

Gangliocytoma Associated with Focal Cortical Dysplasia in a Young-Adult: A Case Report

Erişkin bir Olguda Gangliositomla İlişkili Fokal Kortikal Displazi: Olgu Sunumu

ABSTRACT

Neoplasms and (non-neoplastic) focal dysplasias may coexist as a cause of seizures in both the developing and mature brain. Low grade neoplastic lesions (ganglioglioma/gangliocytoma) may present with seizures, and distinction of these lesions from focal cortical dysplasia is difficult on standard radiological imaging. We report a 24-year-old man who had complaints of tonic-clonic seizures for one week duration and was admitted to department of neurosurgery. He did not have any neurological deficit on his examination. Cranial computerized tomography and magnetic resonance imaging of the patient revealed a calcified, cystic lesion with contrast enhancement, in the left temporoparietal region. Subtotal resection of the mass was performed. Pathological examination revealed focal cortical dysplasia associated with gangliocytoma.

KEY WORDS: Calcified tumor, Focal cortical dysplasia, Gangliocytoma, Ganglioglioma

ÖZ

Gelişmekte olan ve matür beyinde, nöbetlerin bir nedeni olarak neoplazmlar ve fokal displaziler (neoplastik olmayan) birlikte bulunabilir. Düşük gradeli neoplastik lezyonlar (ganglioglioma/gangliositoma) nöbetlerle görülebilir ve standart radyolojik görüntülemelerde bu lezyonların fokal kortikal displaziden ayrımı zordur. Biz burada, bir haftadır olan tonik-klonik nöbet şikayeti nedeniyle kliniğimize başvuran 24 yaşında bir erkek olguyu sunduk. Hastanın değerlendirilmesinde herhangi bir nörolojik defisit bulunmadı. Kranyal bilgisayarlı tomografi ve manyetik rezonans görüntülemelerde sol temporoparietal bölgede kalsifiye, kontrast tutan kistik bir kitle görüldü. Kitle subtotal çıkarıldı. Patolojik inceleme sonucu; fokal kortikal displazi ile ilişkili gangliositom olarak bildirildi.

ANAHTAR SÖZCÜKLER: Kalsifiye tümör, Fokal kortikal displazi, Gangliositom, Gangliogliom

Kudret TÜREYEN¹
Nilgün ŞENOL²
Aydın SAV³

¹ Medical Park Hospital, Neurosurgery, Bursa, Turkey

² Isparta Government Hospital, Neurosurgery, Isparta, Turkey

³ Marmara University School of Medicine, Pathology, Istanbul, Turkey

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Correspondence address:

Kudret TÜREYEN

E-mail: tureyen@usa.net

INTRODUCTION

Gangliocytomas are rare central nervous system (CNS) tumors with a reported frequency of 1.3% (5). This benign neuronal neoplasm occurs most frequently in children and adults under 30 years of age (18). It belongs to the subgroup of the neuroepithelial tumors classed as the "neuronal and mixed neuronal-glial" tumors (15). The majority of patients present with seizures. The vast majority of tumors occur in the temporal lobe (71.3%) (5). They represent one type of ganglion cell tumors and are composed of mature ganglion cells. Gangliogliomas and gangliocytomas occur in cortical and subcortical locations (1,16).

Focal cortical dysplasias (FCD) are defined as circumscribed malformations of cortical development. They occur as a result of impaired neuronal proliferation, migration and differentiation (3). FCD are increasingly diagnosed as a cause of symptomatic focal seizure. Seizures due to FCD are frequently pharmacoresistant.

On magnetic resonance imaging (MRI), it is not possible to easily differentiate FCD from the normal cortex (7). MRI is efficient in identifying developmental, epilepsy-associated tumors such as gangliogliomas, simple and nonspecific forms of dysembryoplastic neuroepithelial tumor, and the rare pleomorphic xanthoastrocytoma. It may be sometimes difficult to differentiate ganglionic tumors from cortical dysplasia. We present a rare case of a gangliocytoma with focal cortical dysplasia.

