿瘤，但其胶质成分多样，纤维基质较明显，可含微囊及黏液样基质，血管周围或肿瘤内可见大量淋巴细胞浸润，这些特征有助于与DNT鉴别，当影像学和形态学特征不典型时，两者鉴别有一定困难。② 少突胶质细胞瘤，好发于成年人，额叶多见，条索状钙化颇具特征，组织学形态相对单一，主要呈蜂窝状形态。③ 低级别弥漫性胶质瘤，好发于年轻人，幕上多见，一般呈浸润性生长，极少表现出多囊性改变和“三角征”，瘤细胞形态、大小相对一致，当间质发生黏液变性时与DNT难以鉴别，GFAP弥漫阳性时支持弥漫性胶质瘤的诊断[6]。

近年来，对于DNT分子机制的研究有了一定进展。在DNT中未检测到1p/19q缺失、*IDH*1[7]或*P*53突变[8]。但一项关于101例DNT患者的研究[9]发现，3例*IDH*1突变，10例1p/19q杂合缺失，2例19q缺失，3例10q缺失，1例1p/19q和10q联合缺失。近年来的研究发现，在DNT中存在*BRAF* V600E突变[10]、TERT启动子突变[11]、mTOR信号过度激活[12]和酪氨酸激酶区FGFR1重复[13]，而FGFR1可以激活MAPK-ERK信号通路[14]。因此，DNT的发生机制十分复杂，并存在肿瘤异质性。这些分子改变可能为未来的靶向治疗提供依据。

手术切除病灶可有效地控制癫痫发作和肿瘤复发[15]，在术中监测脑电活动有助于病灶的完全切除[16]。在病灶全或次全切除的情况下，极少存在肿瘤的复发。极少数患者可以恶变为高级别胶质瘤，主要与放疗相关[17]，当核分裂象增多、出现坏死、微血管增生或Ki-67增殖指数升高时，提示有恶变可能[6]或合并其他类型的肿瘤。本组1例患者术后3年再次出现肢体抽搐，MRI显示，第1次手术只切除小部分肿瘤，癫痫复发时残余病变大小、形态和信号与3年前无明显变化。H-E切片显示，第1次手术时周边脑皮质发育不良，可能导致其癫痫复发。因此，术后定期影像学检查至关重要，可及时发现异常病灶，监测肿瘤复发。

正确认识DNT对于治疗和预后有重要意义，应避免激进的治疗给年轻患者造成进一步损伤。

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