Differentiation of Infective from Neoplastic Brain Lesions by Dynamic Contrast Enhanced MRI

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Introduction:

Magnetic resonance (MR) imaging is commonly used for differentiating infective from neoplastic brain lesion non-invasively. MR imaging techniques like magnetization transfer, MR spectroscopy and diffusion weighted and perfusion weighted imaging has been used to differentiate brain infection from neoplasm; it is still problematic to separate these conditions[1]. Endothelial permeability is a common feature of neo-angiogenesis[2]. Angiogenesis plays a crucial role in the growth and aggressiveness of brain tumor. It is also reported in the infective pathology in response to the expression of various cytokines[3]. The aim of this study is to assess the usefulness of physiological parameters i.e. permeability (k^{trans}) and leakage (v_e) which depend on the integrity of blood brain barrier (BBB), in differentiation of infective from neoplastic lesion.

Materials and Methods:

Study group: A total of sixty six untreated consecutive patients included in this study were classified in to three group 1) infective lesion (mean age±SD=26.6±9.31 years) [brain tuberculoma (n=18), brain abscess (n=6) and fungal granuloma (n=2)], neoplastic lesion containing 2) high grade glioma (HGG, n= 21, mean age±SD=47.5±11.3 years) and 3) low grade glioma (LGG, n=19, mean age±SD=36.28±11.20 years). The final grouping of all these lesions was based on the result of histopathology, microbial culture and response to specific therapy.

Perfusion imaging and Data Analysis: With informed consent all these patients underwent dynamic contrast enhanced MR imaging, using a three dimensional spoiled gradient recalled echo sequence [TR/TE-5.0/1.4 ms, flip angle-15º, The field of view -360x270mm, slice thickness-6mm, matrix size-128x128, NEX=0.5]. At the fourth acquisition, Gd-DTPA (0.2 mmol/kg) was administered intravenously at a rate of 5 ml per second, followed by a bolus injection of 30 ml saline flush. A series of 384 images in 32 time points for 12 slices were acquired with a temporal resolution approximately of 5.25 seconds[4]. Fast Spin echo T_1W and fast double spin echo PD and T_2W imaging was performed for the same slice position to quantify voxel wise pre contrast tissue T_{10}[4]. Images were registered for voxel wise analysis and de-scalped manually. The absolute tissue T_{10} value was used to generate concentration time curve from signal intensity-time curve[4]. Pharmacokinetic model was implemented for permeability (k^{trans}) and leakage (v_e) calculation[4]. k^{trans} and v_e were calculated by placing the region of interest (ROI) on the whole lesion of each slice. Contrast uptake curve using 95% confidence interval of mean was generated separately for infective lesion, HGG, and LGG. Scatter map of infective lesion, HGG and LGG were also plotted for k^{trans} and v_e at Y and X-axis respectively. Group wise descriptive statistics and ANOVA were performed. A linear discriminant analysis was performed to identify which factor is more efficient in classifying the group membership. All the statistical analysis was performed on SPSS-12.

Results:

The mean values of k^{trans} and v_e in infective lesion, HGG and LGG were 2.22±0.66 min^{-1}, 0.62±0.14, 1.23±.29 min^{-1}, 0.35±0.12 and 0.59±0.21 min^{-1}, 0.15±0.09. One way ANOVA showed significant difference ($p < 0.001$) for k^{trans} and v_e among all three groups. Discriminant analysis for classification illustrated that both k^{trans} and v_e combindely could predict 80.8% infective lesion and classified remaining 19.2% as HGG. Similarly it predicted 76.2% HGG correctly while remaining 19.0% as LGG and 4.8% as infective lesion. In case of LGG it classified 78.9% cases accurately and remaining 21.1% as HGG. The v_e classified correctly 84.6% infective lesion, 57.1% HGG and 78.9% LGG. The k^{trans} classified 80.8% infective lesion, 85.7% HGG and 94.7% LGG correctly. Contrast uptake curve at 95% CI of mean clearly showed highest uptake of contrast in the interstitial space of infective lesion compared to the HGG and LGG. Scatter map showed that average k^{trans} and v_e value of five infective lesions and some LGG were overlapping with HGG. A cut-off value of 1.5 min^{-1} for k^{trans} and 0.52 for v_e was derived to differentiate infective lesion from neoplastic lesion based on the scatter plot.

