Glioblastoma Pseudoprogression Diagnosis

- Advances of MR imaging in glioma: what the neurosurgeon needs to know
- [(18)F]FET PET-Guided management of pseudoprogression in glioblastoma (FET POPPING): the study protocol for a diagnostic randomized clinical trial
- Oligodendroglioma pseudoprogression after radiotherapy in a dog: a case report
- Differentiation of tumor progression from pseudoprogression in glioblastoma patients with GRASP DCE-MRI and DSC-MRI
- A self-supervised multimodal deep learning approach to differentiate post-radiotherapy progression from pseudoprogression in glioblastoma
- Liquid Biopsy as a Diagnostic and Monitoring Tool in Glioblastoma
- A Radiologist's Guide to IDH-Wildtype Glioblastoma for Efficient Communication With Clinicians: Part II-Essential Information on Post-Treatment Imaging
- Evaluating Immunotherapy Responses in Neuro-Oncology for Glioblastoma and Brain Metastases: A Brief Review Featuring Three Cases

While pathologic diagnosis is the gold standard to differentiate true progression and pseudoprogression, the lack of objective clinical standards and admixed histologic presentation creates the need to (1) validate the accuracy of current approaches and (2) characterize differences between these entities to objectively differentiate true disease.

Wang et al. demonstrated using an online RNA sequencing repository of recurrent glioblastoma samples that cancer-immune cell activity levels correlate with heterogeneous clinical outcomes in patients. Furthermore, nCounter RNA expression analysis of 48 clinical samples taken from a second neurosurgical resection supports that pseudoprogression gene expression pathways are dominated by immune activation, whereas progression is predominated by cell cycle activity. Automated image processing and spatial expression analysis however highlight a failure to apply these broad expressional differences in a subset of cases with clinically challenging admixed histology. Encouragingly, applying unsupervised clustering approaches over segmented histologic images provides a novel understanding of morphologically derived differences between progression and pseudoprogression. Spatially derived data further highlighted polarization of myeloid populations that may underscore the tumorgenicity of novel lesions. These findings not only help provide further clarity of potential targets for pathologists to better assist stratification of progression and pseudoprogression but also highlight the evolution of tumor-immune microenvironment changes that promote tumor recurrence [1].

With conventional MRI, recurrences often have similar radiologic characteristics as therapy-related changes such as pseudoprogression (PsP) or radionecrosis, and its mutual differentiation remains challenging [2].

Modern multiparametric MRI techniques such as diffusion weighted imaging (DWI) with apparent diffusion coefficient (ADC) mapping, dynamic susceptibility-weighted contrast-enhanced perfusion imaging, and MR spectroscopy (MRS) allow a much deeper and still noninvasive insight into interpretation of brain lesions, resulting in greater specificity of diagnostic imaging, especially in combination with PET with radiolabeled aminoacid [3] [4] [5]. [6]. [7].

However, in routine practice, availability of advanced MRI as well as PET methods is limited with exception of DWI/ADC and MRS. DWI reflects changes in water diffusion as a result of changed tissue

microarchitecture due to tumor infiltration and can be quantitatively assessed with the ADC. MRS enables noninvasive examination of the spatial distribution of multiple metabolite concentrations in normal and pathological tissues.

ADCmean values ≤ 1300 × 10−6 mm2/s and tCho/tNAA ratio ≥ 1.4 are strongly associated with differentiating Glioblastoma recurrence from treatment-related changes indicative of PsP.

Institutional validation of cut-off values obtained from advanced MRI methods is warranted not only for diagnosis of Glioblastoma recurrence, but also as enrollment criteria in salvage clinical trials and for reporting of outcomes of initial treatment [8].

Surgical sampling and histologic review of MRI changes after chemoRT may not serve as a gold standard to distinguish psPD from true progression in Glioblastoma patients. Refinement of the histological criteria, careful intraoperative selection of regions of interest and advanced imaging modalities are needed for early differentiation of PsPD from progression to guide clinical management [9].

Dynamic susceptibility weighted contrast enhanced perfusion imaging

Patients with pseudoprogression (n = 13) had Vp (mean) = 2.4 and Vp (90 %tile) = 3.2; and Ktrans (mean) = 3.5 and Ktrans (90 %tile) = 4.2. Patients with tumor progression (n = 24) had Vp (mean) = 5.3 and Vp (90 %tile) = 6.6; and Ktrans (mean) = 7.4 and Ktrans (90 %tile) = 9.1. Compared with tumor progression, pseudoprogression demonstrated lower Vp perfusion values (p = 0.0002) with a Vp (mean) cutoff <3.7 yielding 85 % sensitivity and 79 % specificity for pseudoprogression. Ktrans (mean) of >3.6 had a 69 % sensitivity and 79 % specificity for disease progression. DCE MRI shows lower plasma volume and time dependent leakage constant values in pseudoprogression than in tumor progression. A cut-off value with high sensitivity for pseudoprogression can be applied to aid in interpretation of DCE MRI [10].

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