Multicentric Gliomas: Still Remains a Controversial Issue

Report of three cases and literature review

Multisentrik Gliomalar: Halen Tartışılan Bir Konu

Üç olgu sunumu ve literatürün gözden geçirilmesi

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ABSTRACT

Multicentric gliomas are uncommon lesions of the central nervous system (CNS) with an unprecise rate of occurrence that diffusely infiltrate large portions of the brain. Glioblastoma multiforme is the most agressive form of gliomas and often has a distinct neuroimaging pattern with poor prognosis.

We present three cases with multicentric gliomas diagnosed as glioblastoma multiforme. The radiological and clinical features of these rare entities were analyzed. We performed surgical treatment and subsequent radiotherapy for each patient.

Although it is difficult to diagnose and treat multicentric gliomas, the aim of the surgeon must be to remove the biggest and/or the nearest and most accessible lesion without causing additional neurological deficit. Further management, either radiotherapy or chemotherapy, must be based on the histopathological diagnosis.

KEY WORDS: Multicentric, Glioma, Etiology, Management

ÖZ

Multisentrik gliomalar santral sinir sisteminin nadir lezyonlarıdır. Görülme sıklığı kesin olarak bilinmemekle birlikte beynin geniş kısımlarını infiltre edebilirler. Glioblastoma multiforme gliomaların en agresif formudur ve genellikle kendine özgü bir görüntüleme özelliği ve kötü prognozu vardır.

Glioblastoma multiforme tanısı olan 3 adet multisentrik glioma olgusu sunuldu. Bu nadir olguların radyolojik ve klinik özellikleri analiz edildi. Her bir hasta için önce cerrahi tedavi sonra radyoterapi uygulandı.

Multisentrik gliomaların tanısı ve tedavisi zor olmakla birlikte, cerrahın hedefi en büyük ve/veya en ulaşılabilir lezyonu ek bir nörolojik defisit olmadan çıkartmaktır. Daha sonraki tedavi histopatolojik tanıya göre radyoterapi veya kemoterapi olmalıdır.

ANAHTAR SÖZCÜKLER: Multisentrik, Glioma, Etyoloji, Tedavi

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INTRODUCTION

Multiple intracranial mass lesions detected on computed tomography (CT) or magnetic resonance imaging (MRI) present a diagnostic dilemma for neurosurgeons. Although multiple contrast-enhancing cerebral mass lesions with surrounding edema commonly represent metastatic disease or an abscess, malignant gliomas must also be kept in mind in the differential diagnosis.

Multicentric gliomas have been previously reported at various incidences from 2.3 to 9.1% by various authors (4). The radiological, clinical and histopathological features separate this group of tumors from the other gliomas and the major problem is their management.

We present three cases of multicentric glioblastoma multiforme from the 20 patients who received a diagnosis of malignant glial tumors of different types and managed at our department over a one-year period.

PATIENTS AND METHODS

A retrospective analysis of 20 consecutive patients with malignant gliomas over a one-year period (between 2000 and 2001) was performed. Cranial CT and MRI with contrast enhancement were obtained from each patient before the treatment. The location, number, shape and the degree of contrast enhancement were noted for all tumors detected radiologically. All patients underwent surgical excision and radiotherapy based on the histopathological diagnosis. Seven patients were diagnosed as glioblastoma multiforme and three were multicentric. No apparent dissemination route was identified in these three cases and the tumors were presumed to be true multicentric gliomas. Cerebrospinal fluid (CSF) examination was also undertaken in each patient for tumor cells and a negative result was obtained in all.

All patients were followed-up by MRI at 3-month intervals after the radiotherapy. We present the case reports of three patients with multicentric gliomas.

Patient 1: A 64-year-old male complaining of headaches and left-sided weakness was admitted to our department. He was otherwise healthy. The neurological examination revealed left hemiparesis and papill edema of the right eye. An emergency cranial MRI was performed and multiple cerebral mass lesions with contrast enhancement and massive edema were found in the right hemisphere (Figure 1). There was no connection between the lesions and they were initially considered to be metastatic tumors. Screening for a possible primary focus was undertaken including thoraco-abdominal CT, prostate ultrasound and serum tumor marker analysis, with negative results. The patient underwent right parietal craniotomy for surgical resection. The histopathological diagnosis was consistent with glioblastoma multiforme (Figure 2), and we performed radiotherapy subsequently. He was followed-up with serial MRI scans and no regrowth was observed at the end of the first year.

