

MAGNETIC RESONANCE SPECTROSCOPY IN THE DIAGNOSIS AND ETIOLOGICAL DEFINITION OF BRAIN BACTERIAL ABSCESSES

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ABSTRACT - We report two patients with bacterial brain abscesses whose etiological diagnosis was correctly proposed by association of diffusion weighted images (DWI) and magnetic resonance spectroscopy (MRS) with conventional MRI. Both patients presented ring enhancing lesions with evidences of restricted diffusion. On MRS, the abscess caused by aerobic bacteria presented lactate and aminoacids peaks and the abscess caused by anaerobic facultative bacteria showed also acetate and succinate peaks. These results are in agreement with an unique previous study that related MRS pattern with bacterial etiology. Conventional MRI, associated with DWI and MRS is effective in diagnosing bacterial abscess and promising in exploring its etiology.

KEY WORDS: pyogenic bacterial abscess, spectroscopy, diffusion, magnetic resonance.

Espectroscopia por ressonância magnética no diagnóstico e definição etiológica dos abscessos bacterianos cerebrais

RESUMO - Apresentamos dois pacientes com abscessos bacterianos cerebrais cujos diagnósticos etiológicos foram corretamente auxiliados pela associação de difusão e espectroscopia à ressonância magnética convencional. Ambos apresentavam lesões com captação anelar de contraste e evidências de restrição à difusão de moléculas de água. Na espectroscopia, o abscesso causado por bactéria aeróbia apresentou picos de lactato e aminoácidos, enquanto o abscesso causado por bactéria anaeróbia facultativa mostrou, além destes, picos de acetato e succinato. Tais resultados concordam com um único estudo prévio que relacionou o padrão de espectroscopia nos abscessos com sua etiologia bacteriana. A ressonância magnética convencional, associada à difusão e à espectroscopia é uma técnica eficiente no diagnóstico de abscessos bacterianos e promissora em explorar suas etiologias.

PALAVRAS-CHAVE: abscesso cerebral piogênico, espectroscopia, difusão, ressonância magnética.

Abscesses can be defined as focal suppurative processes within the brain parenchyma and have been reported to account for 1%-2% and up to 8% of all intracranial space-occupying lesions in patients in developed and developing countries, respectively¹. Instead of the fact that general abscess are usually diagnosed by conventional magnetic resonance images (MRI), some bacterial abscesses may have a nonspecific clinical and morphological presentation, simulating those of cystic ring-enhancing mass lesions of varying etiologies¹. So, bacterial abscess may be misdiagnosed as inflammation caused by other etiologies, as fungal, granulomatous or even as necrotic tumors².

However, some particular details in conventional MRI may suggest the diagnosis and coupling diffusion weighted images (DWI) with magnetic resonance spec-

troscopy (MRS) has been explored by other authors to improve diagnostic specificity in focal brain lesions by enabling better lesion characterization¹. Besides, it may be possible to explore the etiologies of bacterial brain abscesses, differentiating anaerobic from other pyogenic abscess (ie, aerobic or sterile) on the basis of metabolite patterns seen with in vivo MRS¹.

Herein, we demonstrate that MRS coupled with DWI and structural MRI is helpful on characterize the etiology of bacterial abscess once the MRS pattern shows the metabolic products of specific bacterial groups.

METHOD

Patients - Patient 1 is a 16 years old male patient, with headache, fever and alteration in behavior that began 2

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weeks before. He had a previous head trauma and subsequent cerebrospinal fluid (CSF) fistula with spontaneous regression. MRI showed a left frontal lesion.

Patient 2 is a 58 years old male patient with diagnosis of Osler-Weber-Rendu disease since he was seven. He presented with 10 days headache. MRI showed a right temporal lesion.

Procedures – MRIs were performed in a 2T scanner (Elscent Prestige®, Haifa, Israel), with T1 and T2 acquisitions in three orthogonal planes, including T1-weighted “spin echo” (SE) gadolinium enhanced images. MRI acquisition parameters were: sagittal T1 SE, 6 mm thick, flip angle=180°; repetition time (TR)=430, echo time (TE)=12, matrix 200x350, field of view (FOV)=25x25 cm; T2 and proton density “fast spin echo” (FSE), 6 mm thick, flip angle=160°; TR=4800, TE=108/18, matrix 256x256, FOV=22x22 cm and T2- fluid-attenuated inversion recovery (FLAIR), TR=8500 and 2000 or 100 and 2200, TE=72 or 90, matrix of 256x296 and FOV of 22x22 cm. T1 SE gadolinium enhanced images were obtained in the 3 orthogonal planes. DWIs were acquired with TR/TE=500/107 ms, flip angle=180°, 6 mm thick, gap=20%, matrix 128x128, FOV= 37.3x23.1 cm, 1 nex, with 3 orthogonal gradients, B=0-700 s/mm².

