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N. Zamponi  
F. Rychlicki  
A. Ducati  
L. Regnicolo  
U. Salvolini  
R.A. Ricciuti

Abstract  Multiple glioma is a well-recognized but uncommon entity. They are grouped in two categories: multifocal and multicentric gliomas. Multifocal gliomas grow through dissemination along an established route, spreading through commissural pathways, CSF channels, or the blood or by local extension through satellite formation; at the opposite end of the spectrum, multicentric gliomas are widely separated lesions whose simultaneous presence cannot be attributed to any of the above pathways. Reports in the literature refer to single cases or small series of multicentric gliomas, almost always in adult patients, their occurrence in children being even less frequent. We report the case of a 12-year-old boy with multicentric glioma, atypical acute clinical onset and fast growth of three other tumors in 8 months, and then discuss the problems of diagnosis and therapy.

Keywords  Multicentric gliomas · Children · Atypical onset

Introduction
Multiple glioma is a well-recognized but uncommon entity. The incidence ranges from 0.5% to 20% in the various reports [11, 12, 17]. They are grouped in two categories: multifocal and multicentric gliomas.

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Advances in neuroradiological techniques have greatly improved opportunities for discovering multiple tumors, but diagnosis of their nature and differentiation from other pathologies (infections, vascular and demyelinating diseases) can be difficult and may require cerebral biopsy [88, 12, 14, 15, 16, 18].

In the literature, single cases or short series of multicentric gliomas are reported, almost always with reference to adult patients, the occurrence in children being even less frequent [4, 7, 11, 18].

Case report
In August 1998, a 12-year-old boy was admitted to the Pediatric Intensive Care Unit of the Children’s Hospital with a 3-day history of fever and secondarily generalized partial seizure, and in a comatose state. His past history was unremarkable.

A CT scan showed a low-density area on the right temporal lobe with slight enhancement after contrast, consistent with an encephalitic lesion (Fig. 1a, b).

Cytochemical examination of the cerebrospinal fluid (CSF) was normal; there were no anti-herpes simplex virus (HSV) and Epstein-Barr virus (EBV) antibodies in the CSF, but IgM anti-VCA and IgG anti-EA+EBNA 1 were detected in the serum by the immunoblotting reaction, suggesting an EBV reinfection.

The EEG revealed periodic lateralized epileptiform discharges (PLEDs) in the right frontotemporal regions. These disappeared in the next 48 h and were replaced by bilateral, slow, monomorphic background activity (Fig. 2). Medical treatment (antibiotics, steroids, antiviral and antiepileptic drugs) produced a gradual improvement of the neurological status, and the child was discharged.
He still had minimal left facial and upper limb weakness. Twenty days later, he was readmitted with fever, headache, vomiting, partial complex seizures and left hemiparesis. The CT scan revealed an increase in size of the right temporal lesion, which was confirmed by MRI. The previous therapy was restarted as there was persisting serological evidence of EBV reinfection, and the clinical status again rapidly improved.

The second MRI (30 days after the first and 75 days after the onset of the disease) showed a new, deep left frontal lesion with high signal and strong contrast enhancement (Fig. 3). Angiographic examination highlighted an avascular right temporal lesion, while the left frontal lesion appeared to be irregularly and strongly vascularized. A right temporal craniotomy was performed with a large tumor excision, and the histological features showed an anaplastic astrocytoma. Soon after, the child was submitted to radiotherapy (3960 cGy to the frontal-temporal parietal regions and 1600 cCy to the left frontal region).

Thirty days later, CT and MRI showed stability of the right temporal lesion without any sign of growth. In contrast, progression was evident for the left frontal mass. For this reason and because the child’s clinical state had worsened (headache, seizures and drowsiness), a further operation was performed, with subtotal resection of the frontal left tumor, which was an anaplastic astrocytoma but exceptionally aggressive (Fig. 4a–d).

The postoperative course showed an improvement in neurological status, but 15 days later chickenpox developed and 30 days later the MRI detected two more tumors, in the right and left of the retrotrigonal region (Fig. 5a, b).

In April 1999 the child died.

Discussion

Multiple gliomas were described by Gower in 1896 for the first time [11]. Subsequently Batzdorf and Malamud differentiated multifocal from multicentric gliomas, which have an incidence of 2.3–9.1% [7, 11]. Those with different histological appearances account for 2.9%.

Multicentric gliomas are well-separated lesions, localized in different lobes or hemispheres, rarely above and below the tentorium, without macroscopic and microscopic evidence of metastasis. They may be separated not only in location but also in time. In this way they can be divided into synchronous and metachronous (when the next lesions occur months to years after the initial diagnosis of glioma) types.

MRI allows a diagnosis in terms of numeric and spatial localization, and PET can provide data on the biological characteristics and proliferative capabilities of tumor tissue [18]. Multiforme glioblastoma is the most frequent histological pattern of multicentric gliomas, but well-differentiated and mixed gliomas can be found. Many pathogenetic theories have been suggested to explain multicentricity, but the true origin of multicentric gliomas is unknown [11, 12, 17]. Ostertag considers gliomas as coming from primitive cells with blastomatous potential that find expression later. Willis thinks that multicentricity is the result of a two-step proliferation that occurs in a wide area of tissue at the beginning and then in mu-