

CASE REPORT

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A case of an unclassified tumor closely resembling dysembryoplastic neuroepithelial tumor with rapid growth

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Abstract We describe a rare case of a tumor resembling dysembryoplastic neuroepithelial tumor. A 3-year-old girl had a generalized convulsion as the initial symptom, without other neurological deficits. Computed tomography showed a hypodense lesion with calcific hyperdensity in the left frontal lobe associated with deformity of the overlying calvarium. Four months later, she had a second seizure, and computed tomographic scan showed that the lesion had increased in size. Subtotal removal of the tumor was performed, and the postoperative course was uneventful without radiation therapy. Histological examination revealed a cortical lesion in which an oligodendrocyte-like area and an astrocyte-like area with cytological atypia were observed. Although the clinical course and the radiological findings closely resembled those of dysembryoplastic neuroepithelial tumor, specific glioneuronal elements were not found histologically. Daumas-Duport reported a complex form of dysembryoplastic neuroepithelial tumor that contained glial nodules in addition to a specific glioneuronal element. The histological findings of the glial nodules in this case were quite similar to those she described. We conclude that this could be an unclassified tumor closely resembling dysembryoplastic neuroepithelial tumor without a specific glioneuronal element.

Key words Dysembryoplastic neuroepithelial tumor · Rapid growth · Cortical lesion · Epilepsy · Specific glioneuronal element

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Introduction

Dysembryoplastic neuroepithelial tumor (DNT) was first described in 1988 by Daumas-Duport et al.¹ According to the World Health Organization (WHO) Histologic Typing of Tumours of the Central Nervous System, DNT is a benign supratentorial mixed glial/neuronal neoplasm characterized by an intracortical location, a multinodular architecture, and a heterogeneous cellular composition.^{2,3} Patients with DNT usually have intractable seizures without other neurological findings.⁴

We report a patient with clinical and radiological features that strongly suggested a diagnosis of DNT, although the tumor was not confirmed to be DNT according to the recent WHO histological classification because of the lack of specific glioneuronal elements.

Clinical summary

The patient had a normal birth and development without any evidence of phakomatosis. At the age of 3.5 years, she had a generalized seizure. Neurological examination on admission showed no abnormalities. Computed tomography (CT) disclosed a fairly well-demarcated hypodense lesion in the left frontal lobe with calcific hyperdensity and deformity of the overlying calvarium (Fig. 1a,b). She was treated with anti-epileptic medications and underwent a thorough workup. Four months later, a second generalized convulsion occurred. On examination, she had no focal neurological deficits, but CT showed that the lesion had grown larger (Fig. 1c,d). MRI disclosed a well-demarcated hypointense area on T1-weighted images as well as a mixed (hyperintense and isointense) area on T2-weighted images (Fig. 2b,c). The cortical lesion resembled a megagyrus that was about 4cm in diameter and showed heterogeneous central enhancement by gadolinium-DTPA (Fig. 2a). CT and MRI did not show significant perilesional edema, and angiography revealed that the lesion was avascular and had

Fig. 1. **a,b** The initial plain CT shows a calcified lesion in the left frontal lobe. **c,d** The second plain CT demonstrates that the lesion has grown over a 4-month period

