Posttraumatic Glioma: Report of a Case

Aldo Spallone^{a, b} Chiara Izzo^a Augusto Orlandi^b

^aSection of Neurosurgery, Department of Clinical Neurosciences, Neurological Centre of Latium 'NCL', and ^bDepartment of Biopathology, Institute of Anatomical Pathology, Tor Vergata University of Rome, Rome, Italy

Key Words

Head injury · Brain tumors · MRI

Abstract

For a long time, head injury has been considered as a possible causative factor for later development of brain tumors. However, the actual role of previous head trauma in the pathogenesis of intracranial tumors is still a matter of debate, also due to the possible medico-legal implications. Some authors have suggested several criteria for establishing a possible causal relationship between the aforementioned factors. We report a case of a left posterior paraventricular high-grade glioma which developed 20 years after a posttraumatic hematoma occurring in the same area. This case is reported in detail and the relevant literature is reviewed.

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Introduction

For a long time, head injury has been considered as a possible causative factor for later development of brain tumors [1]. However, the actual role of previous head trauma in the pathogenesis of intracranial tumors is still a matter of debate [1], also due to the possible medico-legal implications [2].

Recently, the possibility of an implication of a significant previously occurring head injury in the later development of brain neoplasms has been convincingly suggested as far as intracranial meningiomas are concerned [3]. As regards cerebral gliomas developing after a significant traumatic injury of the head, the reports in the literature are scarce and the causal role of head injury still debated.

Zulch and Mennel [4] and Manuelidis [5] have suggested several criteria for establishing a possible causal relationship between the aforementioned factors, mainly based on the

Aldo Spallone, MD
Section of Neurosurgery, Neurological Centre of Latium 'NCL'
Via Patrica 15, IT-00174 Rome (Italy)
E-Mail segreteria1@nclroma.it

existence of a close anatomical relationship between the traumatic event and the later developing brain tumor, and on sufficiently long time interval between the two occurrences. More recently, other authors have proposed to include the results of neuroimaging investigations as a further proof of the close anatomical relationship between trauma and later developing glioma [5].

We observed a case of a left posterior paraventricular high-grade glioma which developed 20 years after a posttraumatic hematoma occurring in the same area. This case is reported in detail and the relevant literature is reviewed.

Case Report

A 37-year-old man was admitted in October 2002 with a several months history of medically refractory seizures and a more recent onset of headache and confusion. His past clinical history was relevant for a major brain trauma with left temporal hemorrhage, which occurred in 1977 and which was demonstrated by CT scanning as indicated by the clinical charts of another hospital. At admission, he showed mild confusion, short-term memory deficit but no speech impairment. MRI demonstrated a T1 hypointense and T2 hyperintense lesion in the left insular region, which did not enhance with gadolinium (fig. 1a). The lesion was exposed via a pterional approach and wide splitting of the Sylvian fissure and generously removed; however, it was intentionally not radically removed. No clear limit with the surrounding normal parenchyma could be seen at surgery. Histological examination revealed a moderately increased cellularity (fig. 2a, b) compatible with diffuse astrocytoma (grade II according to the WHO classification). In addition, pseudo-cystic areas containing hemosiderin pigment and CD68-positive macrophages, interstitial hemosiderin-loaded macrophages and inflammatory cells were also detected (fig. 2c, d). These findings would indicate the presence of a pre-existing hemorrhage. After surgery, the patient's confusion definitely improved, as did the focal epilepsy. This latter was well controlled with a low medication dosage until 2004, when, due to recrudescence of the seizures, he underwent a MRI that again documented an abnormal area in the deep left temporal region (fig. 1b). The lesion was removed via a transulcal left temporal approach and again removal was not radical. Histological examination in this occasion gave evidence of only local degenerative posttraumatic changes. Again, focal epilepsy improved. He was readmitted in December 2006 because an MRI follow-up study (fig. 3a, b), performed again because of worsening of the seizures, had demonstrated an area of contrast enhancement in the context of the previously abnormal area. The patient was submitted for surgery via the same previous temporal craniotomy, and the lesion was apparently totally removed. Histological examination now revealed (fig. 2e, f) an anaplastic astrocytoma (grade III according to the WHO classification). The postoperative course was uncomplicated. The patient underwent postoperative radiation treatment and chemotherapy. At the last follow-up, 5 years after surgery, the patient was well and had no signs of recurrence.

Discussion

Diagnostic Criteria

As we have already mentioned, several criteria have been proposed for considering the occurrence of a brain tumor after a significant head injury as possibly related causes [4, 6]. Table 1 and table 2 briefly summarize these criteria.

The present case strictly fulfills these criteria as far as time interval and close anatomical relationship between the traumatized area and the glioma are concerned. Moreover, histological examination yielded different results for the initial surgeries, very likely because the biopsies were performed in different areas of the lesion, which showed quite similar characteristics at the various MRI examinations before the malignant transformation of the lesion had taken place.

