MEDICAL IMAGING—CASE LETTER

Modification of MRI pattern of high-grade glioma pseudoprogression in regorafenib therapy

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[Correction added on [09 July 2021] after first online publication: The age of the subject in the study was corrected].

Abstract

Pseudoprogression (PP) is a diagnostic dilemma in the follow-up of brain high grade gliomas (HGG), and the introduction of new therapies has further complicated its identification in Magnetic Resonance Imaging (MRI). We report a case of pseudoprogression after intraoperative radiotherapy (ioRT) and Regorafenib therapy in a patient with anaplastic astrocytoma recurrence. A 65-year-old man, treated in August 2017 for a right frontal anaplastic astrocytoma, with surgical resection and following radiotherapy and Temozolomide, in October 2019 was again treated for peri-surgical bed recurrence with resection and ioRT followed by Regorafenib therapy, interrupted in February 2020, after the onset of adverse reactions. MRI examination showed a large irregular alteration posterior to the surgical bed, T2 weighted hypointense featuring strong diffusion restriction (low ADC values), with an irregular contrast-enhancement (CE) pattern, and surrounded by a vast vasogenic oedema; Dynamic Susceptibility Contrast (DSC) perfusion imaging (PWI) showed no increase of relative cerebral blood volume (rCBV). Particularly, lesion appeared markedly hypointense and dusty-like on susceptibility weighted images (SWI) probably due to a constant hemorrhagic diapedesis promoted by Regorafenib. Therefore, pseudoprogression was suspected. Follow-up MRI exams showed gradual reduction of SWI and CE abnormalities, but a persistent DWI restriction. Unfortunately, the last MRI control showed a secondary cerebellar localisation of the disease. New therapies are changing MRI pattern in HGG imaging and this case underlines how a multimodality approach is increasingly necessary. In particular, when using anti-VEGF drugs, SWI can have a crucial role in identifying therapy-related haemorrhagic changes.

Key words: high-grade glioma; pseudoprogression; Regorafenib; SWI.

Introduction

Pseudoprogression (PP) is a diagnostic dilemma in the follow-up of brain high-grade gliomas (HGG), and the introduction of new therapies has further complicated its identification in Magnetic Resonance Imaging (MRI).

We report a case of pseudoprogression after intraoperative radiotherapy and Regorafenib therapy in a patient with anaplastic astrocytoma recurrence.

Case report

A 65-year-old man was treated in August 2017 for a right frontal anaplastic astrocytoma (IDH 1 and 2 negative, MGMT 7%), with surgical resection followed by radiotherapy (60 Gy) and 12 cycles of Temozolomide. In October 2019, he was treated for peri-surgical bed recurrence by resection and intraoperative radiotherapy (20 Gy) followed by Regorafenib therapy (started in December 2019). New histopathology demonstrated

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glioblastoma (ATRX positive, MGMT 16%, IDH 1 and 2 negative) (Fig. 1). After the onset of adverse reactions, including fever, diarrhoea, oral ulcers, confusion, psychomotor impairment, aphasia and dysphagia, Regorafenib treatment was definitively interrupted in February 2020.

MRI examination (3 Tesla Skyra Siemens, Erlangen, Germany) showed a large irregular alteration posterior to the surgical bed with T2 hypointensity, susceptibility-weighted imaging (SWI) hypointensity, diffusion restriction with low apparent diffusion coefficient (ADC) values, irregular contrast enhancement (CE) and marked vasogenic oedema with cerebral swelling. Dynamic susceptibility contrast (DSC) perfusion imaging showed no increase of relative cerebral blood volume (Fig. 2). Therefore, pseudoprogression was suspected. In fact, the patient clinically improved and MRI performed after 1, 2 and 5 months (Fig. 3) showed gradual reduction of SWI and CE abnormalities, with persistent DWI restriction. Unfortunately, the last MRI showed a secondary cerebellar lesion (Fig. 4), and after few weeks, the patient died.