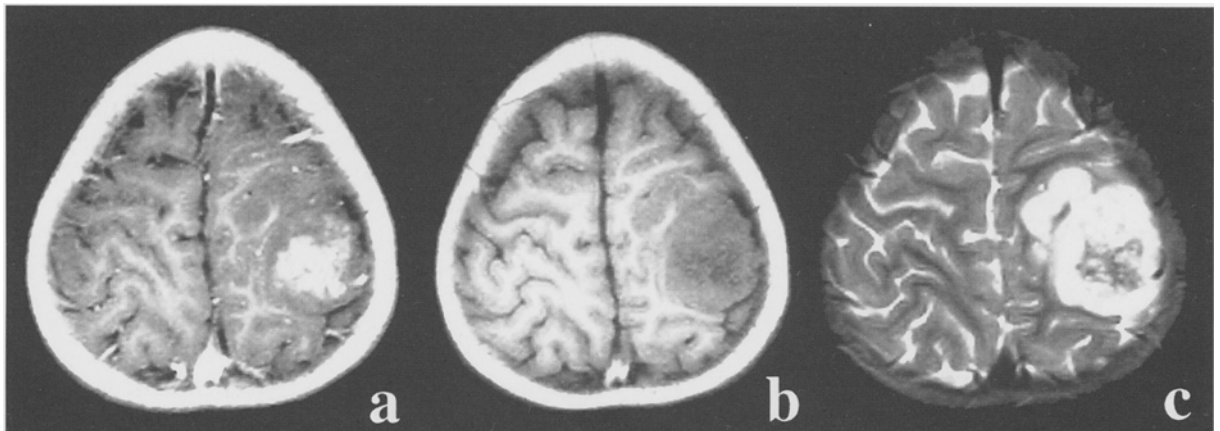
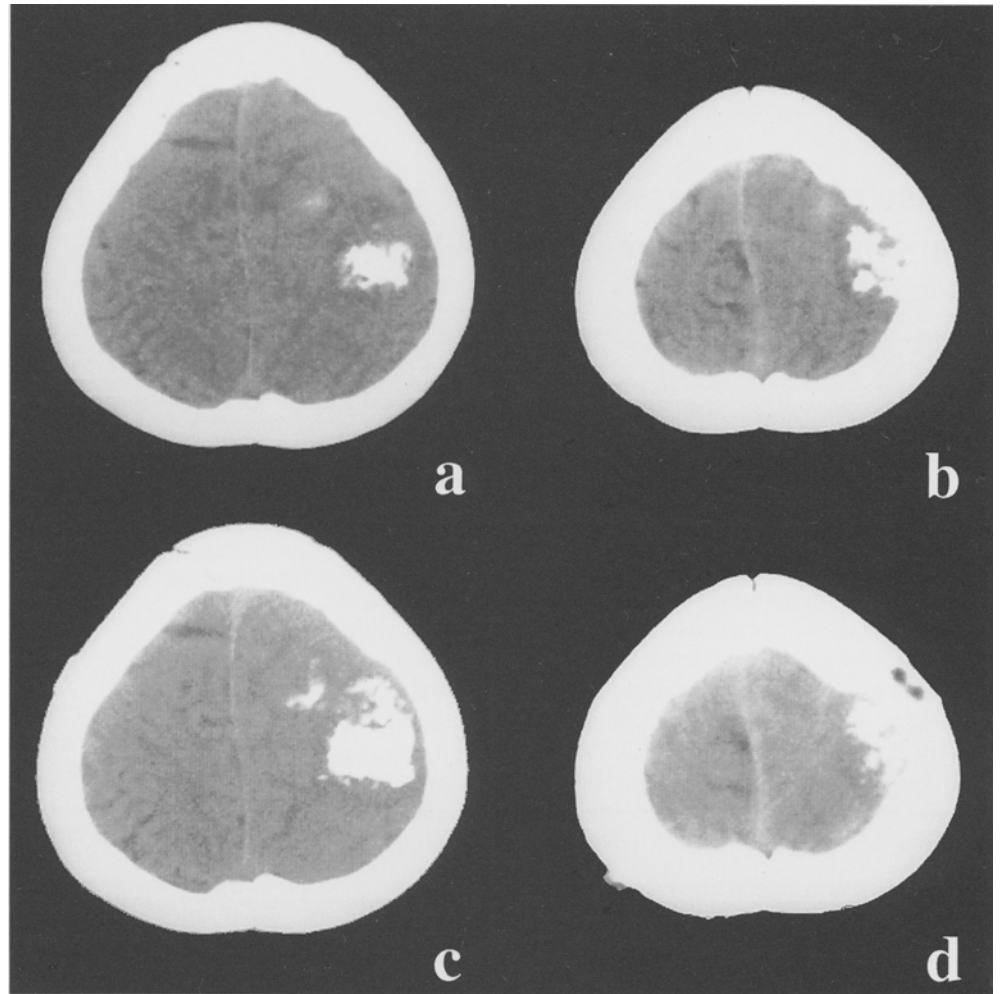


