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Case Report

A Case of Primary Diffuse Leptomeningeal Gliomatosis Predominantly Involving the Cervical Spinal Cord and Mimicking Chronic Meningitis

Kronik Menenjiti Taklit Eden Üst Servikal Primer Diffüz Leptomeningial Gliomatozis

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ABSTRACT

Gliomas may rarely arise in the leptomeninges without any evidence of intraaxial involvement. A case of primary diffuse leptomeningeal gliomatosis (PDLG) histologically diagnosed as oligoastrocytoma is presented. A 50-year-old woman presented with nausea, vomiting and headache. Magnetic resonance imaging (MRI) of cranium and cervical region revealed dural thickening starting from the craniocervical junction to the level of C4 without any parenchymal lesions. CSF examination showed an increase in protein and decrease in glucose levels. There were neither any kind of atypical cells nor any kind of growth in bacterial cultures. The patient underwent biopsy at the level of C1 for diagnosis. The specimen was diagnosed as primary diffuse leptomeningeal gliomatosis, with phenotypic features of astrocytoma and oligodendroglioma.

KEYWORDS: Glial tumor, Meningitis, Primary diffuse leptomeningeal gliomatosis

ÖZ

Gliomaların her hangi parenkimal bir yerleşim göstermeksizin primer olarak leptomeningeal tutulum ile ortaya çıkmaları son derece nadirdir. Histolojik olarak oligoastrositom tanısı konulan bir primer diffüz leptomeningeal gliomatozis olgusu sunulmaktadır. Elli yaşındaki bayan hasta bulantı, kusma ve baş ağrısı şikayetleri ile başvurmuştur. Kranial ve servikal manyetik rezonans (MR) görüntüleme incelemeleri kranioservikal bileşkeden başlayarak C4 seviyesine kadar her hangi bir parenkim tutulumu olmaksızın dura kalınlaşması ile uyumlu görünüm ortaya koymuştur. Beyin omurilik sıvısı (BOS) incelemelerinde her hangi bir atipik hücre saptanmamış olmakla birlikte protein seviyesinde artış, glukoz seviyesinde ise azalma saptanmıştır. Hastaya C1 seviyesinden tanısal amaçlı biyopsi yapılmıştır. Biyopsi materyaline fenotipik olarak astrositom ve oligodendrogliom özellikleri de içeren primer diffüz leptomeningeal gliomatozis tanısı konulmuştur.

ANAHTAR SÖZCÜKLER: Glial tümör, Menenjit, Primer diffüz leptomeningeal gliomatozis

INTRODUCTION

Gliomas may arise primarily in the leptomeninges without any evidence of intraaxial involvement (1, 12, 14). This extremely rare and rapidly progressive condition, which is called primary diffuse leptomeningeal gliomatosis, is thought to originate from heterotrophic neuroglial nests in the subarachnoid spaces (3, 13). Clinical presentation has a broad spectrum of signs and symptoms mostly due to increased intracranial pressure. Symptoms and signs of the disease on admission may be similar to that of chronic infectious meningitis (7, 14,18).

We report a case of a primary diffuse leptomeningeal oligoastrocytoma predominantly involving the cervical spinal cord and initially suggesting tuberculosis meningitis.

CASE REPORT

A 50-year-old, previously healthy female patient had complaints of nausea, vomiting and headache of approximately one month. Physical examination revealed bilateral papilledema with bilateral abducens nerve paralysis. Cranial magnetic resonance imaging (MRI) revealed no other abnormality including hydrocephalus except cystic masses 20x15x13 mm in diameter located bilaterally in the cerebellopontine angles (Figure 1A,B). These cystic masses were isointense with cerebrospinal fluid (CSF) on T1-weighted images and hyperintense on T2-weighted images. The presence of an epidermoid cyst was ruled out as the lesions were hypointense on diffusion MRI. Lumbar puncture was performed, and CSF opening pressure was 600 mm$H_2$0 (Normal <180-200 mmH_2O). Biochemical analysis of the CSF

revealed an increase in protein (189 mg/dl; normal:15-45mg/dl) level. Glucose level was slightly under the normal range (35mg/dl; normal: 40-80mg/dl). CSF/plasma glucose ratio was 25% (Normal: 50%). The cytological evaluation results of the CSF sample were normal. No growth was detected in any of the bacterial cultures.