Discussion:

Significantly higher value of k^{trans} in intracranial infection suggests increased BBB permeability compared to neoplastic lesion. BBB opening in case of brain tumor is primarily depending upon the secretion of VEGF which has early short term effect[5]. Role of Bradykinin and leukotriene-C4 has been reported in long term increased permeability of brain tumor capillaries[6]. In infective brain lesion, a number of cytokines including VEGF are secreted[7]. These cytokines in turn up-regulate the expression of various cell adhesion molecules (CAMs) which are responsible for extravasation of inflammatory molecules and leukocytes through opening of the BBB by widening the endothelial gaps[8]. Weak expression of these CAMs on capillaries and large blood vessels in some HGG is also reported[9]. We hypothesize that these CAMs are responsible for large opening of BBB in infective lesion compared to the glioma and result in higher values of k^{trans} and v_e. Significant higher value of v_e in the intracranial infection suggests the presence of larger extracellular and extravascular space in which pooling of contrast occurred, compared to the neoplastic lesion. In this study, k^{trans} correctly classified 80.8% infective lesion without any overlapping of glioma in infective group and also high prediction of HGG (85.7%) and LGG (94.7%) suggested that k^{trans} can be used specifically for differentiating infective from neoplastic lesion and also HGG from LGG. Highest uptake of contrast in intracranial infection as shown in contrast uptake curve also signified the increased v_e in the current study. We conclude that adding these indices (k^{trans} and v_e) to the current imaging protocol is likely to further improve tissue characterization of these focal brain mass lesions.

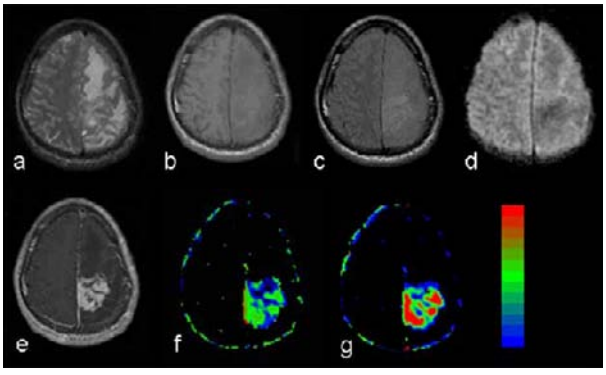

Figure1: Fungal granuloma in left parietal region of 32 year old male.T_2 W image (a) shows iso to slightly hyperintense irregular lesion with perifocal edema which appears isointense on T_1 W image (b) and slightly hyperintense on MT T_1 W image (c) with low signal intensity on DWI image (d). Post-contrast T_1 W image shows contrast enhancement (e). The k^{trans} (f) and v_e (g) for this lesion is 1.75 min^{-1} and 0.53.

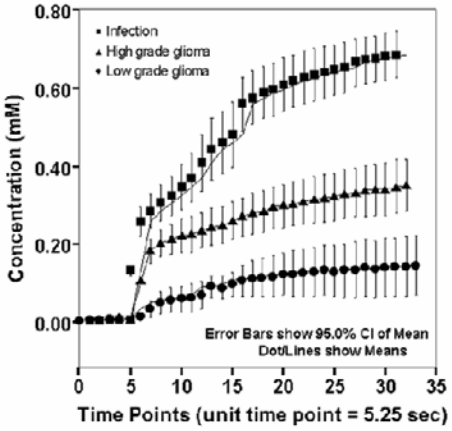

Figure 2: Contrast uptake curve is showing highest uptake of contrast in to the interstitial space of infective lesion

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