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Necrosis in Tumour Bed-is this Radiation Necrosis or Tumour Necrosis: Role of Dynamic Contrast Enhanced Perfusion MRI? First Step- Clinical Feasibility Study

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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ABSTRACT

Purpose of Study: To assess adequacy of relative cerebral blood volume (rCBV) and permeability index in differentiating radiation necrosis and tumour necrosis.
Materials and Methods: In this study we analyzed relative cerebral blood volume rCBV and permeability index from the enhancing areas to the contralateral white matter in 10 post treatment malignant brain lesions. The lesions were compatible with features of MR-morphological tumor progression. The diagnosis (real progression vs. radiation necrosis) was determined by histopathology or by clinical/MRI-follow-up.
Results: There were significant differences between tumor progression (*N* = 5) and radiation necrosis (*N* = 4) and mixed (N=1). An increased rCBV and permeability index are highly predictive of tumour progression.
Conclusion: Initial results of CBV and permeability map in differentiating tumor necrosis and tumor growth were highly promising.

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1. INTRODUCTION

Differentiating between tumor growth versus treatment related changes such as radiation necrosis is always a challenge in post treatment phase of high grade brain lesions.

Different researches have been carried out many MRI sequences to differentiate these [1]. MCDonalds criteria is being used in the assessment of conventional imaging [2]. However, with the addition of new chemotherapeutic agents and their responses to the primary lesion, these methods are becoming relatively less informative.

Advanced imaging techniques like PET and MRI perfusion are more informative [3].

There are certain different MRI Perfusion techniques using dynamic contrast enhanced arterial spin labeling and dynamic susceptibility weighted imaging. The results are very promising [3].

The objective of our study is to assess the role of dynamic contrast enhanced perfusion MRI using rCBV and permeability index as main criteria to differentiate between treatment related changes (radiation necrosis) versus tumor recurrence.

2. MATERIALS AND METHODS

This small size descriptive study was carried out at radiology department of a tertiary care hospital. The study was exempted from formal ethical approval as per institutional policy on retrospective studies. The requirement of informed consent was also waived.

Patients data were collected from January 2011 to December 2015.There were only ten patients who underwent MR perfusion scan since second surgery was not possible. This was either due to patient unfitness for surgery or refusal for a second intervention. The ten patients were referred for MR perfusion scan. All these patients were reported as having increase in size of lesions. We reviewed the medical records of these patients. Data extracted from the case files include age, sex, images, preoperative imaging features, surgical notes on tumor resection, histopathology results, rCBV and pernmeabilty index. The result of followup scan done within 1-3 months were also noted (Table 1).

2.1 MR Perfusion Technique

All patients underwent MR on 1.5 tesla Siemens Avanto with 16 channel head coils.0.2 mm/kg of gadolinium was injected via 18/20 gauge cannula at 3-7 ml/sec using a power injector. Successive images were obtained during first pass of contrast material through the brain. Relative concentration curves were obtained. Relative CBV was obtained by calculating the area under the concentration-time curves, normalized total contralateral uninvolved region. The word r(relative)is used for CBV, since its not a true CBV and the map is obtained and interpreted by comparing with the contralateral cerebral hemisphere map [4].

2.2 Image Interpretation

Images were reviewed on work station using Syngo software by neuroradiologist with either senior resident or neuroimaging fellow. Images were interpreted as tumor necrosis and growth. We found increased rCBV and increased permeability. Lesions were reported as necrosis when we found decrease in both rCBC and permeability. Nine out of ten patients had follow up scan and one had repeat surgery due to increase mass effect.

3. RESULTS

We had ten patients, two females and eight males. Mean age was 50.4 years (range 8-82). Lesion size ranged from 24 mm to 88 mm with a mean size of 5.4mm.The most common location was in the frontal lobe (80%).The lesions were biopsied and eight patients were proven to have GBM, one patient had Ewings sarcoma metastases while the remaining one had anaplastic oligodendroglioma.

All patients had follow up postoperative imaging at standard intervals on follow up. The first follow up was within 24-48 hours, at six weeks and then at three months.

All patients on concurrent radiation and chemotherapy were found to have increased lesion size in follow up scans.