Fig. 2. Preoperative MRI. **a,d** Axial T1-weighted images obtained after Gd-DTPA administration show a heterogeneously enhanced lesion. **b,e** Axial T1-weighted image shows a hypointense lesion. **c,f**

Axial T2-weighted images show a mixed (hyperintense and isointense) intensity lesion

caused shifting of the normal structures. Craniotomy was performed to evaluate and treat the lesion. There was no involvement of the overlying skull or dura, and the exophytic lesion on the cortical surface resembled a soft megagyrus (Fig. 3), findings that did not suggest a common glioma. Macroscopic total removal of the abnormal gyrus was performed, but postoperative CT demonstrated residual tumor with calcification. After the operation, she had no neurological deficits and no epileptic fits. At 1.5 years after surgery, MRI did not show any regrowth of the lesion (Fig. 4a,b).

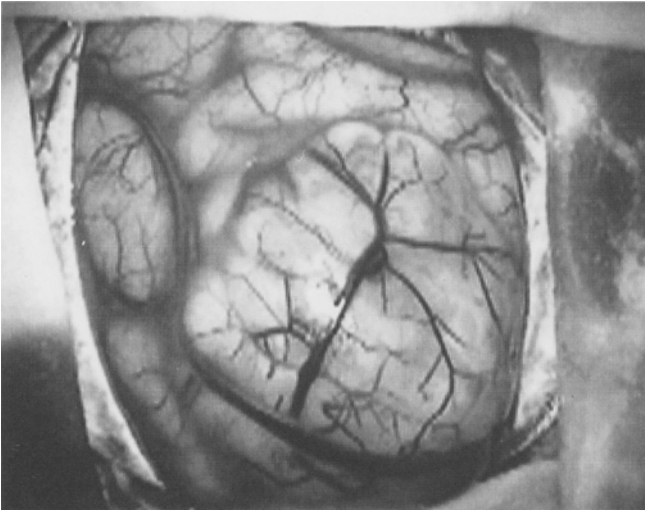


Fig. 3. At operation, an exophytic cortical lesion that resembled a megagyrus was detected

