CASE REPORT

Dysembryoplastic Neuroepithelial Tumor With Probable Sudden Unexplained Death In Epilepsy

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Abstract

A patient with a natural histoty of dysembryoblastic neuroepitelial tumor (DNT) with associated with probable sudden unexplained death (SUDEP) is described. This patient had long period of intractable partial complex seizures, neuropsychological abnormalities and normal neurological examination.

Key Words

DNTs , Neuropsychological Abnormalities, Refractory Epilepsy, SUDEP

Introduction

Dysembryoblastic Neuroepitelial Tumor (DNTs) are benign tumors, arising within the supratentorial cortex. About 100 cases have been reported in the literature since the first description in 1988 by Daumas-Duport (1). A patient with a natural histoty of (DNT) with long period of intractable partial complex seizures, neuropsychological abnormalities and normal neurological examination with parietal cortico-subcortical mass on MRI associated with probable sudden unexplained death (SUDEP) is described for the first time, in this report. By our knowledge this is the first case with probable sudden death in symptomatic epilepsy due to dysembryoplastic neuroepithelial tumors with natural history.

Case Report

A 24- year-old woman was admitted because of long-standing refractory seizures. The seizures started at the age of 11 (1992) and was characterized as frequent complex partial seizure with rare generalized tonic-clonic seizure. Examination revealed no positive finding other than neuropsichological abnormalities.In the patient's background can be mentioned a normal birth, without any incidents and a normal psychomotor development till the age of three, when the mother notices a radical change of behaviour. The sociable, communicative child becomes all of a sudden an introvert, shy girl. Patient's school performance is excellent in the first two grades, later on becoming an average pupil. The moment of the mental decline, which has led to a complete psychological examination, appeared a few month after some atone complex scizure onset. A certain dependence towards the mother and sister appears.At the same age, of 11, the first imagistic investigation was performed. The CT scan shows a left temporo-parietal diffuse hypodense area, quite unhomogenous which doesn't interfere with the position and the shape of the ventricular system (*Fig 1, A*). This is the first time an anticonvulsive treatment was administered, mainly carbamazepin and phenytoin, which can control the seizures to a certain extent. The patient was imagistically reevaluated with MRI a year later when the "brain tumor" diagnosis was given. The patient has taken anticonvulsive medication which didn't manage the seizure.

Over the years, the pattern of the seizures has changed as well, becoming partial, motor, complex, sometimes with second generalisation, worse perimenstrualy in intensity and frequency. The surgery has been refused all the time by the patient's mother. 13 years after desease onset the neurologic examination was normal .The EEG presented an electrical crisis during recording. The biological tests appear to be normal. CT scan with and without intravenous administration of contrast revealed a 4/3 cm unhomogenous hyperdense area with a possible sept in its structure, located in the TP left area. The size mass appears unchanged.

The patient underwent MR imaging with and without intravenous administration of gadolinium that demonstrated a 32,3/43,12mm parietal cortico-subcortical mass. The lesion is divided by septations and looks multicystic and did not display enhancement after contrast material injection (*Fig.1,B,C,D*). As the patiant refuses to have a cerebral biopsy, we decide to perform a complementary imagistic exploration, which could offer us details about the metabolic activity of the tumor. Tc99m-MIBI has been used as potential agent for the

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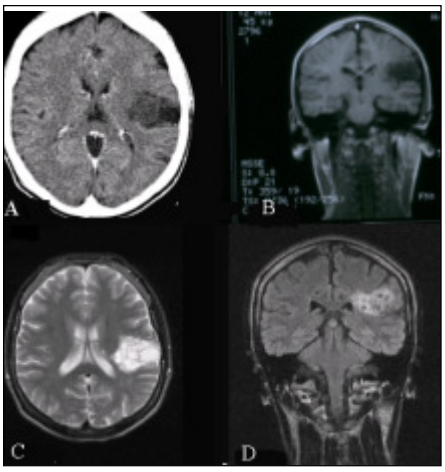

Fig 1. Panel A : First CT Scan ; Panels B,C,D: MRI After 13 Years

imaging of occult brain tumor and for distinguishing between viable brain tumor and necrotic tissue. The tomoscintigraphy (SPECT) was performed 15-25 min after intravenous injection of 1110 Mbq (99m)Tc-MIBI. No MIBI uptake was found. The long hystory, the clinical and unchanged imagistic data, lead us to the, Dysembryoplastic neuroepithelial tumor ".

We dynamically analyze patient cognitive status, which was first tested at the age of 11, when the disease appeared and a second time at the age of 24, when the diagnosis of DNT was given. The cognitive efficiency has been evaluated with the same tests at both examinations: Bourdon-Antimov test, Rey sample, Wecslar test and Raven sample. The mnesic activity, the cognitive efficiency general index, vocabulary, operational efficiency of thinking are decreased by 35% (mean range). For the prosexic activity for focus(exactness), the attention mobility (exactness) and operational efficiency of thinking (quickness) the results are unchanged. Despite the satisfactory control of seizures one year later the patient died during sleep.

