MRI in patients with High Grade Glioma - Pseudoprogression and Recurrence

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Objective:

Retrospective comparison to demonstrate the incidence of radiological progression, pseudoprogression and recurrence of high grade gliomas after treatment, thus highlighting the importance of post-operative day 1 (POD1) MRI.

Introduction:

Patients with histologically proven primary high grade glioblastoma underwent the current standard practice of post-operative concurrent chemoradiotherapy (CCRT) with Stupp's regimen using temozolomide at 75 mg/m2 /day during radiotherapy, and 150 to 200 mg/m2 /day on days 1-5 every 4 weeks for 6 cycles. Our centre established a protocol based scanning schedule with a magnetic resonance imaging (MRI) scan on day 1 after the operation, 2 weeks after completing CCRT, and every 3 months thereafter. Previously, Dr TM Chan et al [1] studied on 28 patients receiving the above treatment from 2005 to 2010, concluding that nearly half of all patients developed early radiological progression within 3 months of completing concomitant chemoradiotherapy, with about one in three of such patients having pseudoprogression. This study serves as a subsequent review of more recent patient data from 2015 to 2020.

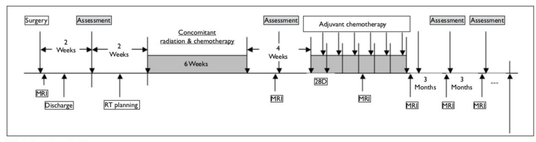


FIG 1. Scanning schedule
MRI denotes magnetic resonance imaging, and RT radiotherapy

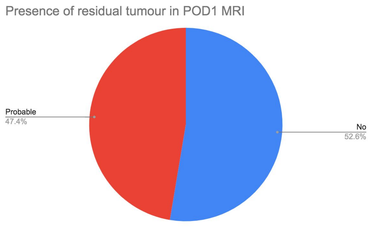
Patients:

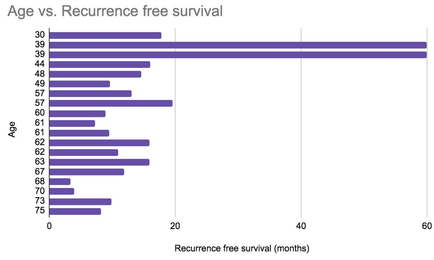
From 2015 to 2020, a total of 114 patients underwent operation for high grade gliomas in our institution. Among them 30 did biopsy, 58 had debulking surgery, and 26 had total resection. 19 patients with glioblastoma who performed total resection, concomitant CCRT and conformed to the above scanning schedule were included in this study. The mean age was 57 years old (range 30 - 75 years). Male to female ratio was 1:1.

Results:

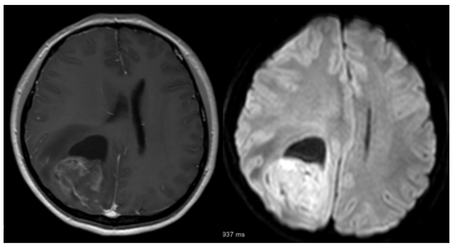
Among the 19 patients included, 10 of them showed no radiological features suggestive of the presence of residual tumour in their post-op day 1 MRI. 9 patients had probable residual tumour with POD1 MRI showing suspicious features including peripheral enhancement, nodular enhancing components, restricted diffusion and enhancement in subtraction series as commented by the reporting radiologists.

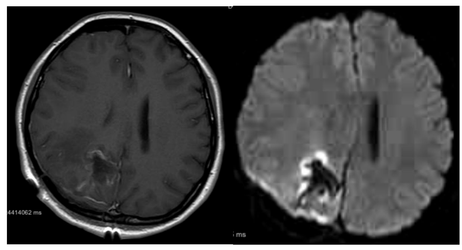
Recurrence free survival referred to the date from total resection surgery to the date of follow-up MRI imaging showing radiological features suggestive of tumour recurrence, or the date of death if MRI was not done beforehand. In the review, most (89%) had true disease progression. 2 patients (~10%) survived without disease recurrence. Their survival was counted as 5 years, with reference to systematic reviews and meta-analysis stating that the five-year survival rate for glioblastoma patients was less than 10%, with average length of survival estimated to be 12 to 18 months only.



