Glioblastoma Pseudoprogression

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Pseudoprogression (PsP) is a transient magnetic resonance imaging (MRI) pattern mimicking tumor progression but not necessarily accompanied by clinical deterioration. It occurs most frequently during the first 3 months after radiation therapy and improvement will usually occur within a few weeks or months. PsP is more frequent in patients treated with concomitant temozolomide than in those receiving radiation therapy alone [1) 2)].

Pseudoprogression is primarily reported in patients who underwent radiotherapy for glioblastoma and was first described by Hoffman et al. in 1979. In a study of 51 patients with high-grade glioma, six patients (12 %) had increased computerized tomography (CT) enhancement following radiation, which later disappeared [3)]

Pseudoprogression (psPD) refers to an increase in size or appearance of new areas of MRI contrast enhancement soon after completing chemoradiation. The term is largely used in brain tumours imaging follow-up, especially for high grade gliomas (e.g. glioblastoma), when observed after chemotherapy and radiotherapy treatment (in about 30% of patients submitted to these therapy) or after just radiotherapy treatment (in about 15%).

Brain post-radiation treatment effects can be divided into pseudoprogression and radiation induced necrosis.

Chemoradiotherapy followed by monthly temozolomide (TMZ) is the standard of care for patients with glioblastoma multiforme (Glioblastoma). Case reports have identified Glioblastoma patients who experienced transient radiological deterioration after concurrent chemoradiotherapy which stabilized or resolved after additional cycles of adjuvant TMZ, a phenomenon known as radiographic pseudoprogression. Little is known about the natural history of radiographic pseudoprogression.

Epidemiology

The incidence of tumor pseudoprogression ranges from 28% to 66% in all glioblastoma patients undergoing chemoradiation and typically occurs within 3 months after the completion of concurrent

radiation and temozolomide [4].

Glioblastoma patients with promoter methylation of the repair enzyme 06-methyl guanine DNA methyltransferase (MGMT) may be at a higher risk of tumor pseudoprogression, with 91% (21 of 23 patients) of such patients developing early radiographic changes in one study [5].

Treatment

Approximately one-third of patients are symptomatic from tumor pseudoprogression and may require treatment with corticosteroids. Bevacizumab (Avastin), a humanized, monoclonal antibody against the vascular endothelial growth factor (VEGF)-A ligand might be efficacious in the treatment of radiation-related brain necrosis but has not been adequately studied or established as an effective therapy for symptomatic tumor pseudoprogression [6].

Although preliminary evidence suggests that concurrent treatment of newly diagnosed glioblastoma patients with chemoradiation and an inhibitor of VEGF may reduce the incidence of pseudoprogression, no VEGF inhibitor is yet approved for newly diagnosed glioblastoma, and follow-up studies are required [7].

Diagnosis of progression is complex given the possibility of pseudoprogression in glioblastoma. The Response Assessment in Neurooncology criteria increase the sensitivity for detecting progression.

Radiation necrosis and other normal responses associated with surgical treatment may lead to mimicking recurrent glioblastoma.

Kim et al. from the University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea, therefore developed and validated a radiomics model using multiparametric MRI to differentiate pseudoprogression from early tumor progression in patients with glioblastoma.

The model was developed from the enlarging contrast-enhancing portions of 61 glioblastomas within 3 months after standard treatment with 6472 radiomic features being obtained from contrast-enhanced T1-weighted imaging, fluid attenuated inversion recovery imaging, and apparent diffusion coefficient (ADC), and cerebral blood volume (CBV) maps. Imaging features were selected using a least absolute shrinkage and selection operator (LASSO) logistic regression model with 10-fold cross-validation. Diagnostic performance for pseudoprogression was compared with that for single parameters (mean and minimum ADC and mean and maximum CBV) and single imaging radiomics models using the area under the receiver-operating-characteristics curve (AUC). The model was validated with an external cohort (n = 34) imaged on a different scanner and an internal prospective registry data (n = 23).

Twelve significant radiomic features (3 from conventional, 2 from diffusion and 7 from perfusion MRI) were selected for model construction. The multiparametric radiomics model (AUC 0.90) showed significantly better performance than any single ADC or CBV parameter (AUC 0.57-0.79, P<.05), and better than single radiomics model using conventional MRI (AUC 0.76, P =.012), ADC (AUC 0.78, P =.014), or CBV (AUC 0.80, P=.43). The multiparametric radiomics showed higher performance in the external validation (AUC 0.85) and internal validation (AUC 0.96) than any single approach, thus demonstrating robustness.

Incorporating diffusion- and perfusion weighted imaging into a radiomics model improved diagnostic performance for identifying pseudoprogression and showed robustness in a multicenter setting [8].

Diagnosis

Glioblastoma Pseudoprogression Diagnosis.

Differential diagnosis

Glioblastoma Pseudoprogression Differential diagnosis.

1)
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