The patient was started on oral methylprednisolone (80 mg TID) to lower the CSF-pressure. A ventriculoperitoneal (VP) shunt was inserted due to hydrocephalus three days after the initiation of the treatment (Figure 1C,D). The patient's symptoms were relieved and she was discharged in good condition. The bilateral abducens paralysis improved two weeks after discharge. The first diagnosis was communicant hydrocephalus due to tuberculosis meningitis. Subsequently, anti-tuberculosis medication was started.

Three months after discharge, the patient was re-admitted to our clinic with nausea, vomiting and headache. Physical examination was unremarkable. Cranial CT scan revealed slit ventricles, consistent with over-drainage of the ventricles (Figure 1E). The VP shunt was revised. The patient's symptoms relieved. On post-operative day 3, the patient was discharged without any neurological deficits.

Three months after the shunt revision, the patient experienced nausea and vomiting again as well as neck pain and paresis in her right arm. Physical examination revealed global muscle wasting and increased deep tendon reflexes on the right arm. A craniocervical junction MRI revealed dural thickening starting from the craniocervical junction to the level of C4, particularly at the level of the tentorium cerebelli (Figure 2A-E). This thickening was hypointense on T1-weigthed images and heterogeneously hyperintense on T2-weigted images. Axial MRI of the craniocervical location with gadolinium contrast agent showed diffuse leptomeningeal enhancement with a nodular lesion at the level of C1 (Figure 2D). There