Single voxel hydrogen magnetic resonance spectroscopy (MRS) was acquired using PRESS sequence (TR/TE=500/135 ms, number of excitation ((NEX)=200) with regions of interest (ROIs) of 8 cm³, centered in the lesions. Prior to the ac-

quisition, a localized shimming at the ROI was performed, followed by water suppression adjustment. Localized shimming was repeated to ensure good field homogeneity and until the 'H signal from water within the ROI became as narrow as possible. The spectra were post-processed using software supplied by the machine manufacturer (Elscent Prestige 2T, Haifa, Israel).

RESULTS

Both lesions were hyperintense in T2 weighted images (WI) and FLAIR and hypointense in T1WI with a ring of hyperintense signal on T1WI and hypointense signal on T2WI, with contrast peripheral enhancement and extensive surrounding edema (Fig 1).

DWI showed hyperintensity in both with a low signal in apparent coefficient diffusion (ADC) map (Fig 2). MRS showed many differences between the lesions. Patient 1 had aminoacid peak (0.9 ppm) and elevated lactate signal intensity (1.3 ppm) while patient 2 had a succinate (1.9 ppm) and acetate (2.4 ppm) peaks and also elevated lactate signal intensity (1.3 ppm) (Fig 3).

The lesions were surgically removed and culture revealed infection by *Streptococcus pneumoniae*, aer-

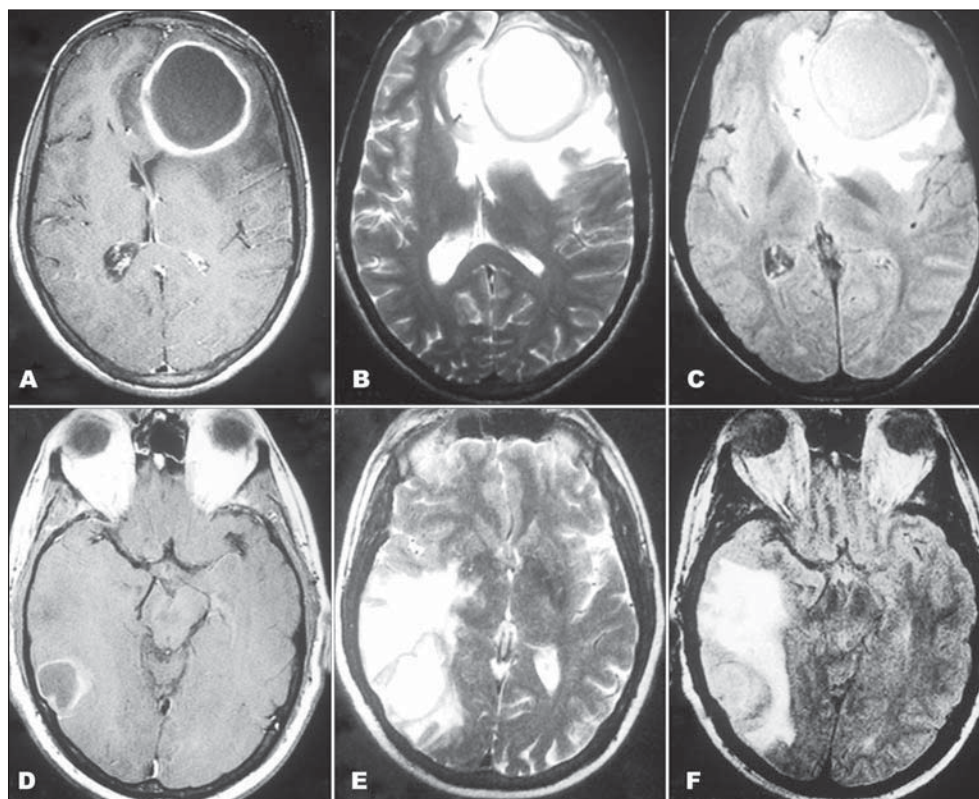


Fig 1. Large frontal rounded lesion in patient 1 (A, B, C) and temporal lesion in patient 2 (D, E, F) both with similar signals: hyperintense with hypointense halo in T2 (A and D) and FLAIR (B and E), hypointense in T1 with peripheral enhancement (C and F). Both are surrounded by extensive edema with mass effect.