CASE REPORT

A 24-year-old male presented with one week history of tonic-clonic seizures. No abnormality was found on general examination. The cranial nerves were intact. There were no visual symptoms or speech problems. He was right handed with no neurological abnormalities in the upper or lower limbs.

Cranial computerized tomography (CT) revealed a calcified mass with low attenuation in the left temporoparietal region (Figure 1). MRI showed a left temporal lesion with cystic component and calcification with contrast enhancement (Figure 2). Functional MRI showed close relationship of tumor with the speech center. The speech center was left dominant and was behind and above the lesion in the temporal lobe. A subtotal tumor excision was therefore performed via temporoparietal craniotomy. During the procedure, a grayish region with increased vascularity was seen on the cortical

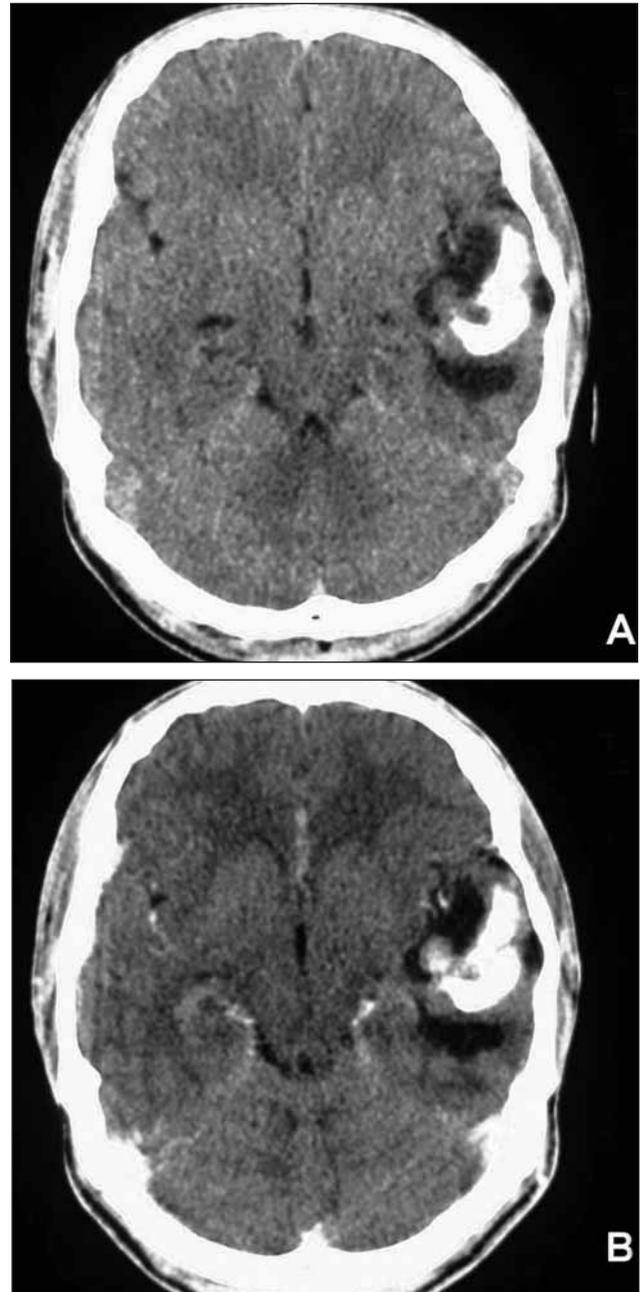


Figure 1: Axial CT shows a calcified, cystic mass in the left temporoparietal region (A). Post-contrast CT shows the non-uniform contrast enhancement (B).

surface. There was a cystic mass about 1 cm beneath the surface, from which yellow homogeneous fluid was aspirated. Subtotal resection was performed because of the close relationship with the speech center. Intraoperative histopathological results were benign. Anti-epileptic medication (phenytoin 300mg/day) was prescribed to the patient after the operation. The histopathological diagnosis was low grade gangliocytoma (Grade I, World Health

