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ORIGINAL ARTICLE

Usefulness of the apparent diffusion coefficient for the evaluation of the white matter to differentiate between glioblastoma and brain metastases☆

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Abstract
Objective: To determine whether there are significant differences in the apparent diffusion coefficient (ADC) between the apparently normal peritumor white matter surrounding glioblastomas and that surrounding brain metastases.
Material and methods: We retrospectively reviewed 42 patients with histologically confirmed glioblastomas and 42 patients with a single cerebral metastasis. We measured the signal intensity in the apparently normal peritumor white matter and in the abnormal peritumor white matter on the ADC maps. We used mean ADC values in the contralateral occipital white matter as a reference from which to design normalized ADC indices. We compared mean values between the two tumor types. We calculated the area under the receiver operator characteristic curve and estimated the sensitivity and specificity of the measurements taken.
Results: Supratentorial lesions and compromise of the corpus callosum were more common in patients with glioblastoma than in patients with brain metastases. The maximum diameter of the enhanced area after injection of a contrast agent was greater in the glioblastomas ($p < 0.001$). The minimum ADC value measured in the apparently normal peritumor white matter was higher for the glioblastomas than for the metastases ($p = 0.002$). Significant differences in the ADC index were found only for the minimum ADC value in apparently normal peritumor white matter. The sensitivity and specificity were less than 70% for all variables analyzed.
Conclusions: There are differences in the ADC values of apparently normal peritumor white matter between glioblastomas and cerebral metastases, but the magnitude of these differences is slight and the application of these differences in clinical practice is still limited.

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PALABRAS CLAVE
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Utilidad del coeficiente de difusión aparente en la evaluación de la sustancia blanca para diferenciar glioblastoma de metástasis cerebral

Resumen
Objetivo: Encontrar diferencias significativas en la sustancia blanca peritumoral aparentemente normal entre gliobastoma y metástasis cerebral mediante la valoración del coeficiente de difusión aparente (CDA).
Material y métodos: Se revisaron retrospectivamente resonancias magnéticas de 42 pacientes con histopatología de glioblastomas y 42 pacientes con metástasis cerebral única. Se realizaron mediciones de intensidad de señal en el mapa de CDA sobre la sustancia blanca peritumoral aparentemente normal (SBPAN) y la sustancia blanca peritumoral alterada (SBPAlt). Se diseñaron índices normalizados de CDA utilizando valores medidos en la sustancia blanca occipital contralateral como referencia. Se compararon las medias para establecer diferencias entre ambos tipos de tumores. Se calculó el área bajo la curva (ROC) y se estimaron la sensibilidad y la especificidad para las mediciones realizadas.
Resultados: Los pacientes con glioblastoma presentaron con mayor frecuencia lesiones supratentoriales y compromiso del cuerpo calloso que los pacientes con metástasis cerebral. El diámetro máximo del área de realce tras la inyección de contraste fue mayor en los glioblastomas ($p < 0,001$). El valor mínimo de CDA medido en la SBPAN fue mayor en los glioblastomas que en las metástasis ($p = 0,002$). Solo se encontraron diferencias significativas en el índice de CDA para el valor mínimo de CDA en la SBPAN. Los valores de sensibilidad y especificidad fueron inferiores al 70% para las variables evaluadas.
Conclusiones: Existen diferencias en los valores del CDA de la SBPAN entre glioblastomas y metástasis, pero la magnitud de dicha diferencia es escasa y su aplicación en la práctica clínica aún es limitada.

Introduction

Brain metastases and glioblastomas are the most frequent encephalic tumors in adults resulting both in approximately 70% of parenchymatous intracranial neoplasms.[1] When it is a single metastasis, it is difficult to differentiate them from high-grade gliomas, since both their clinical manifestations and behavior in conventional magnetic resonance images (MRI) can be similar (both signal intensity in the basal study and the contrast enhancement pattern). On the other hand, the therapeutic strategies are different in both cases and this is why on certain occasions, biopsies are performed before initiating treatment, even with a known primary tumor. Nevertheless, biopsies are not the best option for some patients given their general functional condition or the location of the lesion in an eloquent area.[2,3]

Both metastases and glioblastomas can show extensive peripheral edema: the former of vasogenic origin, while in glioblastomas it is secondary to the infiltration of neoplastic cells in the perilesion region. Vasogenic edema is the result of the alteration of the hematoencephalic barrier and the neocapillaries that allow the escape of endovascular proteins into the interstice, with the subsequent increase of osmotic pressure and also of the amount of extracellular water. The peritumoral edema in glioblastomas, in addition to the changes in fluids homeostasis, correlates to the infiltration of tumor cells in the fibers of the white matter.[2] This is the difference that we have tried to identify through advanced MRI techniques such as spectroscopy (MRS), perfusion and diffusion through diffusion tensor with tractography (DTI) and apparent diffusion coefficient (ADC), since conventional MRI techniques do not allow us to identify the microscopic invasion of the adjacent white matter.[2,4] Although advanced techniques are useful to reduce the diagnostic spectrum of brain neoplasms, some authors have confirmed that the MRS has greater difficulties discriminating metastases from glioblastomas.[5,6]

The physical concept of diffusion refers to the molecular movement of water, which results isotropic when the means is homogeneous or disorganized, without barriers, whereas in the tissues both the cellular membranes and some architectural characteristics of the interstice limit the free directionality of movement (diffusion) of these molecules. MRI diffusion techniques provide us with information on the movement of the water protons in normal or pathologic brain tissue. The ADC shows mobility of both inter- and extracellular free water fraction, and the signal is smaller when movement is restricted, and greater when it is facilitated, that is, the image will be hypointense or hyperintense, respectively. This is so in such a way that, for instance, it is used to infer tumor degree based on cellularity and the probable nucleus-cytoplasm index of mass from the value shown in the diffusion restriction.[2,7]

Some studies have shown that there are no significant differences in the ADC measurements, in the tumor mass, between tumor metastases and glioblastomas.[8–10] Others have proven that the ADC in the abnormal peritumoral white