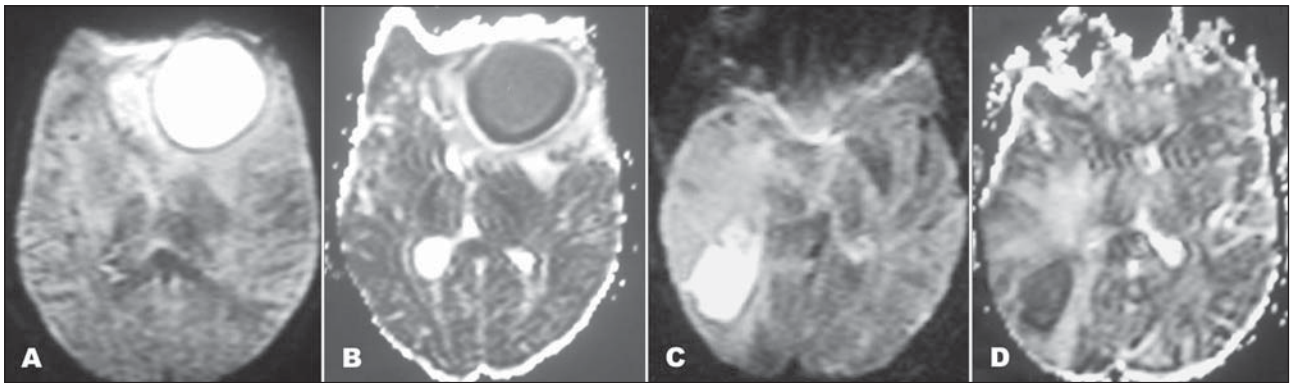


Fig 2. Patient 1 (A and B) and patient 2 (C and D) show lesions with restricted diffusion on DWI (A and C) and ADC map (B and D).

