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Multicentric Glioblastoma Mimicking Demyelinating Plaque Disease

Demiyelinizan Plak Hastalığını Taklit Eden Multisentrik Glioblastom

Evren AYDOĞMUŞ[a],
Ahmet Kasım KILIÇ[b],
Sezen GÜLEÇ AYDOĞMUŞ[c]

Clinics of
[a]Neurosurgery,
[b]Neurology,
Health Sciences University
Kartal Dr. Lütfi Kırdar Training and Research Hospital,
[c]Clinic of Radiology,
İstanbul Maltepe State Hospital,
İstanbul, TURKEY

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Correspondence:
Evren AYDOĞMUŞ
Health Sciences University
Kartal Dr. Lütfi Kırdar Training and Research Hospital,
Clinic of Neurosurgery, İstanbul,
TURKEY/TÜRKİYE
evren.aydogmus@gmail.com

ABSTRACT Demyelinating plaque disease in acute phase may simulate gliomas. The multicentricity is most frequently found in glioblastoma which is the most common and most malignant primary brain tumor. The differential diagnosis of demyelinating plaque diseases and multicentric gliomas is difficult since the neurological and radiological findings of each are similar in most cases. Multiple tumor-like brain lesions may mimic multicentric gliomas or metastases and they may be mistreated. Accurate diagnosis may need a histological examination following the surgical excision of the suspicious lesion. We report a patient with multicentric glioblastoma mimicking demyelinating plaque disease.

Keywords: Glioblastoma; demyelinating disease

ÖZET Demiyelinizan hastalıkların akut fazları, gliomları taklit edebilir. Multisentrisite, çoğunlukla, en sık ve en malign primer beyin tümörü olan glioblastomda gözlenir. Nörolojik ve radyolojik bulguları açısından birçok vakada benzerlikler gösterebilmeleri nedeniyle, demyelinizan hastalıklarla multisentrik gliomların ayırıcı tanısı zordur. Beyindeki multipl tumor benzeri lezyonlar, multisentrik gliomları ya da multipl metastazları taklit edebildiği için bazen yanlış tanı ve tedaviler yapılmasına neden olabilmektedirler. Kesin tanı için, şüpheli lezyona yönelik cerrahiyi takiben histolojik inceleme yapılması gerekli olmaktadır. Biz bu çalışmada, demiyelinizan plak hastalığını taklit eden bir multisentrik glioblastoma vakasını sunduk.

Anahtar Kelimeler: Glioblastom; demiyelinizan hastalık

Multiple gliomas have been classified as multicentric if they arise independently in more than one parenchymal areas without any continuity and as multifocal if they arise in a primary parenchymal focus and spread to other cerebral areas.[1-4]

Multiple cerebral tumor-like lesions are usually considered as a metastatic disease in patients with systemic cancer. However, in some patients, multiple tumor-like brain lesions may mimic multicentric gliomas or multiple metastases and they may be mistreated.[5] We report a patient with multicentric glioblastoma mimicking demyelinating plaque disease.

CASE REPORT

A 66-year-old male patient presented to the hospital with severe frontal headache progressing for the last two months. In his neurological examination, motor dysphasia was detected. He had a history of radical prostatec-

tomy surgery in 2016 and he was diagnosed with prostate adenocarcinoma. Computed tomography (CT) revealed, a right frontal lobe localized hypodense lesion (Figure 1). On contrast-enhanced magnetic resonance imaging (MRI), a cortico-subcortical irregular lesion was detected in right internal capsule extending up to the level of corpus callosum with heterogeneous enhancement and peripheral edema. Beside this lesion, there were other lesions with contrast enhancement, in superior and middle frontal gyrus, genu of corpus callosum extending to left cerebral hemisphere through the midline and in left centrum semiovale (Figure 2). The chest x-ray revealed a cavitary lesion in the right middle lobe (Figure 3). Radiographically, this lesion appeared to be a consolidation but underlying malignancy could not be excluded. For further investigation of a possible primary metastatic tumor, whole-body positron emission tomography (PET) was performed. According to Ga68-PET, slightly high Ga68 metabolic activity was detected in right frontal and left parietal lobes suggesting metastatic prostate cancer (Figure 4).