Discussion

By our knowledge this is the first case with probable sudden death in symptomatic epilepsy due to DNT. DNTs is a newly described, pathologically benign tumor, arising within the supratentorial cortex. About 100 cases have been reported in the literature since the first description in 1988 (1). This concept has been developed much so far, due to the imagistic support. The majority of cases are found in the temporal lobe where can coexisted with mesial temporal sclerosis , followed by the frontal, parietal and rarely the occipital lobe (2). From the epidemiologic point of view, the incidence is between 6 and 35 years old, with an average of 21.5 years and an equal repartition female/male. Histologic study shows that DNT has multinodular architecture, mainly in the cortex, and is composed of oligodendrocytes, astrocytes, neurons, and the gliconeural elements. This cortical structural abnormality that disrupts normal neuronal circuitry becomes an epileptogenic focus. Neuronal cells in the lesion may also secrete neurotransmitters or express receptors (3). Neuronal markers (synaptophysin, neuronal specific enolase) and glial markers (GFAP, S-100) are positive. Despite benign behavior, it may have high MIB-1 labeling index. Aberrant expression of apoptosis-associated proteins (bcl-2,bcl-x,bax) similar to what has been previously described in gangliogliomas (another epilepsy-related, dysplasia-associated tumor), may play a role in the pathogenesis of DNTs (4). Today, DNT refers to polimorphyc tumors that appear during embriogenesis. In the revised WHO classification, DNTs have been incorporated among the category of neuronal and mixed neuronoglial tumours (5). Noncontrast-enhanced CT scans show well-demarcated lesions that are hypodense to surrounding brain, even with intratumoral calcification and multicystic appearance.

Routine MR imaging sequences reveal lesion to be well demarcated, hypointense on T1- weighted images, and hyperintense on T2-weighted images. Edema and mass effect on midline structures are lacking, although they may be observed in case of hemorrhagic complications (6). The lobular aspect with presence of septations can occur sometimes (as in our case). Single-photon emission CT has been used in limited fashion with DNTs, and this shows hypoperfusion or poor isotope uptake. MR spectroscopy allows the determination of certain biochemical properties of the brain in vivo and reflects the biologic characteristics of benign tumor (7). The combination of preoperative positron emission tomographic metabolic studies with functional brain mapping allowed for prediction of tumor type, defined eloquent areas of cortical function, and improved approach and resection of the tumors with minimal risk of neurological impairment (8).Differential diagnosis includes oligodendrogliomas, mixed gliomas and gangliogliomas. Treatment options and prognosis differ significantly between these lesion (6). It is important that DNT and glioma are correctly distinguished at diagnosis, because patients with DNT need not be subjected to potentially harmful adjuvant therapies such as radiation or chemotherapy. Treatment for DNT is surgical resection, however , there is no cohort of untreated patients to serve as controls. DNT relationship to the epileptogenic foci can be determined by extensive interictal and ictal EEG recordings. Noninvasive recording and careful mapping show that a structural lesion is not the source of epileptic activity. There is a little correlation between the lesion site and epileptogenic foci of the ictal onset zone as well as the irritative zone(the widespread

epileptogenicity beyond visible tumor) (9). Seizure control after surgery is good: 80-90% seizure free (10). Although the majority of children remain seizure free after surgical excision of DNTs, a considerable number have recurrent seizures. Short-term outcome is influenced by older age at surgery and longer duration of epilepsy. Residual tumor is a significant risk factor for poor seizure outcome (11). DNTs have a benign course. Rushing reports a case of DNT with malignant transformation but after radiation and chemotherapy (12). Our patient was found by her mother in a prone position at the time of death. The patient fulfills criteria used in most SUDEP studies: recurrent unprovoked seizures, died unexpectedly and suddenly while in a reasonable state of health, during normal and benign circumstances, and the death was not the direct result of a seizure or status epilepticus. The probable SUDEP is given because of lack of autopsy. In 60% of the cases, the event was related to sleep, which might indicate involvement of a sleep-related event. Seizures are known to cause central apnea by direct propagation of the electrical discharge to the respiratory center. Cardiac arrest can cause secondary cardiopulmonary stop (13). Cardiac arrhythmia during the interictal state is another potentially fatal condition. Asphyxiation secondary to an obstructive cause has been postulated to play a role in the deaths of patients who were found in a prone position at the time of death (14). Annual risk of SUDEP is estimated to be 1 per 100 for patients with symptomatic seizures and 1 per 1000 for patients with idiopathic seizures. Our patient presented several risk factors: generalized seizures, lower age of onset of seizures, duration of seizure disorder longer than 10 years, age 20-40 years, poorly controlled seizure disorder (15).DNTs are more frequant with children and young adults than it was believed till recently (16). Early and complete surgery, with functional studies before and during the surgery, leads to a control of seizure, avoiding evolutive accidents and neuropshichological changes as in this case. Moreover, the recently published National Institute for Clinical Excellence(NICE) guidelines states that individuals with epilepsy and their families should be given and have access to information on SUDEP' (17).

Conclusion

Sudden death in symptomatic epilepsy due to DNT is quite possible, thus SUDEP information should be given to such subjects and early and complete surgery, lead to a control of seizure, avoiding such accidents & neuropshichological changes.

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