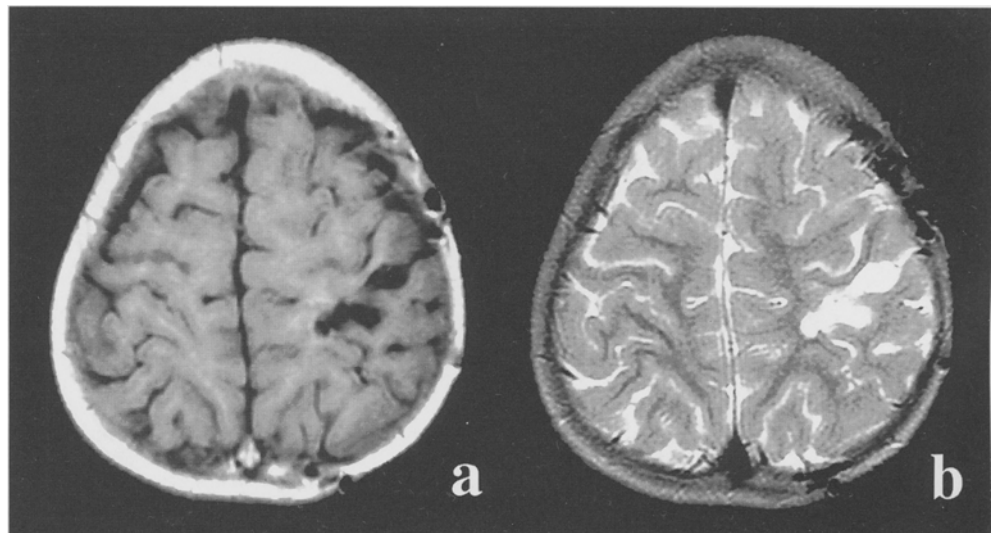
Pathological findings

The cortex contained a solitary nodule (Fig. 5a) with varied cellularity, including an astrocytoma-like area with small round nuclei, an oligodendrocytoma-like area (Fig. 5b), and undifferentiated cells. Multinucleated giant cells resembling fleurettes were often found (Fig. 5c). In some areas, the cells were arranged in parallel rows, forming a pattern similar to that of a polar spongioblastoma (Fig. 5d). Calcification (Fig. 5d,e), and necrotic foci were occasionally encountered. Small tumor cells with irregular nuclei were also seen in the mucoid background material along with microcysts (Fig. 5f). However, differentiated neurons or typical specific glioneuronal elements were not observed, and there was no cortical dysplasia. Immunohistologically, the tumor cells were negative for glial fibrillary acidic protein, vimentin, epithelial membrane antigen, and cytokeratin. Synaptophysin was faintly positive in the fibrillar matrix, but the cytoplasm of the tumor cells was not stained. In some area, numerous mitotic figures were observed (Fig. 5g), and the MIB-1 (Ki-67 nuclear antigen) staining index in these areas was greater than 10% (Fig. 5h). These findings suggested that the tumor was neuroectodermal in origin and showed minimal glioneuronal differentiation.

Discussion

In our present patient, the age, symptoms, neurological findings, and good response to surgical treatment suggested a diagnosis of DNT.^{1,5} The angiographic avascularity, CT density, MRI intensity, contrast enhancement on CT and MRI, and deformity of the overlying calvarium on CT were also consistent with the radiological features of DNT.^{1,5} Moreover, histological examination of this tumor revealed an intracortical lesion showing cellular heterogeneity with

Fig. 4. MRI 1.5 years after operation: **a,b** Axial T1-weighted images and **c,d** T2-weighted images show no evidence of tumor regrowth



