Pseudoprogression after proton radiotherapy for pediatric low grade glioma

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To the Editor,

Pseudoprogression after photon radiotherapy for childhood low grade glioma has been recently reviewed [1]. Pseudoprogression is difficult to distinguish from real tumor progression with conventional magnetic resonance imaging (MRI); functional imaging techniques, such as perfusion MRI or amino acid positron emission tomography (PET) scans may be of diagnostic help [2,3].

We report the case of a 17-year-old child who developed pseudoprogression after proton radiotherapy for a low grade glioma.

Case presentation

In 2011, a 13-year-old girl, presented with symptoms of increased intracranial pressure, headache, nausea and intermittent double vision. An MRI demonstrated hydrocephalus caused by a left-sided non-enhancing mass, extending from the inferior thalamus into the tectum of the mesencephalon with occlusion of the aqueduct. A ventriculostomy was performed and biopsy of the lesion revealed a diffuse astrocytoma. Initial symptoms resolved without further intervention. The tumor was observed closely with MRI scans every six months.

In 2014, a small area of enhancement on post-contrast T1-weighted images was noted (Figure 1a). The patient remained asymptomatic. As a result of suspected tumor progression, the patient was referred for proton radiotherapy. She was treated with 50.4 GyRBE in 28 fractions to the tumor volume and a boost of 1.8 GyRBE in 1 fraction to the enhancing volume to a total dose of 52.2 GyRBE (the assumed RBE was 1.1). The treatment was well tolerated. An MRI six weeks after radiotherapy showed stable disease.

Four months after radiotherapy, the patient developed right-sided hypo- and dysesthesia, dysgeusia and diplopia. MRI revealed progression of the contrast enhancement (Figure 1b) and of high signal changes on T2-weighted series. Review of the radiation dose distribution showed that the area of increased enhancement was mainly located in the boost area, whereas the high signal changes on T2-weighted images were mostly located in the left side of the target volume. Pseudoprogression was suspected.

Perfusion-weighted MRI and ^{18}fluoro-ethyl-thyrosine(FET)-PET were performed for differential diagnosis. Perfusion-weighted MRI showed a small region with increased cerebral blood volume in the area of the enhancement, but it was difficult to interpret due to many vascular structures in the vicinity. FET-PET revealed tracer uptake in this area with a tumor/background ratio of 2.2, suspicious for pseudoprogression.

The patient was treated with high dose steroids (96 mg methylprednisolone), and the diplopia rapidly resolved. After two weeks, the steroid dose was

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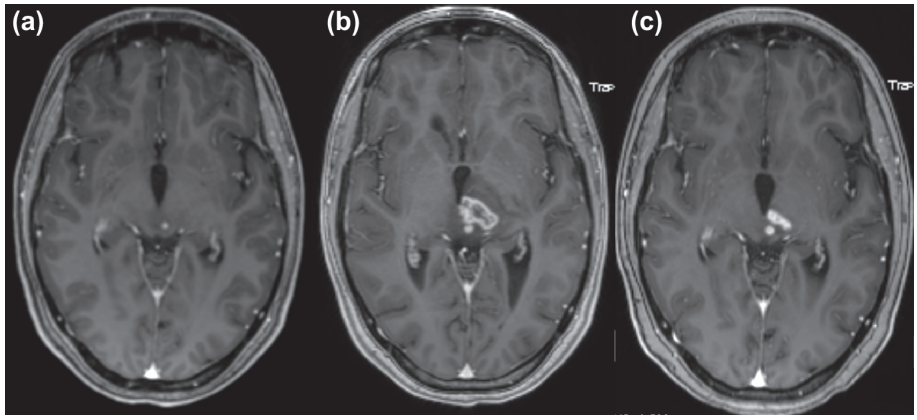

Figure 1. MRI T1-weighted image with contrast before and after proton radiotherapy. (a) MRI before proton radiotherapy showing a small area of contrast enhancement in the left superior colliculus. (b) MRI four months after completion of proton therapy showing progression of contrast enhancement. (c) MRI 10 months after completion of proton therapy showing decrease in contrast enhancement.

reduced and subsequently tapered. During this period, the patient experienced left-sided numbness in addition to the other symptoms, but this resolved rapidly after a short increase of the steroid dose. The right-sided dysesthesia resolved slowly. Right-sided numbness and dysgeusia were reduced but did not resolve completely. The girl continued to follow her high school education with a good performance. Treatment was complicated with a herpes zoster infection and the development of Cushingoid appearance leading to some social isolation. Steroid treatment was discontinued after six months.

MRI scans at Week 6, 12, and 24 showed decreasing T2 hyperintensity and contrast enhancement (Figure 1c), confirming the diagnosis of transient pseudoprogression.

Discussion

The occurrence of pseudoprogression after photon radiotherapy for pediatric low grade glioma appears to be more frequent and to develop later than in adult high grade glioma series. Patients with tumors in the brainstem or cervicomedullary regions seem to be at greater risk for pseudoprogression with more prolonged symptoms [1,4].

Pseudoprogression after proton radiotherapy for low grade glioma has been described in a 14-year-old boy after proton radiotherapy and in two patients from a mixed adult and pediatric series treated for low grade glioma [2,5].

The differential diagnosis between pseudoprogression and real progression is difficult. Increased blood perfusion volume in perfusion MRI in contrast enhancing lesions is suspicious for tumor progression [2,3]. In our case, perfusion MRI showed elevated blood perfusion volume, but the analysis was difficult to interpret because of the proximity of blood vessels that may have physiologically caused an increase in perfusion volume.

Amino acid PET has been used to distinguish tumor progression from radionecrosis [6]. FET-PET was also useful in our case study.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

[1] Naftel RP, Pollack IF, Zuccoli G, Deutsch M, Jakacki RI. Pseudoprogression of low grade gliomas after radiotherapy. Pediatr Blood Cancer 2015;62:35–9.

[2] Meyzer C, Dhermain F, Ducreux D, Habrand JL, Varlet P, Sainte-Rose C, et al. A case report of pseudoprogression followed by complete remission after proton-beam irradiation for a low-grade glioma in a teenager: The value of dynamic contrast-enhanced MRI. Radiat Oncol 2010;5:9.

[3] Kruser TJ, Mehta MP, Robins HI. Pseudoprogression after glioma therapy: A comprehensive review. Expert Rev Neurother 2013;13:389–403.

[4] Bakardjiev AI, Barnes PD, Goumnerova LC, Black PMcL, Scott RM, Pomeroy S, et al. Magnetic resonance imaging changes after stereotactic radiation therapy for childhood low grade astrocytoma. Cancer 1996;78:864–73.

[5] Hauswald H, Rieken S, Ecker S, Kessel KA, Herfarth K, Debus J, et al. First experiences in treatment of low-grade glioma grade I and II with proton therapy. Radiat Oncol 2012;7:189.

[6] Galldicks N, Dunkel V, Stoffels G, Hutterer M, Rapp M, Sabel M, et al. Diagnosis of pseudoprogression in patients with glioblastoma using *O*-(2-[-^{18}F]fluoroethyl)-L-tyrosine PET. Eur J Nucl Med Mol Imaging 2015;42:685–95.