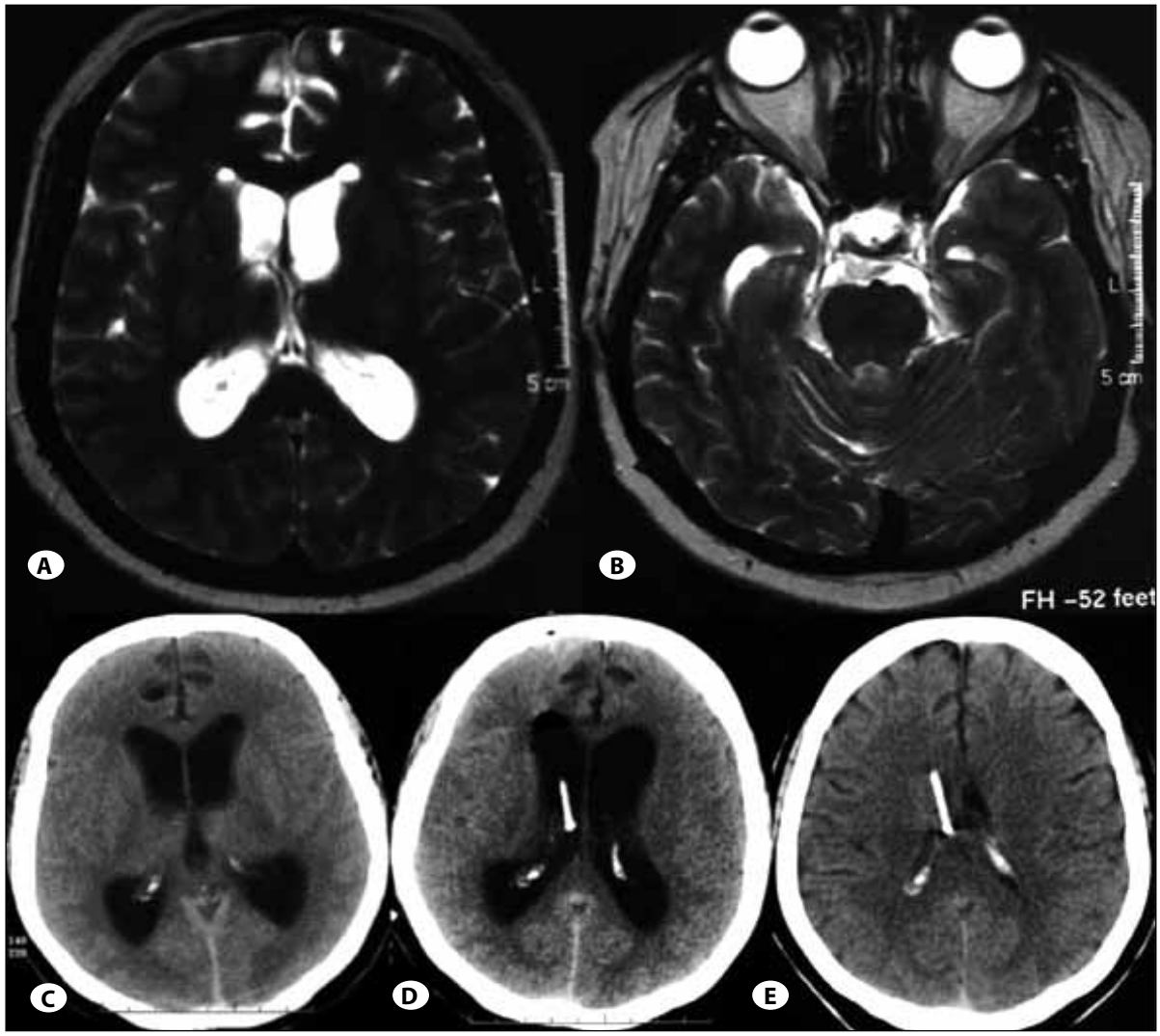

Figure 1: The T2-weighted MR image excluded hydrocephalus on the first admission **(A-B)**. During her hospitalization, the ventricules began to dilate **(C)** and eventually a VP shunt system was inserted **(D)**. The patient was admitted for her increased ICP symptoms several weeks after her first discharge **(E)**.

were no parenchymal lesions. A biopsy at the level of C1 was performed for the diagnosis.

Microscopic Examination

Histopathology of the lesion showed a neuroepithelial tumor infiltrating the leptomeninges with a pattern suggestive of astrocytoma. The neoplastic cells had ovoid nuclei, and the cytoplasm was eosinophilic with presence of fibrillary processes (Figure 3A). However, other parts of the tumor showed the typical appearance of oligodendroglioma with round uniform nuclei and clear cytoplasm. Microgemistocytes of the gliofibrillary oligodendrocytic type were observed. Moderate cellular atypia and mitotic activity were evident. There was no vascular endothelial proliferation and no necrosis. The following immunostains were conducted, using the streptavidin-biotin peroxidase complex (ABC) method in all: i) Glial Fibrillary Acidic Protein (GFAP) (clone GA-5, diluted 1:250; Neomarkers, CA), ii) S100 protein (clone 4C4.9, diluted 1:250; Neomarkers, CA), iii) Epithelial Membrane Antigen (EMA) (clone E29, diluted 1:20; Neomarkers, CA) and iv) Ki67 labeling index (clone MIB-1, ready to use ; Neomarkers, CA). A large percentage of tumor cells expressed glial fibrillary acidic protein (GFAP) (Figure 3B) and S100 (Figure 3C) in immunohistochemistry. The Ki67 labeling index was 10% at hot spots (Figure 3D).