Discussion

Pseudoprogression is defined radiologically as a new or enlarging area of contrast enhancement occurring after combined adjuvant therapy of HGG, in the absence of true tumour growth, which subsides or stabilizes without a change in therapy and its diagnosis is essentially retrospective, with a typical time interval from the end of treatment of 3–6 months.[1-2]

Few studies have examined the MRI pattern in those patients with HGG undergoing Regorafenib therapy, a multikinase inhibitor targeting vascular endothelial growth factor (VEGF) receptors.[3,4]

Imaging findings of new therapies may be challenging, though some aspects may lead to the correct diagnosis. In our case, the lesion showed a conspicuous dusty-like SWI hypointensity, not previously reported in

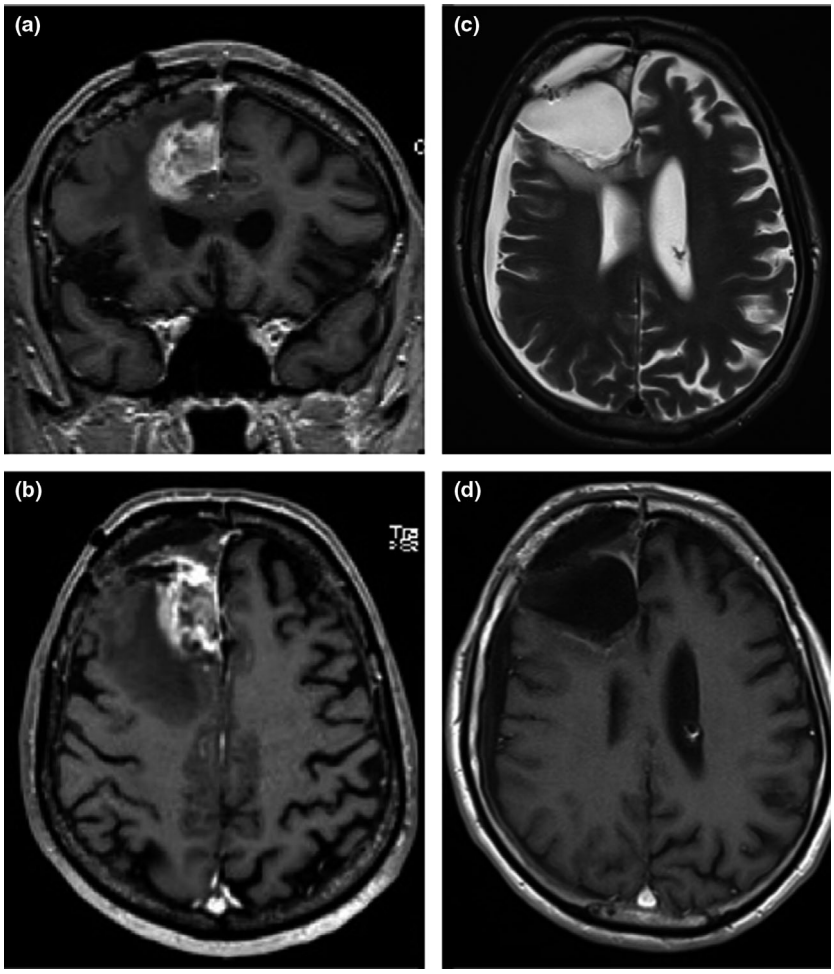

Fig. 1. Coronal (a) and axial (b) T1 contrast-enhanced (CE) MRI showing right frontal glioma recurrence. First post-operative MRI showing slight ring of contrast enhancement (d) and T2 hyperintensity outside the surgical bed (c).