Histological Studies

The fact that one biopsy was diagnosed as a low-grade glioma and another one as a posttraumatic gliosis is a clear proof of the close anatomical relationship between the two pathological events. This is a fundamental factor for considering the glioma to be posttraumatic. This latter evolved to a high-grade tumor as it happens quite often with low-grade brain gliomas [6]. A total removal of a histologically benign intracranial glioma, localized in a functionally critical area, has been recently advocated as a possibly preventive measure against later malignant transformation of such a lesion [7]. However, clear evidence is still lacking, and a less aggressive surgical behaviour as the one we had in the present case, can be considered acceptable. Moreover, the results of the histological examinations were apparently conflictive, and the possibility of the first diagnosis being erroneous was also considered, since no lesion growth was observed by MRI examination. Furthermore, focal epilepsy – the only symptom of the patient – improved significantly after both surgeries, from which the patient recovered without any deficit. In addition, the long survival of the patient following the last gross total surgical removal is very uncommon, and the MRI data before the last surgery suggested the possibility of malignant transformation of a benign glioma, and the revision of the histological material confirmed the previous diagnosis of high-grade glioma.

Posttraumatic Gliomas

Posttraumatic intracranial gliomas are rare [1, 2, 5]. As we have already stated above, the fact that significant head injury can cause a brain glioma is a matter of great controversy.

Experimental Glioma Tumorigenesis

A possible evidence of such a causal relationship has been the goal of several experimental studies. In fact, a significant proliferative astrocytic activity early after a trauma has been demonstrated in animal studies [8]. Areas of alternative neurogenesis have also been found at some distance from the site of the experimental traumatic lesion and were more prominent in the areas of blood brain barrier breakdown [9]. Moreover, an increase in the number of C6-SP cells (tumor stem cells for rat glioma) was observed as a consequence of trauma [10].

Experimental studies on glioma tumorigenesis also yielded controversial results concerning the role of trauma [11], although there are indications that, in the presence of several carcinogenesis-promoting factors, head injury would enhance the risk of developing brain glioma in experimental animals [12].

Clinical Epidemiological Studies

However, it is quite difficult to translate these findings to the actual clinical scenario. In fact, evidence of a possible causal role of previous brain traumatic injury in the oncogenesis of intracranial gliomas is lacking in epidemiological studies [2, 13]. Some evidence has been found only for intracranial meningiomas [14]. This would mean that, concerning gliomas, there is not enough evidence for possible medico-legal implications between previous

trauma and tumorigenesis [15]. Nevertheless, it cannot be excluded that, in some exceptional circumstances, previous head injury would have played a role in the pathogenesis of a later occurring brain glioma, particularly if the aforementioned criteria for postulating such a causal relationship are strictly fulfilled, as it was the case in the patient reported here.

Conclusions

In conclusion, we reported the case of a young adult who presented with an initially benign glioma, which later underwent a malignant transformation, who showed exactly the same location of a brain contusion which had occurred 25 years before. Although clear evidence of a causal relationship between previous trauma and later developing brain glioma is still lacking in epidemiological studies, the present case seems to indicate a true posttraumatic glioma due to the strict adherence to the criteria proposed in order to suggest a causal relationship between these two factors.

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Table 1. Criteria for diagnosing post-traumatic glioma [4]

- 1 The patient must have been in good health before the accident
- 2 The head injury must have been severe enough to cause brain contusion and scar formation
- 3 The site of the trauma and the tumor must correspond at either biopsy or autopsy, and the location of the injury must be morphologically demonstrable either in the meninges, the bone or the brain. The mode of injury must be elicited from the past history
- 4 The latent period between the injury and the development of the tumor must be adequate. It was consider that tumors arising less than 1 year after an accident are more likely to have caused the accident than to have resulted from it
- 5 The tumor must be characterized histologically or be obvious macroscopically. Confusion of tumor with glial scar tissue should be avoided.

Table 2. Criteria for diagnosing post-traumatic glioma [5]

- 1 Trauma should be histologically proved
- 2 Bleeding – edema and scars, either recent or old – should be distinguished clearly from the traumatic injury
- 3 The tumor should be in direct continuity with the traumatic scar and not merely in its vicinity or separated by a narrow zone of healthy or slightly altered tissue

Fig. 1. a MRI scan, T2 imaging and axial view: a deep left insular lesion in the temporal lobe is shown. b MRI scan, T2 imaging, and axial view: the lesion can be clearly seen as well as the partial resection of its anterior portion.

Fig. 2. **a** Histological sections of cerebral tissue with moderately increased cellularity constituted by astrocytes showing monotony in their appearance, elongated or round nuclei with occasional atypia, absence of mitosis, and somewhere gemistocytic aspect, featuring a diffuse astrocytoma. **b, c** Immunohistochemical examination reveals the positivity for glial fibrillary acid protein in the majority of cells (**b**) and CD68 in an area of pseudo-cystic degeneration (**c**). **d** Interstitial cells containing hemosiderin pigment are also present. **e, f** Examination of recurrent tumor biopsy at different magnification reveals marked hypercellularity with nuclear pleomorphism and mitotic figures (arrowhead), compatible with the diagnosis of anaplastic astrocytoma. **a, d–f** HE staining. **b, c** Diaminobenzidine as chromogen. **a–c, e** Original magnification, 100×. **d, f** Original magnification, 200×.

Fig. 3. **a** MRI scan, T1 imaging, and axial view: a deep slightly hyperintense lesion localized to the cavity related to the previous resections can be seen. **b** MRI scan, T1 imaging, and axial view: the lesion enhancement following gadolinium is shown.