Patient 2: A 53-year-old man was admitted with left-sided weakness, personality changes and visual disturbance. There was no history of malignancy in his background. Left hemiparesis and bilateral papilledema were found on the neurological examination. Three mass lesions with contrast enhancement were detected on cranial MRI; the biggest one was located in the right frontal lobe with massive edema while the others were in the left frontal and left posterior parietal lobe (Figure 3). The results of all screening examinations to detect

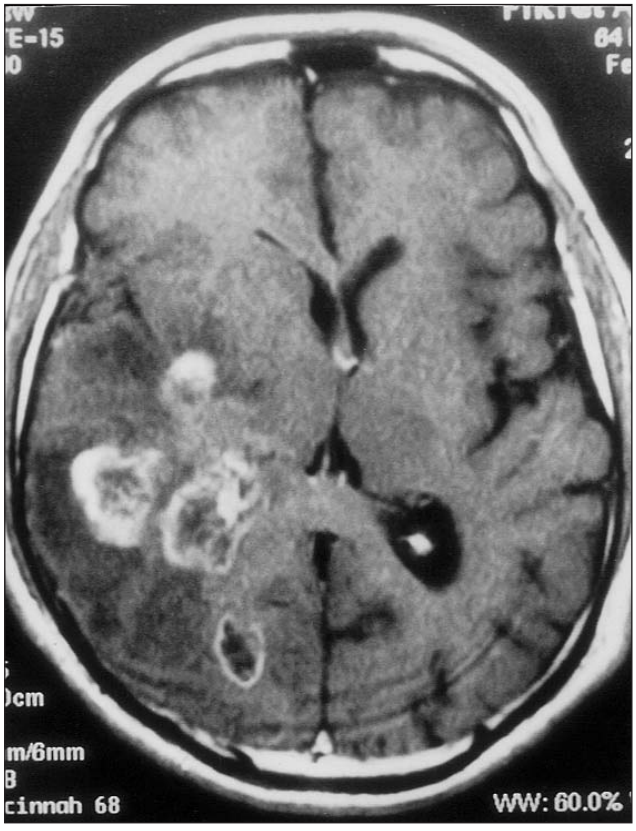

Figure 1: The axial MRI scan of patient 1 showing synchronous multiple contrast-enhancing mass lesions located in the right hemisphere.

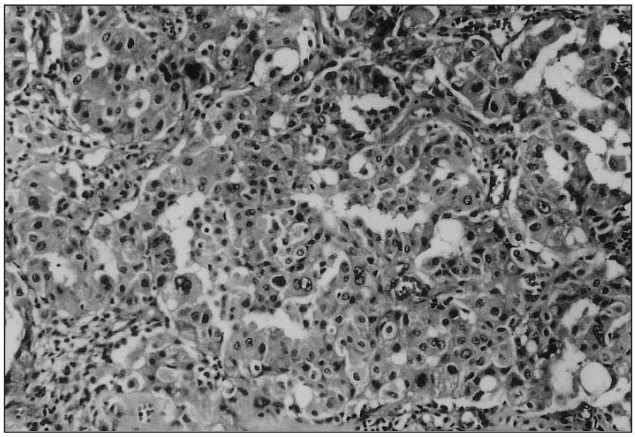

Figure 2: The histopathological appearance of patient 1 showing pseudopalisading around necrosis and pleomorphic multinucleated astrocytes (Haematoxylin & Eosin, x100).

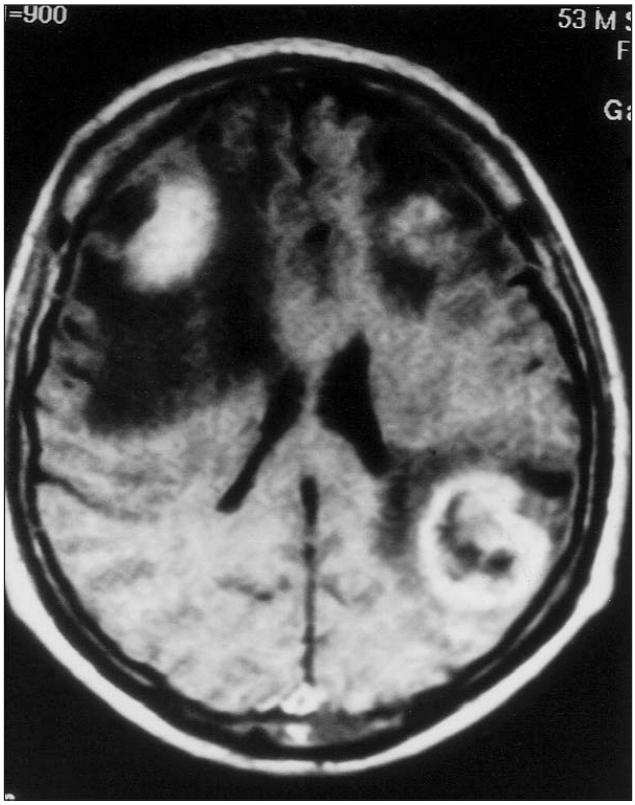

Figure 3: The axial MRI scan of patient 2 with three synchronous contrast-enhancing mass lesions located in both hemispheres. The right frontal lesion is responsible for the clinical status because of surrounding massive edema, while the left frontal and left posterior parietal lesions have caused relatively less edema.

primary foci were normal. The patient underwent left frontal craniotomy and removal of the left frontal mass lesion. The histopathological diagnosis was consistent with glioblastoma multiforme (Figure 4). The left hemiparesis improved slightly postoperatively and the patient underwent radiotherapy as further treatment. He was alive at the end of one year after surgery.