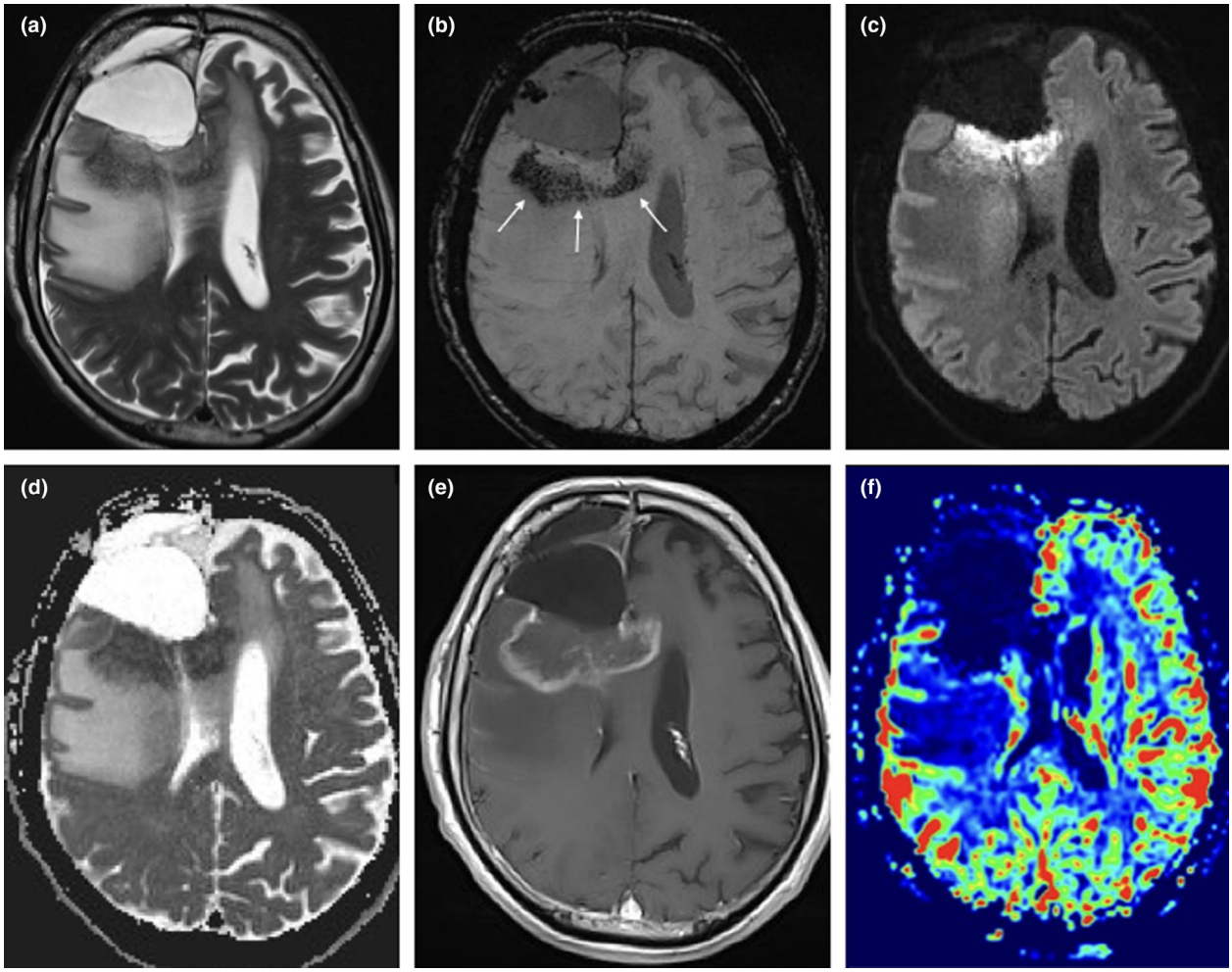

Fig. 2. Diffuse T2 hypointensity along surgical borders surrounded by a diffuse oedema (a), with marked SWI hypointensity (b, white arrows), strong DWI restriction (c) with low ADC values (d) and T1 irregular contrast enhancement (e). PWI showed no higher rCBV with respect to surrounding parenchyma (f). DWI, diffusion-weighted imaging; PWI, perfusion-weighted imaging; rCBV, relative cerebral blood volume; SWI, susceptibility-weighted imaging.

literature to our knowledge, and probably due to a constant haemorrhagic diapedesis promoted by Regorafenib. The lesion also showed DWI restriction, in most cases consistent with tumour recurrence. Nevertheless, a stable and prolonged (up to more than 3 months) restriction has been described in patients treated with Bevacizumab, resulting in a better overall survival.[2,5] The prolonged lesional 'benign' diffusion restriction could also be explained by a constant haemorrhagic diapedesis. In our case, persistent low perfusion values of the lesion established the leading sign of a pseudoprogression of the disease.[1]

New therapies are changing the MRI pattern in HGG imaging in some cases. This case underlines how a multimodality approach is increasingly necessary. In particular, when using anti-VEGF drugs, SWI can have a crucial role in identifying therapy-related haemorrhagic changes.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request. The data are not publicly available due to privacy or ethical restrictions.