Radiological diagnosis of metastatic prostate cancer was accepted and after obtaining the freely given informed consent, he underwent stereotactic biopsy from the most significant lesion localized in the right frontal lobe (Figure 5). Histological examination of the biopsy material revealed inflammation and demyelination without detecting any malignant cells. Cerebrospinal fluid cytology was non-specific for infectious or demyelinating diseases. Neurology consultation recommended a clinical and MRI follow-up under antiepileptic and steroid therapy. Since the lesions regressed in first follow-up MRI Figure 6, they were accepted as demyelinating plaques and continued with antiepileptic and steroid therapy. Control MRI examination in the first month, revealed a significant progression in all lesions (Figure 7). After obtaining the freely given informed consent, considering that progressive radiological findings were relevant with tumoral lesions instead of demyelinating plaques, a right frontal craniotomy was planned for the excisional biopsy from the largest lesion (Figure 8). The pathological diagnosis was IDH wild-type Glioblastoma (WHO Grade IV) (Figure 9, Figure 10, Figure 11, Figure 12, Figure 13, Figure 14). All the lesions were considered as multicentric glioblastoma and patient was submitted to whole brain radiotherapy and chemotherapy.

DISCUSSION

Multicentric cerebral lesions do not exhibit a clear path of spread, but multifocal lesions involve multiple cerebral areas interacting each other with a definite path of spread.[1-4] Some authors define these lesions as multicentric only if they are separated by 2 cm or presented in contralateral lobes.[5,6]

The multicentricity is most frequently found in glioblastoma which is the most common and most malignant primary brain tumor.[4,7-9]

Metastases, demyelinating plaque diseases, and infections should be considered in differential diagnosis of multicentric gliomas. Clinical and radiological assessments are useful at first step but not enough for the accurate diagnosis in some of the cases. Histological examination by stereotactic biopsy is a relatively invasive option offering higher certainty for the diagnosis of the undefined

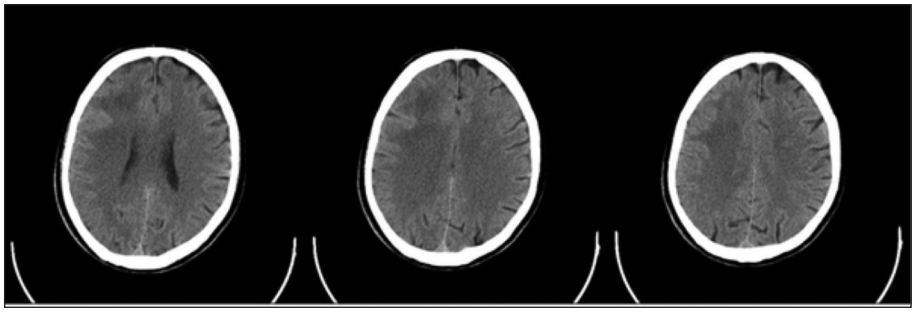

FIGURE 1: Cranial CT: A right frontal lobe localised hypodense lesion.