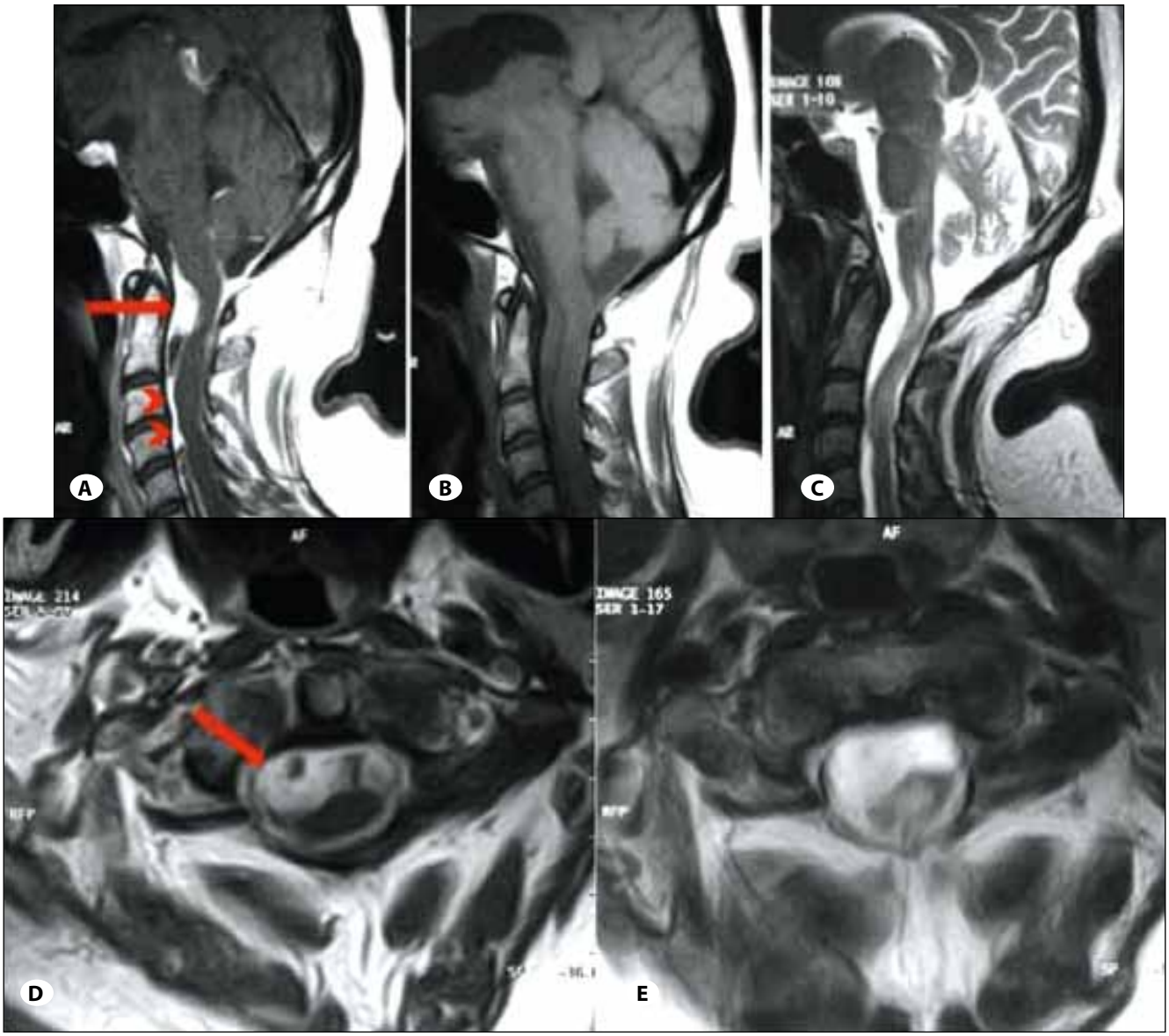

Figure 2: The MRI-scan of craniocervical junction with gadolinium contrast agent shows no sign of pathology consistent with presence of intracranial mass lesion **(2A)**. Note that the dural thickening exhibits intense contrast material enhancement (2a, arrows), shows hypointensity on T1-weigthed images **(B)** and is heterogeneously hyperintense on T2-weigted images **(C)**. The axial section of MRI-scan with gadolinium contrast agent showing C1 level reveals diffuse leptomeningeal enhancement with a nodular lesion **(D, arrow)**. T2-weighted axial section of MRI image shows hyperintensity anterior to the spinal cord **(E)**.