Table 1. Patients demographics

No	Sex	Age	Primary characteristics of lesion on MRI	Histopathology	Post op resection	Post op radiation	Chemotherapy	CBV	PI	Follow up scan
1	M	8	Peripheral enhancement	Ewings	Biopsy	Yes	Yes	Increased	Increased	Increased in size
2	F	60	Large necrosis	GBM	Biopsy	Yes	Yes	Increased	Increased	Increased in size
3	M	40	Central necrosis	GBM	Gross total resection	Yes	Yes	Increased	Increased	Increased in size
4	M	32	Necrosis	GBM	Gross total resection	Yes	Yes	Increased	Increased	Increased in size
5	M	24	Solid and cystic	ANAPLASTIC OLIGO	Gross total resection	Yes	Yes	Increased	Increased	Increased in size
6	M	64	necrosis	GBM	Gross total resection	Yes	Yes	Reduced	Increased	Reduced in size
7	M	82	Peripheral enhancement	GBM	Gross total resection	Yes	Yes	Reduced	Reduced	Reduced in size
8	F	70	necrosis	GBM	Gross total resection	Yes	Yes	Reduced	Reduced	Reduced in size
9	M	64	Central necrosis	GBM	Gross total resection	Yes	Yes	Reduced	Reduced	Reduced in size
10	M	60	Central necrosis	GBM	Gross total resection	Yes	Yes	Reduced	Reduced	Reduced in size

The dose of radiation given was 4500 Gy administered over 5-6 days per week in doses of 1.8-2 Gy. Chemotherapeutic agents Temozolamide and Avastin were used concomitantly with the radiation.

The immediate postoperative scan showed increase in size of the lesion.

Five of our patients had a recurrence on follow up with increased r CBV and permeability index (Fig. 1). Four patients were reported as having radiation necrosis on the basis of decreased rCBV and permeability index. One patient was reported as inconclusive as there were decreased rCBV with increased permeability index. Despite technical corrections we were unable to exclude tumour necrosis since radiotherapy can disrupt blood brain barrier and consequently increase permeability. This patient had massive progression in size of the lesion and mass effect and underwent surgery. It was found to be a mixed picture of tumor growth with necrosis.

All patients including the one that had surgery underwent follow scans. Radiation was discontinued on four of the patients who had radiation necrosis. Chemotherapy continued with commencement of steroids and these patients showed significant reduction in size of lesions on follow up scans.

Five of the patients with a recurrence were continued on radiotherapy and chemotherapy and they also showed reduction in size of the lesion.

4. DISCUSSION

Necrosis can be seen in high grade neoplasms or it can occur as a complication of radiotherapy. It is important while planning for radiotherapy to have information on the following: amount of brain tissue included in the radiation port, type of radiation, location of the primary malignancy, and amount of time elapsed. It is also important in determining whether the imaging abnormality represents radiation necrosis or recurrent tumor [5]. Conventional magnetic resonance (MR) imaging findings of these two types overlap considerably, and even at histopathologic analysis, tumor mixed with radiation necrosis is a common finding. This we also found in one of our cases. Advanced imaging modalities such as diffusion tensor imaging and perfusion MR imaging, MR spectroscopy, and positron emission tomography can be useful in differentiating recurrent tumor and radiation necrosis [6]. Imaging plays a major role in the assessment of response to various treatment regimens for CNS malignant lesions. Mac Donalds criteria were used in assessing tumor response. According to this criteria, response is reported as complete response (when there is disappearance of all enhancing tumor on consecutive CT or MRI examination at least 1 month apart, no steroids and clinically stable or improved. Partial response is more than 50 percent reduction in size of enhancing tumor on consecutive CT or MRI examination at least one month apart on steroids or reduced steroids and clinically stable or improved. Progressive disease is more than 25 percent increased in size of enhancing tumour or new tumor on CT or MRI clinically worse stable or steriod stable disease or increased. Stable disease occurs in all other situations [7].

The current treatment regimens for all high grade primary lesions is surgery followed by concomitant radiation and chemotherapy with temozolamide. The use of conventional MRI in the assessment of pseudo progression and radiation necrosis is now limited as newer techniques such as MRI perfusion and PET scanning are now generating much interest.