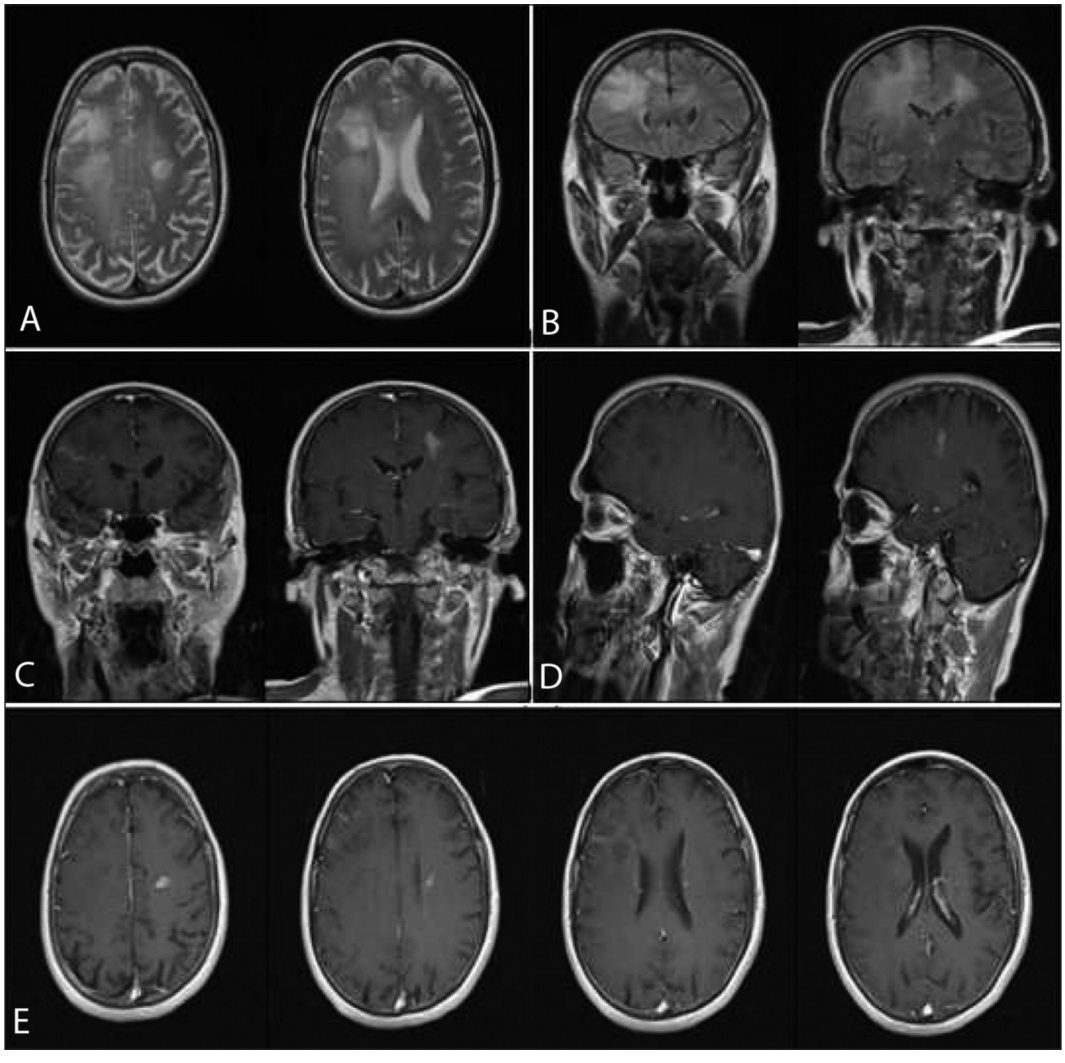

FIGURE 2: Cranial MRI, **(A)** T2-FLAIR axial and **(B)** T2-FLAIR coronal views: A cortico-subcortical irregular lesion in right internal capsule. **(C)** T1 with contrast coronal, **(D)** T1 with contrast sagittal and **(E)** T1 with contrast axial views: Multiple lesions, in superior and middle frontal gyri, genu of corpus callosum and in left centrum semiovale.

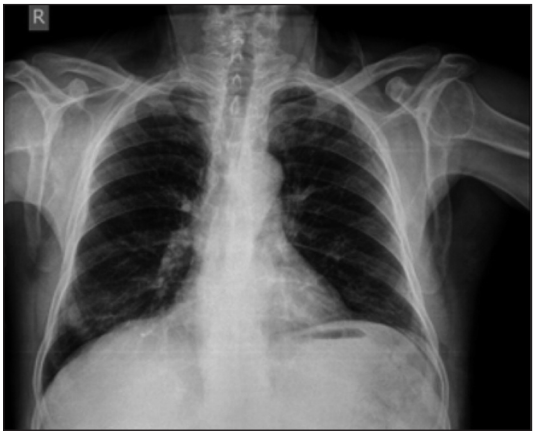

FIGURE 3: Chest x-ray: A cavitary lesion in the right middle lobe.

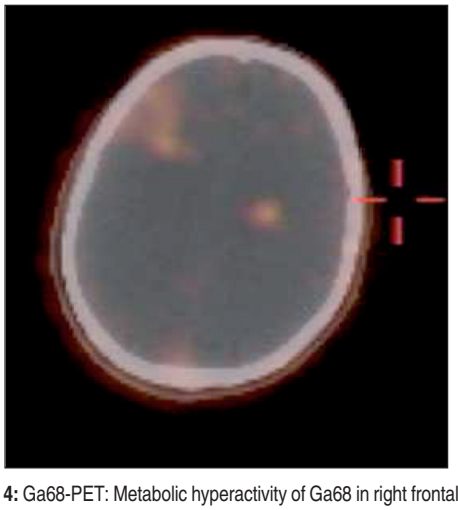

FIGURE 4: Ga68-PET: Metabolic hyperactivity of Ga68 in right frontal and left parietal lobes suggesting metastatic prostate cancer.