Patient 3: A 48-year-old woman was admitted with the complaint of right leg weakness. She was otherwise healthy. Right hemiparesis, dominant in the lower part, and bilateral papilledema were found on her neurological examination. Cranial MRI showed multiple cerebral contrast-enhancing mass lesions in both hemispheres (Figure 5). A primary

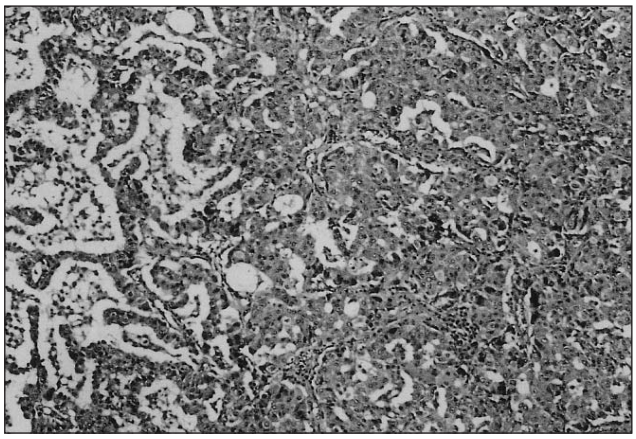

Figure 4: The histopathological appearance of patient 2 showing marked vascular endothelial proliferation and multinucleated giant cells (Haematoxylin & Eosin, x100)

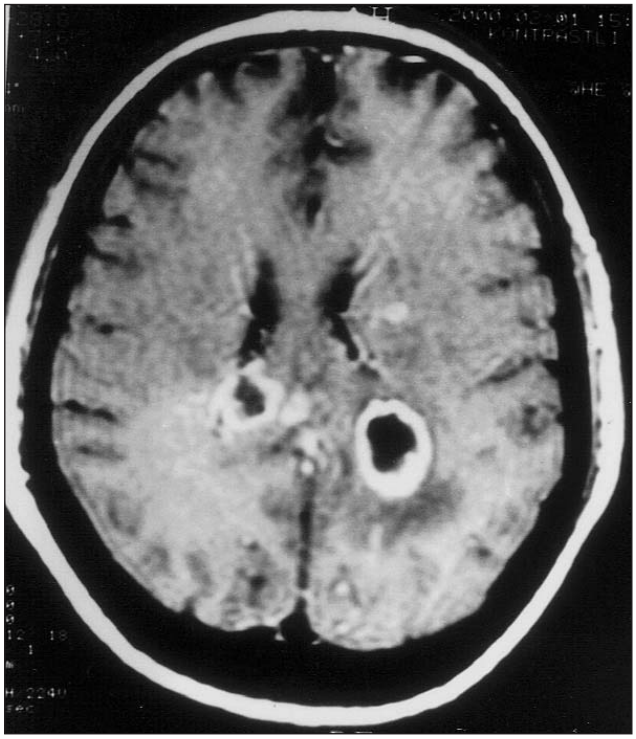

Figure 5: The axial MRI scan of patient 3 with synchronous lesions in both hemispheres. The biggest is located just behind the occipital horn of the left lateral ventricle.

focus was searched with negative results. The patient underwent left occipital craniotomy and the mass lesion behind the occipital horn of the left lateral ventricle was removed. The histopathological diagnosis was consistent with glioblastoma multiforme (Figure 6A and 6B). Radiotherapy was performed following the surgery. The patient's clinical status deteriorated rapidly despite radiotherapy and she died within three months.

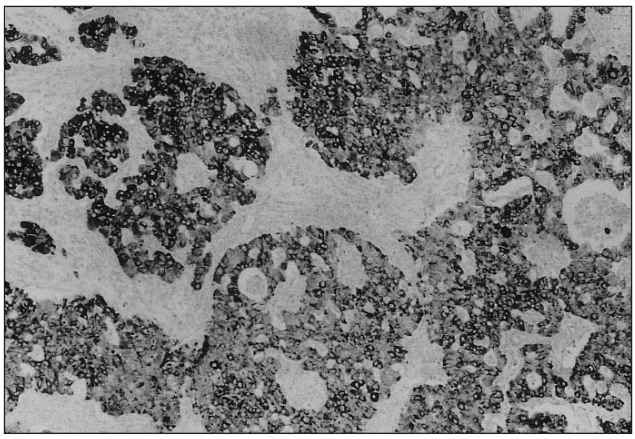

Figure 6A: The histopathological appearance of patient 3 showing an anaplastic and highly cellular tumor consisting of small, poorly differentiated round cells (Haematoxylin & Eosin, x200).