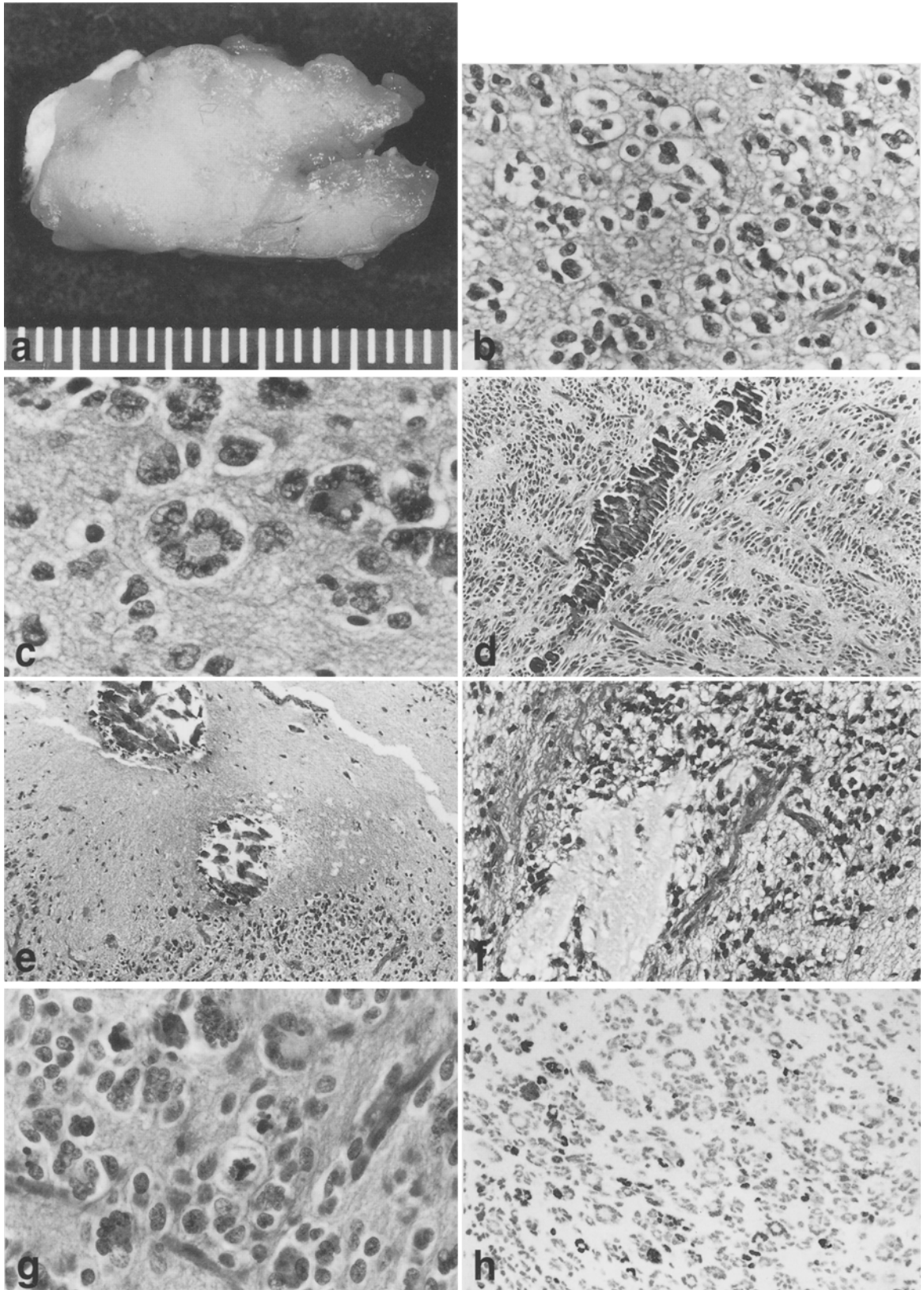


Fig. 5. Photomicrograph and photomicrographs of the surgical specimen. **a** Macroscopic appearance of the resected tumor. Nodular architecture was seen in the cortex and white matter. **b** The oligodendrocytic components have a typical fried-egg appearance. ($\times 400$) **c** Multinucleated giant cells with eccentric nuclei resemble fleurettes. ($\times 400$) **d** In some regions, the cells form a polar spon-

gioblastic pattern with calcification. ($\times 100$) **e** Calcification was often found. ($\times 100$) **f** Small tumor cells with irregular nuclei were seen in the mucoid substance along with microcysts. ($\times 200$) **g** Mitoses were very common in some areas. ($\times 400$) **h** MIB-1 immunostaining shows a high labeling index. ($\times 200$)

minimal glioneuronal differentiation. These clinicopathological features all suggested the possibility that the lesion might be a DNT, although the typical specific glioneuronal element (SGE) was not found.^{1,5} Daumas-Duport reported that there are variants of DNT without the usual specific histological features,⁵ and there has been a case report of DNT without any SGE.⁶ However, such opinions have not been well supported, because SGE is still generally considered essential to define DNT.