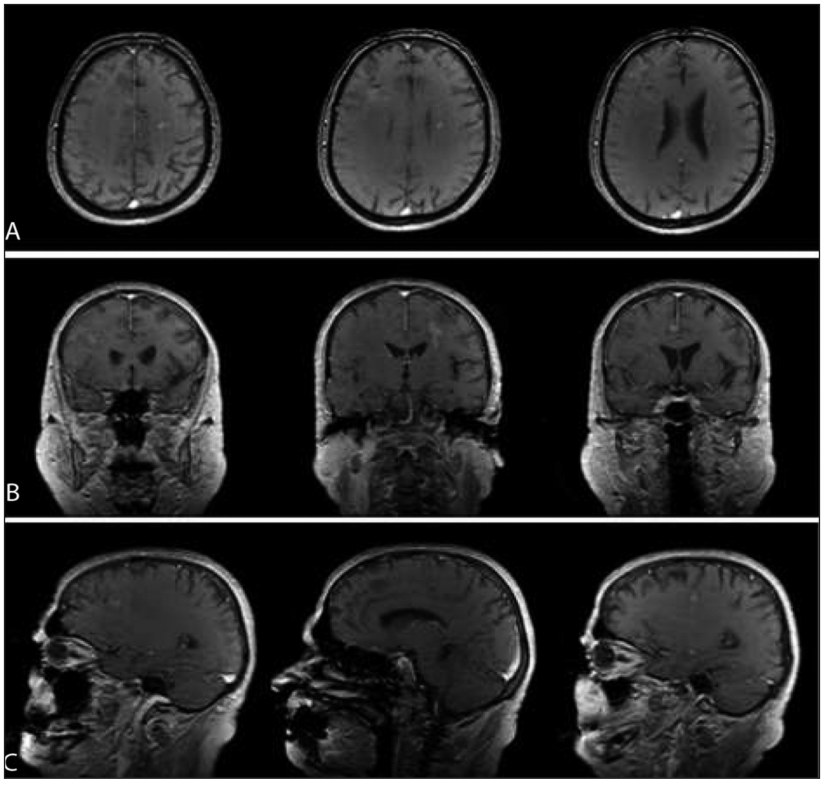

FIGURE 5: Postoperative Cranial MRI, T1 with contrast **(A)** axial, **(B)** coronal and **(C)** sagittal views: Following stereotactic biopsy from the most significant lesion localised in the right frontal lobe.