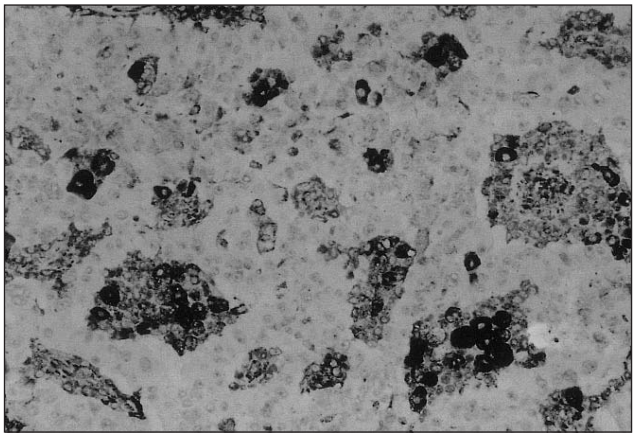

Figure 6B: Pleomorphic multinucleated astrocytes in the histopathological specimen of patient 3 (Haematoxylin & Eosin, x200).

DISCUSSION

Multicentric gliomas are fascinating lesions of the brain. They have a poor prognosis despite all treatment modalities. Making the differential diagnosis and choosing the management strategy are the main difficulties encountered with this rare entity. Multiple cerebral masses should be thoroughly evaluated and not always presumed to be of metastatic origin (5). Although multicentric gliomas can mimic metastatic diseases, the treatment of these two lesions is considerably different with respect to adjuvant radiotherapy and chemotherapy (6, 7, 11, 12).

The incidence of multicentric gliomas is still matter of debate. Djalilian (3) estimated the rate of multiplicity in malignant glioma as 9%, in contrast to Russel and Rubinstein's rate of 4.5% (8). Barnard reported the largest post mortem series of 241 gliomas in the literature on multifocal cerebral gliomas and these tumors accounted for 2.9% of the series (1). Multicentric gliomas made up 15% of our patients with malignant gliomas who underwent surgery over a one-year period. This rate is higher than reported in the literature, but the time interval of our study was short.

Gliomas can either be multiple at the time of diagnosis or develop subsequently. There is still uncertainty on the origin and mode of spread of malignant gliomas. Many theories on the pathogenesis of multicentric gliomas exist (2, 13, 14). Willis suggested that the evolution of multicentric gliomas is a two-step process. In the first step, a large area of brain parenchyma undergoes neoplastic transformation. During the second phase, various rates of tumor proliferation within the larger field give rise to separate lesions (13). Zülch suggested that the multicentric lesions represent metastasis from a primary focus via a yet unknown pathway (14). Tumor dissemination via CSF pathways has been proposed as another reason for multicentric gliomas (2) but we did not encounter any tumor cells in the CSF examination of our three cases. Despite the many theories on multicentric gliomas, no single theory can explain the pathophysiology of this rare entity.

Multifocal gliomas have been classified into four main categories as diffuse, multiple, multicentric and multiple-organ by Salvati in 1991 (10). He reported 7 cases with multicentric glioma and pointed out the distinctive features of these tumors. He also reported 40 patients divided into two groups as multicentric and multifocal tumors in 1997 and stated that there were no significant differences between these groups (9).

Djalilian analyzed 100 consecutive patients with malignant gliomas in 1999 and he found that 9% of the patients had multicentric lesions, either synchronous or metachronous, on radiological

evaluation. He suggested that the metachronous lesions could represent dissemination of tumor through the CSF pathways, radiation-induced tumors, radiation necrosis, or new tumor foci (3). Sundaresan also reported six cases with multicentric glioma and stated that metachronous lesions occur more frequently than synchronous lesions (12). In our three cases, the lesions were synchronous initially and we did not detect an additional lesion on MRI after radiotherapy. Actually, we do not definitely know why these tumors are multiple and the management is therefore always a problem.

The multiplicity of the lesions has an obvious effect on the management choices. The mass lesion mostly responsible for the clinical status must be removed for histopathological examination and to obtain clinical improvement. The location and size of the tumor are also important in surgical removal. The aim of the surgeon must be to remove the biggest and nearest lesion that is most accessible without causing additional neurological deficit. Further management, either radiotherapy or chemotherapy, must be based on the histopathological diagnosis.

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