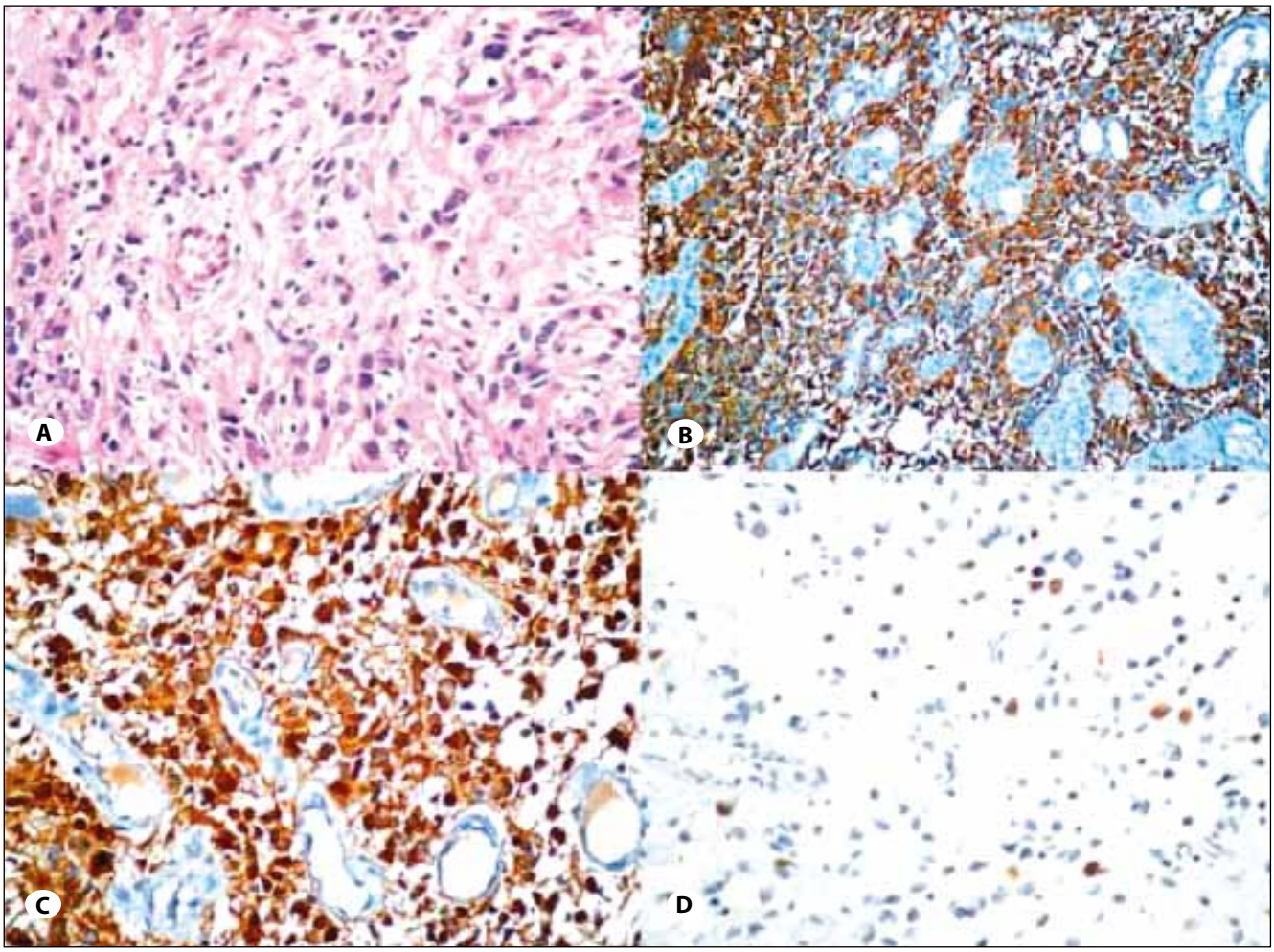

Figure 3: Astrocytes with severe atypical characteristics seen in high magnification (HE, x400) **(A)**. Tumor cells with diffuse cytoplasmic GFAP reactivity (Neomarkers, GFAP, Streptavidin-biyotin, x400) **(B)**. Tumor cells with diffuse cytoplasmic and nuclear S-100 reactivity. (Neomarkers, GFAP, Streptavidin-biyotin, x400) **(C)**. MIB-1 index measured as 10%. (Neomarkers, anti-Ki67, Streptavidin-biyotin, x400) **(D)**.

Based on the histopathology and immunohistochemical results, this case was diagnosed as primary diffuse leptomeningeal gliomatosis, with phenotypic features of astrocytoma and oligodendroglioma (WHO grade III). .

DISCUSSION

PDLG is thought to originate from leptomeningeal heterotopic neuroglial nests, which have separated during the embryogenesis of the central nervous system (3, 13). Heterotopic glial nests occur in the subarachnoid space in about 1% of randomized necropsies, with a higher incidence (25%) in patients with congenital malformations of the nervous system (1). These heterotopic neuroglial nests are mostly composed of astrocytic cells but may also include oligodendroglial component, and thus, primary diffuse leptomeningeal oligodendrogliomatosis cases have been reported (6, 14).

PDLG is a very rare and distinct central nervous system neoplasm occurring due to focal or diffuse infiltration of the leptomeninges without any intraparenchymal involvement by any kind of glioma or metastases (1, 3, 4, 7, 14, 15). PDLG usually appears as a contrast-enhancing lesion with thickening of the leptomeninges with imaging methods. (2, 4, 10-12, 14, 15, 17). Although non-enhancing or minimally enhancing leptomeningeal lesions in the cranium have been reported, they may be located in the spinal cord (1, 6, 7). The disease may occur at any age group. It may also occur in the pediatric population (4). The clinical manifestations