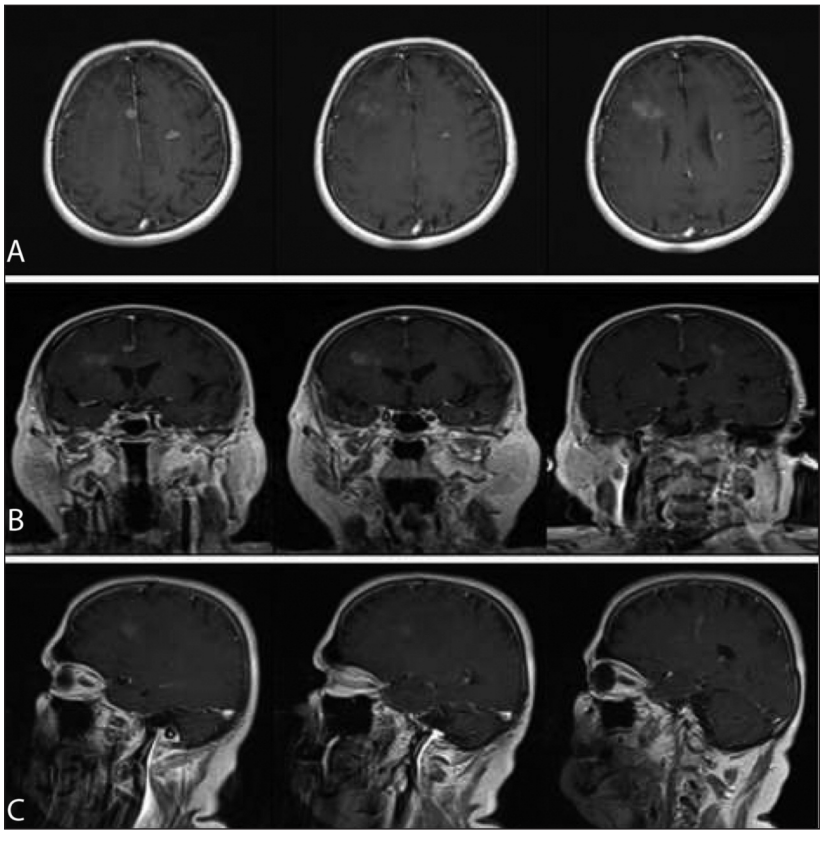

FIGURE 6: First follow-up Cranial MRI, T1 with contrast **(A)** axial, **(B)** coronal and **(C)** sagittal views: Lesions regressed under antiepileptic and steroid therapy.

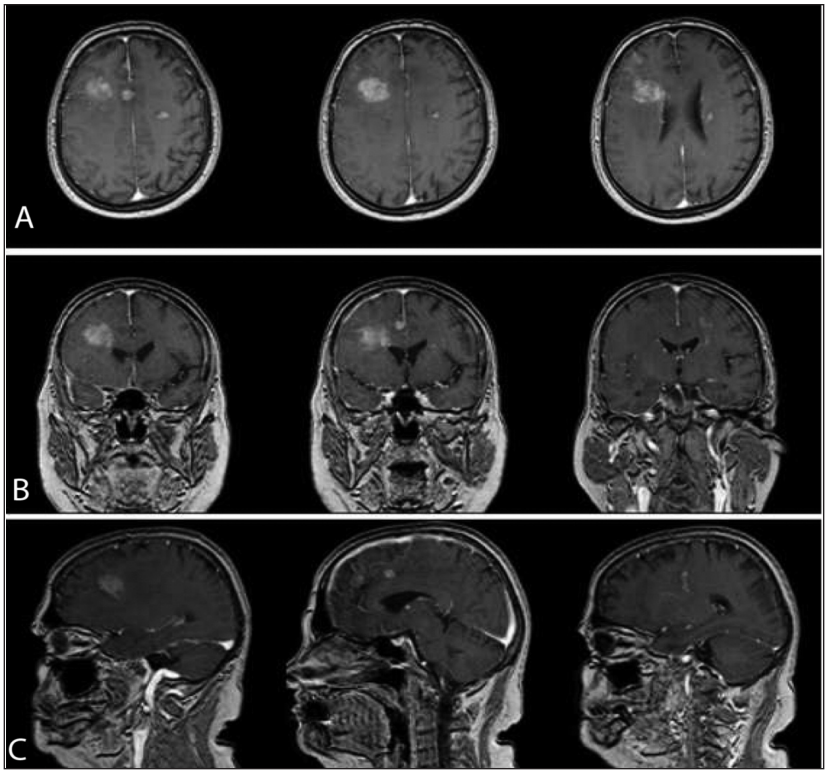

FIGURE 7: Second follow-up Cranial MRI in the first month, T1 with contrast **(A)** axial, **(B)** coronal and **(C)** sagittal views: Significant progression in all lesions suggesting tumoral invasion instead of demyelinating plaques.