Although our study is just an initial descriptive study it can be a beneficial tool in the future. We used rCBV and permeability index to assess radiation necrosis and tumor recurrence, Increased CBV and permeability index indicated tumor recurrence and reduced rCBV while permeability index indicated necrosis [8]. Out of the 10 cases we had, five had a recurrence, four had necrosis while one had a mixed picture.

Our major limitation was small sample size and inclusion of a metastatic deposit from Ewings sarcoma.

The results of our study was akin to earlier studies [9,10,11,12] in Table 2. This further encourages neurooncologists, neurosurgeons and neuroradiologits that it is a reliable tool.

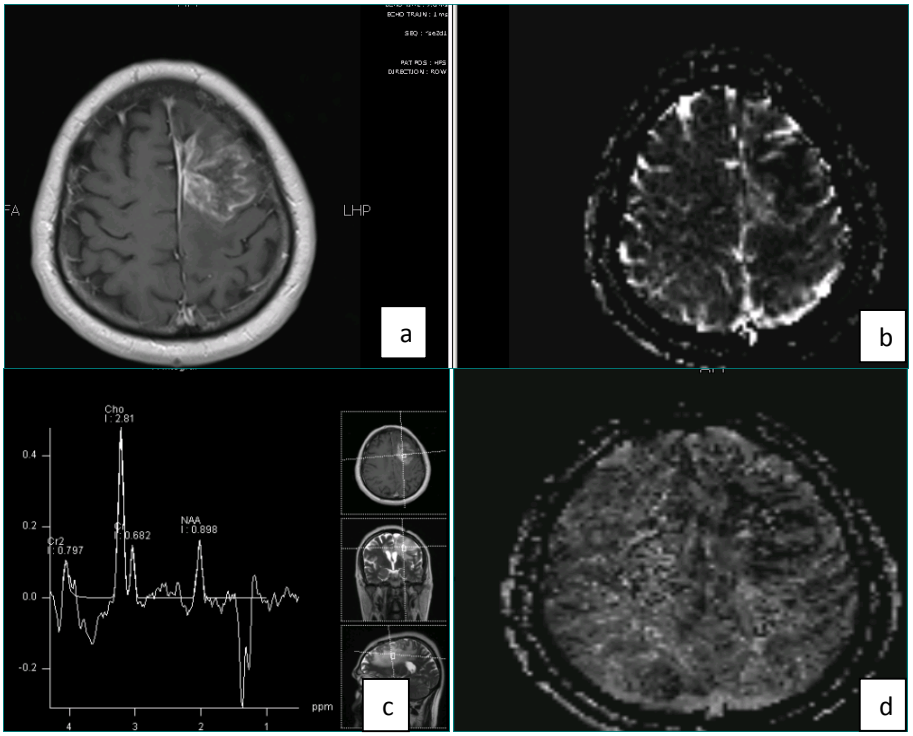

Fig. 1. A young male with diagnosed glioblastoma multiforme on follow up scan(a) shows tumour necrosis as evident by increased r CBV(b) and permeabilty index(d). MR spectroscopy(c) also performed which shows significant necrosis with tumour recurrence in surgical bed

Table 2. Comparative analysis with prior studies

S.no	authors	Results
1.	William R. Masch et al	The combined assessment of DTI and DSC MR perfusion properties of new contrast-enhancing lesions is helpful in distinguishing recurrent neoplasm from radiation necrosis in patients with a history of brain neoplasm previously treated with radiotherapy with or without surgery and chemotherapy.
2.	Ming-Tsung Chuang et al	There was evidence of heterogeneity regarding the rCBV values among the 10 studies (Q statistic = 311.634, I^2 = 97.11%, P < 0.001); therefore, a random-effects model of analysis was used. Pooled differences in means (2.18, 95%CI = 0.85 to 3.50) indicated the mean rCBV in a contrast-enhancing lesion was significantly higher in tumor recurrence compared with radiation injury
3.	S. Wanga et al	A combination of fractional anisotropy and maximum relative cerebral blood volume differentiated pseudoprogression from nonpseudoprogression (true progression and mixed) with an area under the curve of 0.807.
4.	Stella Blasel et al	The $rCBV_{max}$ differentiates tumor progression from TRC in unselected recurrent glioblastomas

5. CONCLUSION

We found CBV and permeability index as highly valuable tools in discrimination of tumor necrosis and radiation necrosis in highly malignant brain lesions.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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