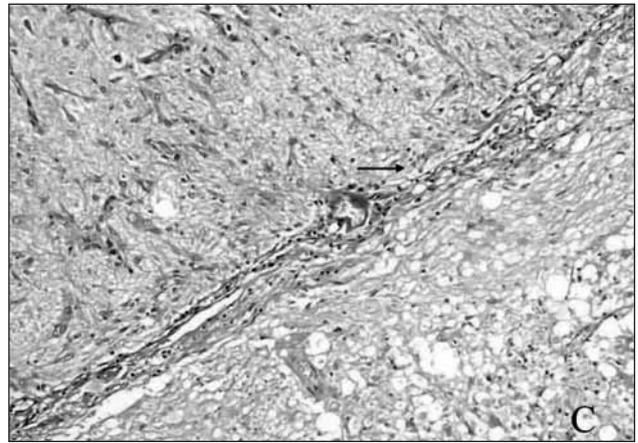
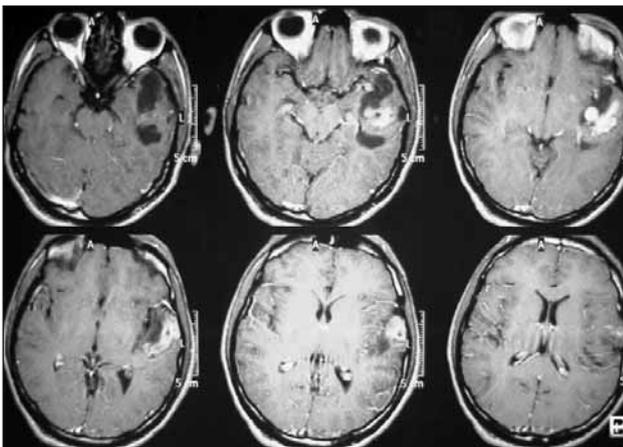
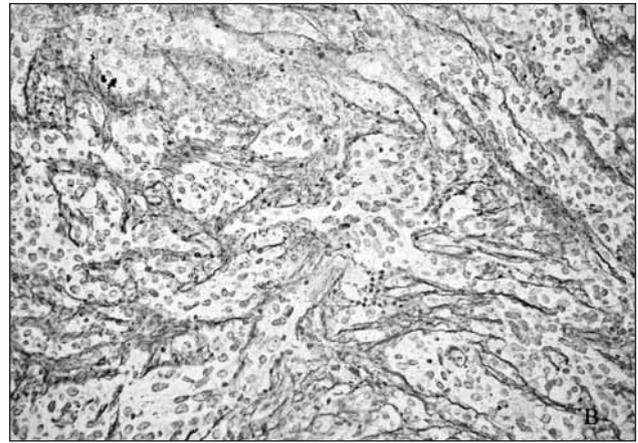
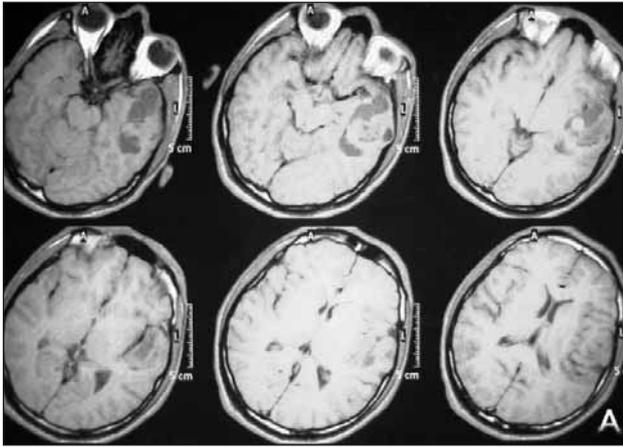


Figure 2: Pre (A) and post-gadolinium (B) T1-weighted images show a left temporal lesion with a cystic component and contrast enhancement.

Organization (WHO) 2000) with focal cortical dysplasia (Figure 3). The patient is doing very well without seizures, and there is no tumor growth 20 months after the operation.