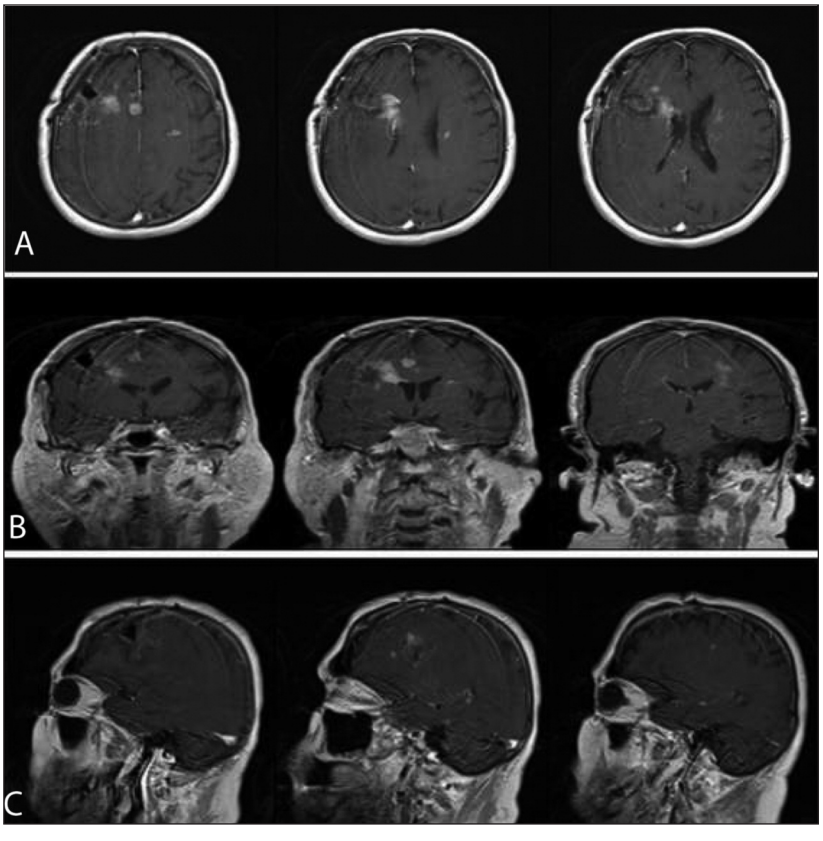

FIGURE 8: Postoperative Cranial MRI, T1 with contrast **(A)** axial, **(B)** coronal and **(C)** sagittal views: Following the right frontal craniotomy and the excisional biopsy from the largest lesion localised in the right frontal lobe.

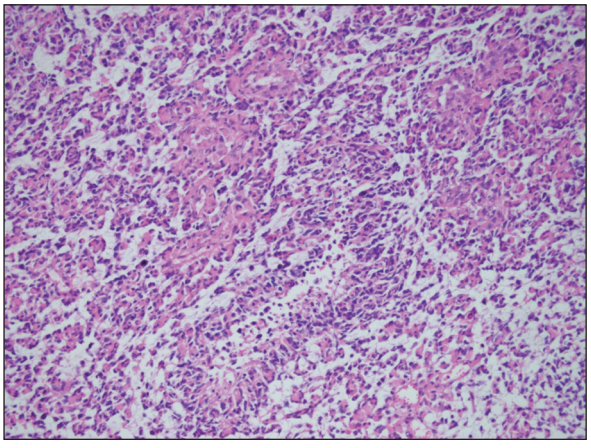

FIGURE 9: Necrotic areas presented with palization.

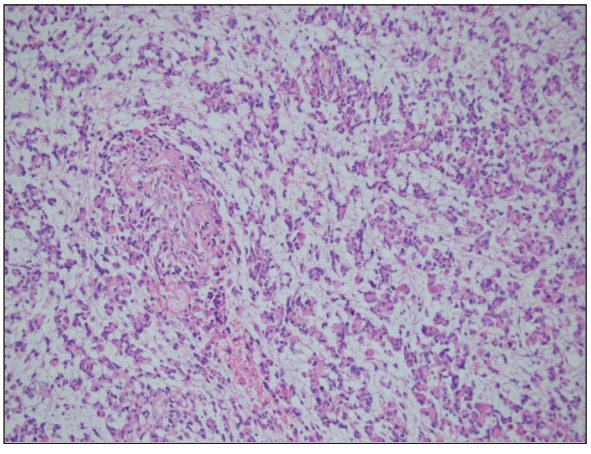

FIGURE 10: Microvascular proliferation areas.