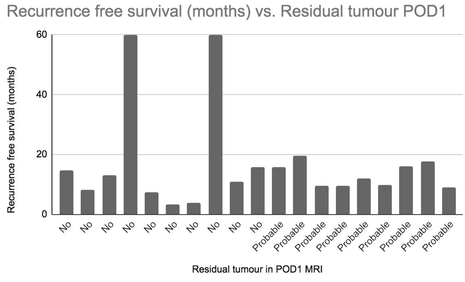


Below shows an example of having suspicious features of residual tumour in POD1 MRI. Pre-operative there is a large heterogeneously-enhancing mixed solid/cystic mass centered in the right medial parieto-occipital region with moderate amount of perilesional edema. In the POD1 MRI, there is a cystic defect compatible with post-excision change. The rim of the cystic defect shows restricted diffusion signal, residual malignancy cannot be excluded. Post-contrast scan shows mild internal enhancement and peripheral nodular enhancement.



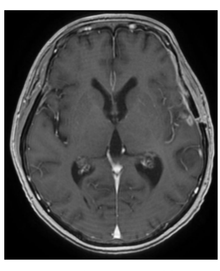


(Top left: Pre-operative stereotactic planning MRI series T1W with contrast. Top right: pre-op DWI sequence
Bottom left: POD1 T1W+C. Bottom right: POD1 DWI)

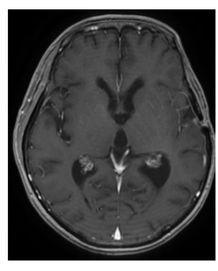


In the group of patients with probable features of residual tumour in POD1 MRI, there is a 100% recurrence rate. The mean time from operation to radiologically evidenced recurrence was 11.9 months, which is nearly a year. Among the patients without residual tumour shown on POD1 MRI, 2 out of 10 had no documented recurrence

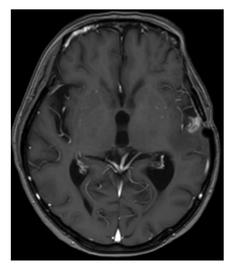
Pseudoprogression is defined as a new or enlarging area(s) of contrast agent enhancement occurring early after the end of radiotherapy, in the absence of true tumor growth, which subsides or stabilizes without a change in therapy. Only 1 out of the 19 patients had no radiological progression observed in follow-up imaging. 18 patients had different degrees of radiological progression, in which 7 of them (around 39%) had pseudoprogression. However, having pseudoprogression did not exclude the possibility of having tumour recurrence at other sites or in subsequent imaging.



2 weeks after completing CCRT



3 months after CCRT



6 months after CCRT

In the imagings above, there is an enhancing foci at the posterior surgical margin in MRI 2 weeks after the completion of CCRT, which is not seen in the POD1 MRI. It does not show restricted diffusion. Small volume of residual or recurrent tumour remains a consideration. In the MRI 3 months later, the previously seen enhancing foci shows interval partial resolution, suggesting that it is more likely treatment-related change. However, a new enhancing focus is found over the superior part of the curvilinear residual lesion in the left temporal fossa which is suspicious of local recurrence in the MRI 3 months after.

Conclusion:

Pre-operative and post-treatment MRI scans, together with careful interpretation, are pivotal in the assessment of disease progress of patients with high grade glioma. Despite best surgical efforts, around half of the patients had probable residual tumour after total resection. Patients who had suspicious features of residual tumour in POD1 MRI had a 100% recurrence rate, with a mean onset of recurrence of around 1 year. The pseudoprogression rate was about 39% among those with radiological progression, although pseudoprogression did not exclude future tumour recurrence.

References:

1. Danny TM Chan et al (2012). Pseudoprogression of malignant glioma in Chinese patients receiving concomitant chemoradiotherapy. Hong Kong Med J 2012;18:221-5
2. Oliver DM et al (2018). Utility of early postoperative magnetic resonance imaging after glioblastoma resection: implications on patient survival. World Neurosurg 2018;120:e1171-4
3. Michael TC Poon et al (2020). Longer-term (≥ 2 years) survival in patients with glioblastoma in population-based studies pre- and post-2005: a systematic review and meta-analysis. Nature 11622.