DISCUSSION

Gangliocytoma is an extremely rare, benign intraparenchymal neuronal tumor comprised

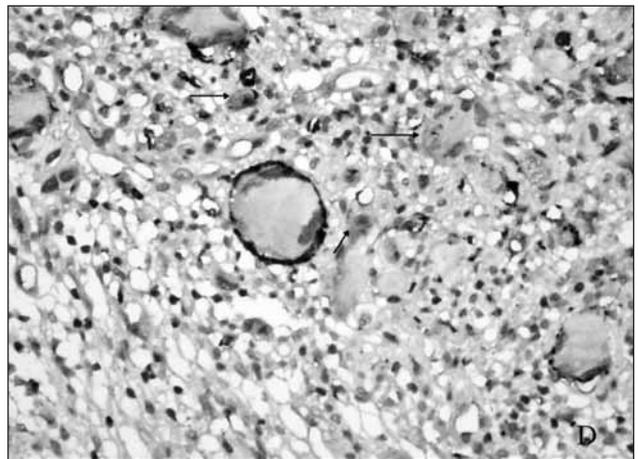
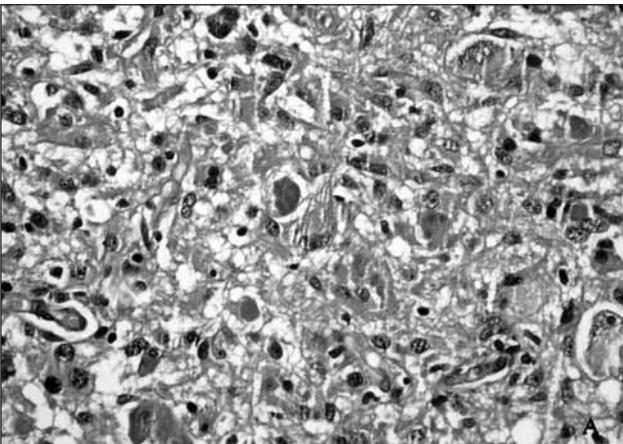


Figure 3: A: Bizarre binucleate ganglion cells and several eosinophilic granular bodies among them (HE, x100)
 B: Reticulin-rich framework of tumor (Gomori reticulin, X100)
 C: Dysplastic cortex next to tumor tissue (arrow) on surfaces of adjacent gyri (HE, x40)
 D: Bizarre ganglion cell with abundant cytoplasm surrounded by synaptophysin-reactive dot-like material (arrows) (anti-synaptophysin, Streptavidin-biotin, X400).

mainly of ganglion cells, and a relatively few number of stromal glial cells, that have little or no evidence of mitosis (11,13,18). It belongs to a subgroup of neuroepithelial tumors classified as the "neuronal and mixed neuronal-glial" tumors. According to the WHO grading system, it is a grade I tumor (15). In 1993, the WHO affirmed a new classification of neoplasms affecting the central nervous system. The classification of brain tumors is based on the premise that each type of tumor results from the abnormal growth of a specific cell type. Neuronal and mixed neuronal-glial tumors are classified as gangliocytoma, dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos), ganglioglioma, anaplastic (malignant) ganglioglioma, desmoplastic infantile ganglioglioma, central neurocytoma, dysembryoplastic neuroepithelial tumor and olfactory neuroblastoma (esthesioneuroblastoma) (12). Malignant variants of ganglioglioma have been reported at a rate of 4 to 32%. Malignant changes appear to be confined to the glial component, but a single case of anaplastic transformation affecting both neuronal and glial cells has been reported. The mechanisms are not clear but radiotherapy results in an increased risk of malignant progression in gangliogliomas/ gangliocytomas by DNA damage (10).

Gangliocytoma occurs most frequently in children and young adults usually under the age of 30 years (13,15,18). Seizures are the most common symptoms (18). Other rare manifestations are increased intracranial pressure due to third ventricle location or mass effect, endocrine disorders (in tumors located in sellar region), and focal symptoms (15). The most frequent site is the temporal lobe, but they can arise anywhere in the CNS including the cerebellum, brainstem, floor of the third ventricle and spinal cord (15,18).