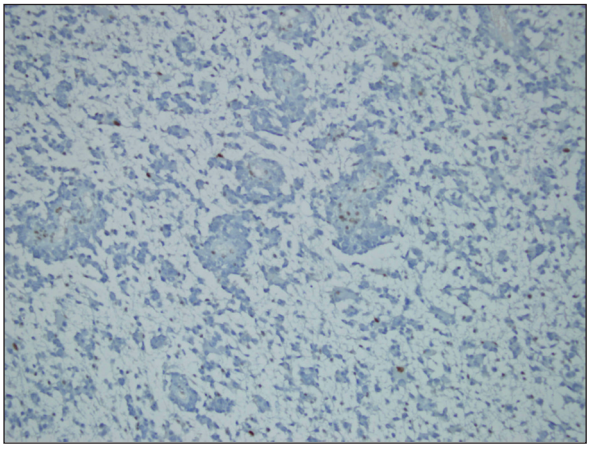

FIGURE 11: ATRX expression loss in tumor cells.

cases after conventional investigation techniques. However, since the malignant glial tumors usually generate a zone of demyelination, it is possible that it may be the only tissue enclosed in the specimen, especially when evaluating small biopsy materials like in stereotactic brain biopsy.[10]

Scherer (1938), Russell and Rubinstein (1971) reported cases of glial tumors (WHO Grade IV) in coincidence with multiple sclerosis, suggesting that glial tumors might arise from hyperplastic plaques of multiple sclerosis.[11,12] In case of 29-year-old female patient died from an unknown progressive neurological disease, Scherer observed periventricular atypical multiple demyelinating plaques resembling findings of acute multiple sclerosis and focal transitions between reactive astrocytes in plaques and neoplastic cells and hypothesized that neoplastic transformation of hyperplastic glial cells in plaques resulted in glioma formation.[11] That hypothesis was also supporting

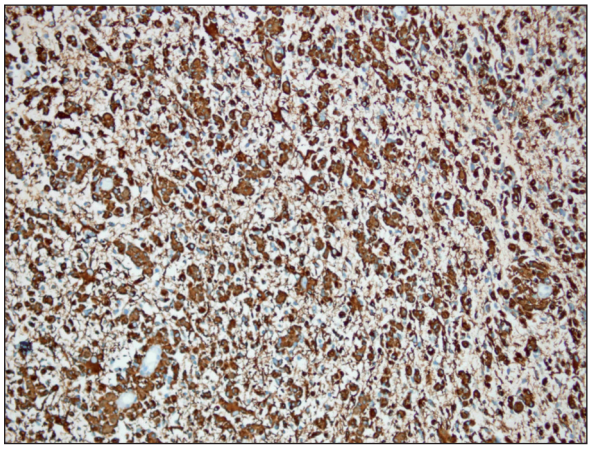

FIGURE 12: GFAP positive tumor cells.

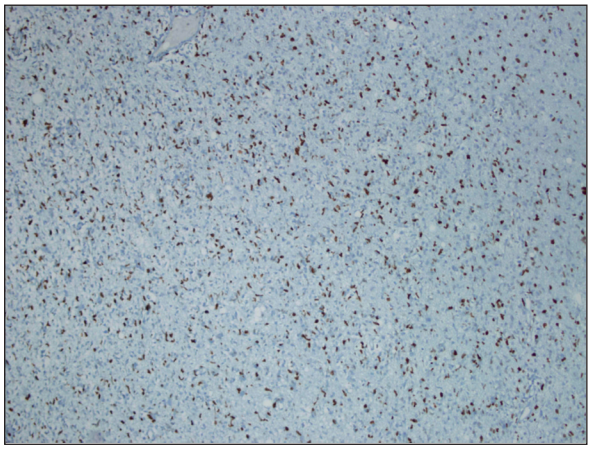

FIGURE 13: High Ki-67 proliferation index.

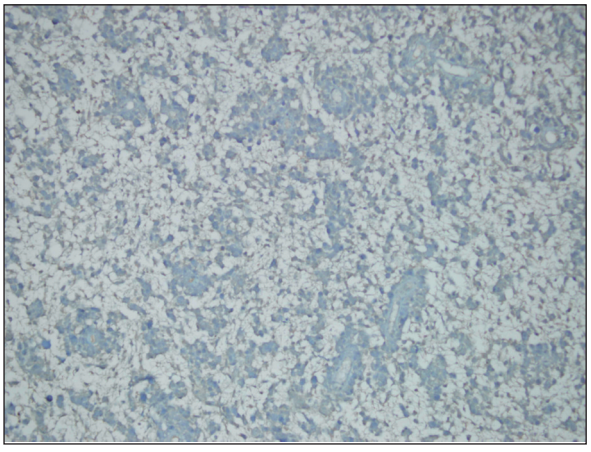

FIGURE 14: IDH-1 negative tumor cells.

the multicentricity of gliomas accompanying multiple sclerosis.[11,13]

Our patient with clinical and radiologic findings strongly suggestive of demyelinating plaque disease was shown by the excisional biopsy to have glioblastoma. Such patients emphasize the importance of considering the multicentric gliomas in the differential diagnosis of demyelinating lesions before establishing the therapeutic strategy even in case of a previous cancer history. Following laboratory tests and radiological examinations, patients with multicentric lesions need further evaluation including stereotactic biopsy for accurate diagnosis.