In DNT, mitoses are rarely encountered, and necrosis is absent or very rare,^{1,3,5,7-12} so the lesions remain stable in size.^{1,5,7,8-10} Immunostaining for MIB-1, a marker of cellular proliferation, was performed in 18 cases of DNT by Daumas-Duport⁵ and in 11 cases by Prayson.³ Among them, only two tumors exhibited a high labeling index,⁵ but both lesions remained perfectly stable. It was interesting that our patient's tumor increased in size after only 4 months and that it contained foci with a high MIB-1 labeling index. There have been some other cases where DNT has shown growth, including two patients reported by Ostern,⁴ four patients reported by Prayson,³ one patient reported by Yamaguchi,¹¹ and one patient reported by Hanavar.¹² However, all of these tumors grew slowly over at least 14 months. If our tumor fits into the category of DNT as reported by Ostern, Prayson, Yamaguchi, and Hanavar, its growth was the most rapid that has been detected. Despite its previous rapid growth, however, the tumor remained stable after surgery, so its clinical course was quite different from that of glioma. Recently, Hanavar and co-workers reported that the morphological spectrum of DNT is broader than has been previously recognized. Their histological examination of DNT showed a range of features shared by three subtypes, known as the multinodular, solitary, and diffuse types.¹² If our tumor fits any of these categories of DNT, it might be the solitary nodular type. All the solitary nodular tumors reported by Hanavar and co-workers were large nodules with a complex form, like classical DNTs.¹² Their solitary nodular lesions also showed necrosis and a high mitotic index when compared with multinodular and diffuse tumors. Although our tumor partially resembled their solitary nodular lesion, Hanavar and co-workers emphasized that the essential diagnostic point was the existence of a mixed cellular component, including oligodendroglia-like cells, astrocytes, and mature neurons.¹² Therefore, our tumor did not fit their definition of solitary DNT, because it lacked any mature neurons.

In accordance with the accepted strategy for treating DNT,⁵ we have not performed reoperation or radiosurgery for the residual tumor, and there has been no regrowth after 1.5 years. However, careful follow-up will be necessary. In conclusion, this patient's tumor closely resembled a DNT without SGE, although it did not fit exactly into any category of the recent WHO histological classification.

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References

1. Daumaous-Duport C, Scheithauer BW, Chodkieweis JP, et al (1988) Dysembryoplastic neuroepithelial tumor: a surgically curable tumor of young patients with intractable partial seizures. *Neurosurgery* 23:545-556
2. Kleihues P, Burger PC, Scheithauer BW (1993) *Histological typing of tumours of the central nervous system*, 2nd edn. Springer, New York, p 23
3. Prayson RA, Morris HH, Estes ML (1996) Dysembryoplastic neuroepithelial tumor: a clinicopathologic and immunohistochemical study of 11 tumors including MIB 1 immunoreactivity. *Clin Neuropathol* 15:47-53
4. Ostertun B, Wolf HK, Campos MG, et al (1996) Dysembryoplastic neuroepithelial tumor: MR and CT evaluation. *Am J Neuroradiol* 17:419-430
5. Daumaous-Duport C (1993) Dysembryoplastic neuroepithelial tumours. *Brain Pathol* 3:283-295
6. Iwanaga K, Takahashi H, Kameyama S, et al (1995) Dysembryoplastic neuroepithelial tumor: report of a case without typical glioneuronal elements. *Acta Neuropathol* 89:284-289
7. Adachi H, Shinohara C, Ono Y, et al (1995) Dysembryoplastic neuroepithelial tumor: a case report. *JOSPA* 32:41-46 (in Japanese)
8. Chang BC, Chen CY, Wei YH, et al (1996) Mesial temporal dysembryoplastic neuroepithelial tumor mimicking oligodendroglioma. *Chang Gung Med J* 19:382-387
9. Kimura S, Kobayashi T, Hara M (1996) A case of dysembryoplastic neuroepithelial tumor of the parietal lobe with characteristic magnetic resonance imaging. *Acta Paediatr Japon* 38:168-171
10. Kuroiwa T, Bergey GK, Rothman MI, et al (1995) Radiologic appearance of the dysembryoplastic neuroepithelial tumor. *Radiology* 197:233-238
11. Yamaguchi N, Oonishi H, Tachibana O, et al (1998) An enlarging dysembryoplastic neuroepithelial tumor during a 6-year period. *No Shinkei Geka* 26:1097-1101 (in Japanese)
12. Hanavar M, Janota I, Polkey CE (1999) Histological heterogeneity of dysembryoplastic neuroepithelial tumour: identification and differential diagnosis in a series of 74 cases. *Histopathology* 34:342-356