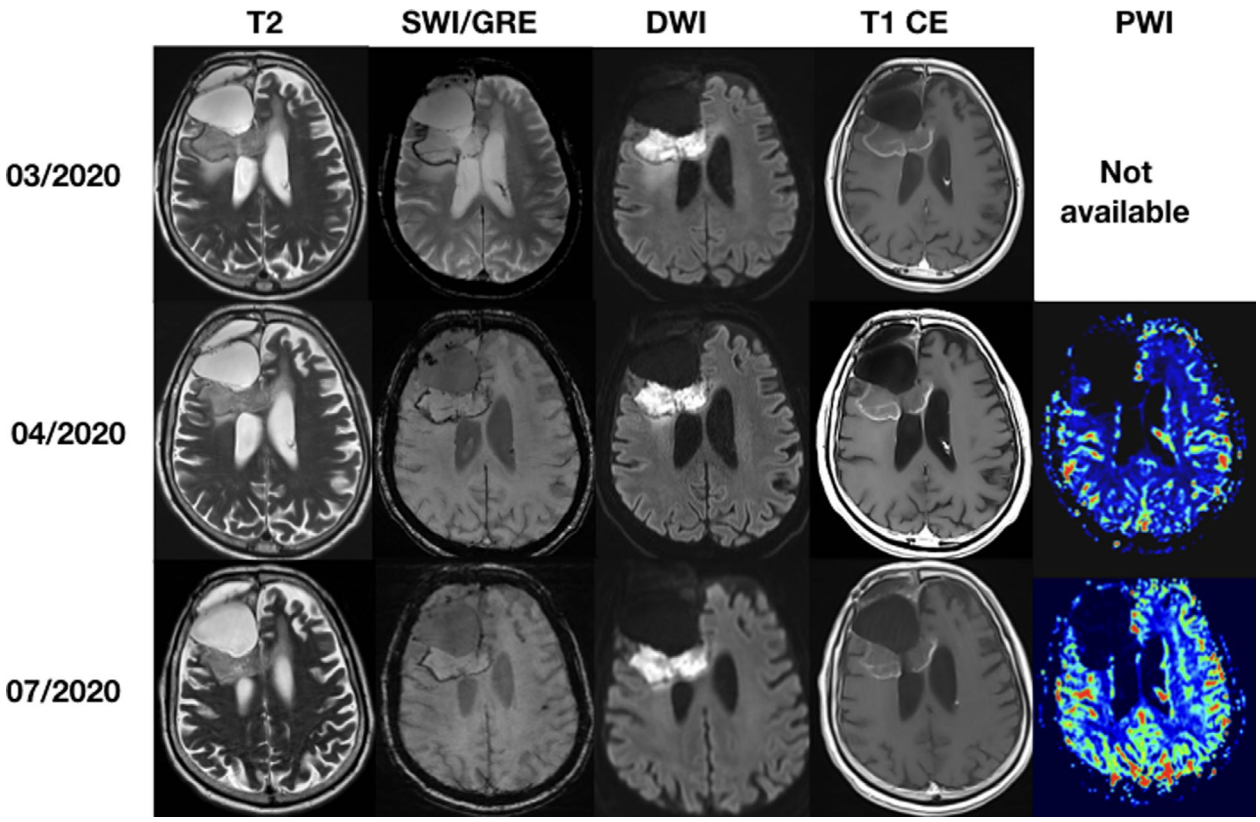

Fig. 3. MRI examinations after 1 (first row), 2 (second row) and 5 months (third row) showing progressive reduction of oedema and SWI-T2 hypointensity (first and second column), more regular linear contrast enhancement (CE) (fourth column) and persistent DWI restriction (third column). PWI (fifth column) showed persistent low rCBV values.

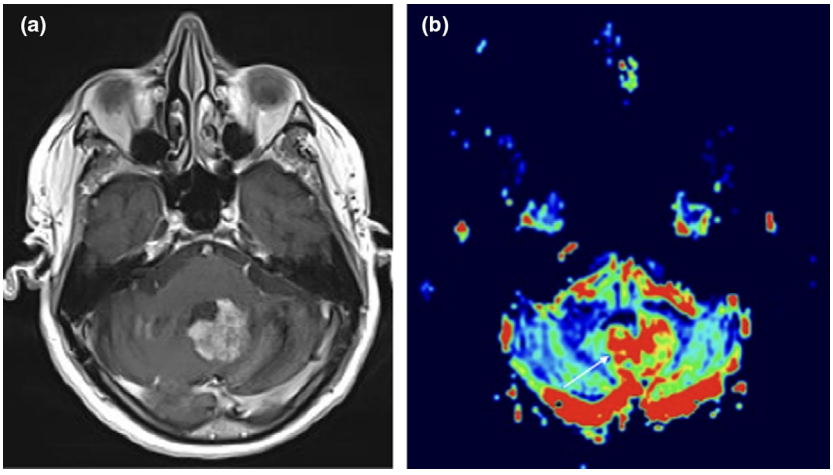

Fig. 4. MRI after 5 months: axial T1 contrast-enhanced scan showing cerebellar lesion near the fourth ventricle (a) with high rCBV values (b, white arrow).

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