Source of Finance

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Evren Aydoğmuş, Ahmet Kasım Kılıç;* ***Design:*** *Evren Aydoğmuş;* ***Control/Supervision:*** *Evren Aydoğmuş, Sezen Güleç Aydoğmuş;* ***Data Collection and/or Processing:*** *Evren Aydoğmuş, Ahmet Kasım Kılıç;* ***Analysis and/or Interpretation:*** *Evren Aydoğmuş, Sezen Güleç Aydoğmuş;* ***Literature Review:*** *Evren Aydoğmuş;* ***Writing the Article:*** *Evren Aydoğmuş, Ahmet Kasım Kılıç, Sezen Güleç Aydoğmuş;* ***Critical Review:*** *Evren Aydoğmuş, Ahmet Kasım Kılıç, Sezen Güleç Aydoğmuş;* ***References and Fundings:*** *Evren Aydoğmuş;* ***Materials:*** *Evren Aydoğmuş.*

REFERENCES

1. Batzdorf U, Malamud N. The problem of multicentric gliomas. J Neurosurg. 1963;20:122-36. [Crossref] [PubMed]
2. Budka H, Podreka I, Reisner T, Zeiler K. Diagnostic and pathomorphological aspects of glioma multiplicity. Neurosurg Rev. 1980;3(4):233-41. [Crossref] [PubMed]
3. Salvati M, Oppido PA, Artizzu S, Fiorenza F, Puzzilli F, Orlando ER. Multicentric gliomas. Report of seven cases. Tumori. 1991;77(6): 518-22. [Crossref] [PubMed]
4. Thomas RP, Xu LW, Lober RM, Li G, Nagpal S. The incidence and significance of multiple lesions in glioblastoma. J Neurooncol. 2013;112(1):91-7. [Crossref] [PubMed]
5. Giannopoulos S, Kyritsis AP. Diagnosis and management of multifocal gliomas. Oncology. 2010;79(3-4):306-12. [Crossref] [PubMed]
6. Hassaneen W, Levine NB, Suki D, Salaskar AL, de Moura Lima A, McCutcheon IE, et al. Multiple craniotomies in the management of multifocal and multicentric glioblastoma. Clinical article. J Neurosurg. 2011;114(3):576-84. [Crossref] [PubMed]
7. Kyritsis AP, Levin VA, Yung WK, Leeds NE. Imaging patterns of multifocal gliomas. Eur J Radiol. 1993;16(3):163-70. [Crossref]
8. McLendon RE, Rich JN. Glioblastoma stem cells: a neuropathologist's view. J Oncol. 2011;39:7195. [Crossref]
9. Stark AM, van de Bergh J, Hedderich J, Mehdorn HM, Nabavi A. Glioblastoma: clinical characteristics, prognostic factors and survival in 492 patients. Clin Neurol Neurosurg. 2012;114(7): 840-5. [Crossref] [PubMed]
10. Love S. Demyelinating diseases. J Clin Pathol. 2006;59(11):1151-9. [Crossref] [PubMed] [PMC]
11. Scherer HJ. [La 'glioblastomatose en plaques': sur les limites anatomiques de la gliomatose et des processus sclerotiques progressifs (sclerose en plaques, sclerose diffuse de Schilder, scl6rose concentrique)]. Journal Belge de Neurologie et de Psychiatrie. 1938;38:1-17.
12. Russell DS, Rubinstein LJ. Pathology of Tumours of the Nervous System. 3rd ed. London: Arnold; 1971. p.179.
13. Werneck LC, Scola RH, Arruda WO, Torres LF. Glioma and multiple sclerosis: case report. Arq Neuropsiquiatr. 2002;60(2-B):469-74. [Crossref] [PubMed]