Various CT and MRI appearances of gangliocytoma have been described in the literature. The CT findings range from hypodense to hyperdense, cystic to solid, enhancing or non-enhancing lesions with or without edema or mass effect. Calcifications have been reported on CTs in up to 35% of cases (18).

The differential diagnosis of gangliocytoma includes oligodendroglioma, ependymoma, astrocytoma and meningioma. The honeycomb-like clear cell architecture is a histopathological hallmark

of oligodendrogliomas. However, clear cell elements can also be encountered in gangliocytomas. In addition, both tumor entities can be associated with chronic epilepsies. Since oligodendrogliomas harbor the risk of tumor recurrence and malignant progression, they must be carefully distinguished from gangliocytomas. The recently reported pattern of MAP2 immunoreactivity in oligodendrogliomas can be helpful in this respect. Similar to diffuse astrocytomas, proliferation activity is significantly higher compared to gangliocytomas (5).

Gangliocytomas with a diffuse pattern and predominant glial differentiation may be difficult to differentiate from diffuse astrocytomas. Labeling of MAP2-positive neoplastic glial cells and lack of CD34 staining corroborate this diagnosis. Proliferation activity in diffuse astrocytomas is approximately 5% and significantly higher than in gangliogliomas (5).

CT demonstrated a hypodense enhancing lesion associated with calcifications causing a mass effect that was surrounded by edema in our patient. MRI revealed a well-defined lesion that had a low signal on T1W and a high signal on T2W sequences. The tumor showed homogeneous enhancement in the solid parts. These MRI findings are consistent with the recently published studies (18).

Cortical dysplasia is the second most common cause of seizures that show resistance to medical therapy (6). In normal neurogenesis, the vast majority of neurons and glia are generated in the germinal zone (matrix) that is located at the ventricular surfaces. This is the area where the majority of cells proliferate. As the cells mature, they migrate from the germinal zone to their final destination. Most neurons of the cerebral cortex migrate to their destinations along specialized radial glial fibers that span the entire thickness of the hemispheres from ventricular surface to piamater. This radial glia is then transformed to astrocytes (2). A standard classification of malformations of abnormal cortical development divides lesions into those due to neuronal and glial proliferation versus those due to cellular migration. Proliferation and migration do occur synchronously, therefore some of these abnormalities have overlapping features (13). In developmental cortical malformations, FCD takes place both in the non-neoplastic group and the neoplastic group (especially gangliocytomas) (14).

Payson & Estes reported a histopathological study of 52 cases with cortical dysplasia who underwent partial lobectomy with epilepsy. Coexistent tumors including ganglioglioma (8 patients), dysembryoplastic neuroepithelial tumor (3 patients), and low-grade astrocytoma (2 patients) were present in 13 patients (17).

Hamiwka et al reported ten-year follow-up of surgery for epilepsy due to cortical malformations. Pathological diagnosis of the frontal lobe resections included cortical dysplasia in 14 cases and developmental tumors in four (one ganglioglioma and three gangliocytoma). The temporal lobe cohort had 11 cases of cortical dysplasia and two cases of developmental tumor (gangliocytoma). Two parietal cases (one cortical dysplasia, one gangliocytoma) were found. Outcome analysis for seizure freedom with regard to location of the resection showed that cortical dysplasia cases and developmental tumor cases showed no difference when compared independently for temporal versus extratemporal location (9).

Fauser et al showed that patients with dual pathology almost always had temporal lobe epilepsy and dual pathology did not imply a worse outcome with regard to postsurgical seizure-freedom. The outcome is affected not only by the high coincidence of histological abnormalities but also by the histological subtypes (8).

Blumcke et al noted CD34 (a stem cell marker) immunoreactivity in the majority of gangliocytomas and FCD. This study not only established a definitive role of CD34 as a diagnostic marker in glioneuronal lesions associated with epilepsy, especially in dual lesions, but also indicated a possible pathogenetic relationship between FCD and gangliocytoma (4).

CONCLUSION

Ganglion cell tumors, and less frequently some benign glial tumors in the CNS can be associated with a variety of mild developmental abnormalities of the cerebral cortex. Surgery alone results in a long progression-free survival in these dual lesions.

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