Pseudoprogression

see also Pseudoprogression in Intracranial Metastases.

A purely radiological diagnosis of recurrence or progression can be hampered by flaws induced by pseudoprogression, pseudoresponse, or radionecrosis.

Peri-ictal pseudoprogression

Peri-ictal pseudoprogression

Terminology

Due to a overlap between the definitions of both pseudoprogression and radiation necrosis, it is not incorrect to say that pseudoprogression represents a mild and self-limiting variant of treatment-related necrosis.

Currently the most reliable and robust criteria for disease progression are the Response Assessment in Neurooncology (RANO) 2D criteria established in 2010, updated from the earlier established McDonald criteria

In particular, the newly recognized phenomenon of PsP (the transient treatment-related increase of contrast enhancement suggestive of tumor progression) and pseudoresponse (the early and rapid decrease of contrast enhancement without a true tumoricidal effect) are addressed in the RANO criteria. This pseudoresponse is most likely related to the introduction of TMZ and antiangiogenic targeted therapies in treatment protocols

Epidemiology

In almost 60% of cases pseudoprogression occurs within the first 3 months after completing treatment, but it may occur from the first few weeks to 6 months after treatment.

PsP can develop after radiotherapy alone but more frequently is present after concomitant radiotherapy and TMZ with occurrence in up to 30% of patients, especially those with O(6)-methylguanine-DNA methyltransferase (MGMT) promoter methylation [1) 2)].

Clinical presentation

Pseudoprogression can be observed in a context with or without clinical deterioration. However, it is asymptomatic in most patients.

Pathology

It is related to endothelial damage and consequent tissue hypoxia observed after treatment and it has an early occurrence (~60%), usually in the first 3 months after the treatment, but it may occur from the first few weeks to 6 months after treatment.

Impact of extent of resection

MGMT status and extent of resection EOR have a significant impact on psPD. Gross total resection GTR can reduce the side effects of psPD and prolong survival [3].

Differential diagnosis

Tumor progression

Radionecrosis

Case series

Of 43 evaluable patients, 25 (58%) exhibited radiographic progression on the first MRI after concurrent treatment. Twenty of these went on to receive adjuvant TMZ, and subsequent investigation demonstrated radiographic pseudoprogression in 10 cases (50%). Median survival (MS) was better in patients with pseudoprogression (MS 14.5 months) compared to those with true radiologic progression (MS 9.1 months, p=0.025). The MS of patients with pseudoprogression was similar to those who stabilized/responded during concurrent treatment (p=0.31). Neither the extent of the initial resection nor dexamethasone dosing was associated with pseudoprogression.

These data suggest that physicians should continue adjuvant TMZ in Glioblastoma patients when early MRI scans show evidence of progression following concurrent chemoradiotherapy, as up to 50% of these patients will experience radiologic stability or improvement in subsequent treatment cycles [4].

Glioblastoma Pseudoprogression

see Glioblastoma Pseudoprogression.

1)
Chakravarti A., Erkkinen M. G., Nestler U., et al. Temozolomide-mediated radiation enhancement in glioblastoma: a report on underlying mechanisms. Clinical Cancer Research. 2006;12(15):4738–4746. doi: 10.1158/1078-0432.ccr-06-0596
2)
Brandes A. A., Franceschi E., Tosoni A., et al. MGMT promoter methylation status can predict the incidence and outcome of pseudoprogression after concomitant radiochemotherapy in newly diagnosed glioblastoma patients. Journal of Clinical Oncology. 2008;26(13):2192–2197. doi: 10.1200/JCO.2007.14.8163

3)
Park HH, Roh TH, Kang SG, Kim EH, Hong CK, Kim SH, Ahn SS, Lee SK, Choi HJ, Cho J, Kim SH, Lee KS, Suh CO, Chang JH. Pseudoprogression in glioblastoma patients: the impact of extent of resection. J Neurooncol. 2015 Nov 25. [Epub ahead of print] PubMed PMID: 26608521.
4)
Roldán GB, Scott JN, McIntyre JB, Dharmawardene M, de Robles PA, Magliocco AM, Yan ES, Parney IF, Forsyth PA, Cairncross JG, Hamilton MG, Easaw JC. Population-based study of pseudoprogression after chemoradiotherapy in Glioblastoma. Can J Neurol Sci. 2009 Sep;36(5):617-22. PubMed PMID: 19831132.