of the disease are quite variable. The most common presenting symptom is headache followed by vomiting, seizures, and neck stiffness (1, 4, 5, 7). The signs are also quite different including cranial nerve palsies, papilledema, altered level of consciousness, and those depending on spinal cord involvement (1, 2, 4, 8, 9, 16, 18). CSF evaluation is usually consistent with elevated protein levels, absence of atypical cells in almost all cases. Low glucose levels and increased opening pressure in some cases may raise the suspicion of chronic meningitis. (1, 4, 7, 14, 18). Besides, CSF should be examined in terms of any

microorganisms in order to rule out any type of bacterial or viral meningitis.

In this report, similar to the previously reported cases, a middle-aged woman with symptoms mimicking meningitis (neck pain, nausea, vomiting, and elevated CSF protein levels) has been presented. Neuroimaging methods indicated contrast enhancing leptomeningeal lesion predominantly involving spinal cord with a nodular lesion at the level of C1. As in other cases, empirical anti-tuberculosis therapy was initiated.

The histopathology findings in this case of neoplastic leptomeninges infiltration by a mixed tumor of astrocytoma and oligodendroglioma are unique. Most of the cases reported in the literature were astrocytomas (1, 7, 11, 12).

Despite the misleading clinical presentation, with findings suggestive of chronic meningitis and the absence of a parenchymal lesion, the diagnosis of PLDG must be considered. Cases with spinal cord involvement or cases without any contrast-enhancing lesions are especially challenging. However, the prognosis of PDLG is poor. The case presented here indicates that PDLG may exist with clinical symptoms mimicking those of chronic meningitis, and may histologically contain different phenotypic features.

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