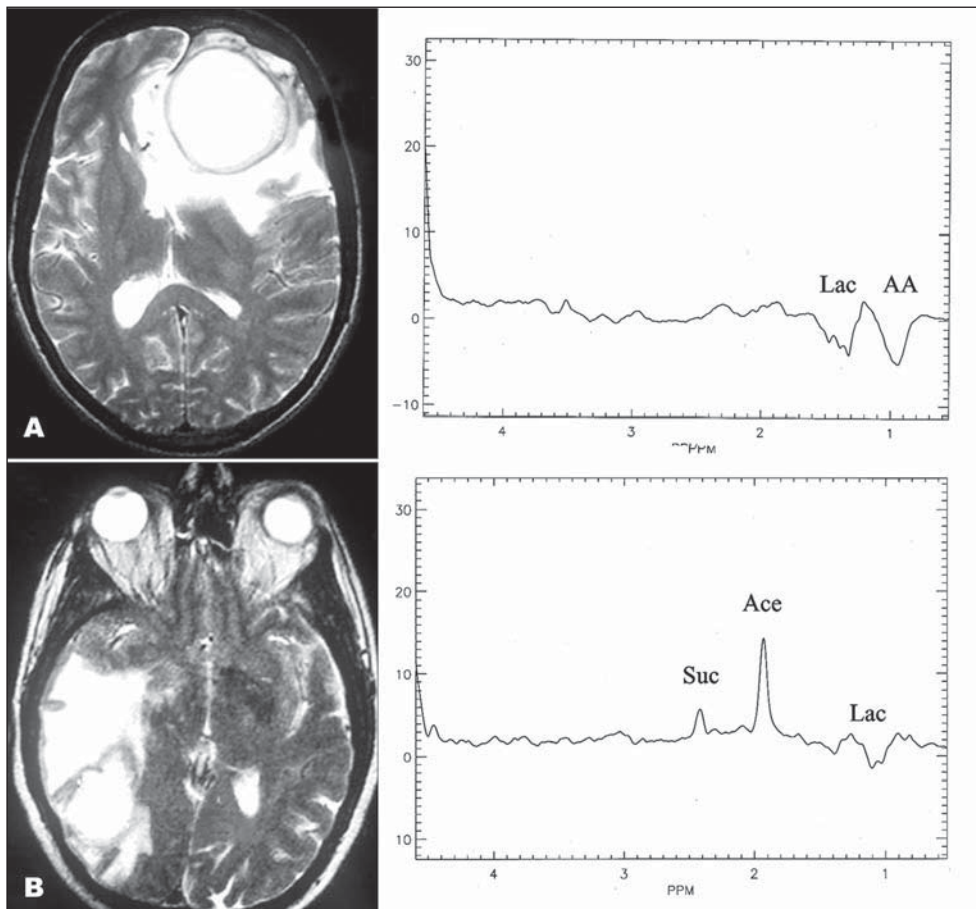


Fig 3. Proton MRS. Patient 1 (A) shows aminoacid peak (AA) and elevated lactate signal intensity (Lac), inverted in TE of 135 ms which makes it easy to differentiate from lipids signal. Patient 2 (B) had succinate (Suc) and acetate (Ace) peaks and also elevated lactate and aminoacid signal intensity. Both MRS performed in necrotic area display absence of characteristic peaks of brain tissue.

obe bacteria, in patient 1 and *Streptococcus milleri*, facultative anaerobe bacteria, in patient 2.

DISCUSSION

Abscesses usually are hyperintense in T2WI and hypointense in T1WI (as the most part of brain lesions) but bacterial abscesses have a particular con-

tinuous peripheral ring hypointense on T2WI and and hyperintense on T1WI, a feature that could relate to coagulative necrosis, increased accumulation of hemorrhagic products and paramagnetic materials such as iron, magnesium and manganese³, and production of free radicals, secondary to bacterial metabolism⁴. Unfortunately, some tumors and frequently fungal or

granulomatous abscesses (as occur in tuberculosis)^{5,6} present hemorrhagic areas producing the same alteration in peripheral signal intensity, making this finding suggestive of bacterial etiology, but nonspecific.

In addition to conventional MRI, DWI appears to be almost characteristic of bacterial abscesses. Pus is a viscous fluid content of inflammatory cells, mucoid protein, bacteria and necrotic tissue. Microscopic diffusion movement of water molecules are expected to be decreased in the cavity containing pus, whereas in necrotic tumor or cystic metastases, the cystic contents are less viscous, containing less inflammatory cells and more serous fluid^{7,8}. So, bacterial abscess produce high signal on DWI and low ADC values, ranged from 0.45 to 0.8⁹. This variation might be related to a difference in the concentration of inflammatory cells, and differences in necrotic tissue debris, bacteria, and viscosity of abscess fluid⁸⁻¹⁰. Other inflammatory processes as fungal disease, toxoplasmosis and necrotic portions of the tumors usually show lower signal intensity on DWI and higher ADCs¹¹.

However, recent studies have shown that restricted diffusion value is an important sign but is not specific for cerebral abscess. Restricted diffusion has been found in metastatic squamous cell carcinoma and radiation necrosis. The underlying pathophysiology is not known but probably due to sterile liquefaction necrosis. In sterile liquefaction necrosis, it may contain creamy pus like material with polymorphonuclear leukocytes¹².

Not enough, MRS also may corroborate the diagnosis of bacterial abscess and progress in etiological diagnosis. MRS is a noninvasive method to access, *in vivo*, the biochemical environment of a tissue producing direct or indirect information about the mechanisms of the disease progression and/or the host reaction to the aggression factor. Clinically, it may help to define the nature of different types of brain lesions by the metabolic profile. In some cases, it helps the differentiation among infections from other etiologies when conventional MR images are incomplete or inconclusive¹³.

Bacterial abscesses are completely necrotic lesions and so, all metabolites that characterize the SNC tissue are absent if the region of interest (ROI) is full located in the necrotic center. In fact, in both patients reported, peaks that characterize brain, as N-acetyl aspartate (NAA), considered a neuronal and axonal marker; choline, a constituent metabolite of cell membrane and myelin; and creatine, which plays a major role in energy metabolism, are absent¹⁴.

Lactate, an end product of anaerobic glycolysis and a considered marker of hypoxia, is elevated in both patients (identified as a reversed J coupled peak in 1.3 ppm in this applied TE (135 ms), that avoid lipid overlap). However, its elevation is nonspecific. Large lactate peaks have been commonly identified in necrotizing high-grade neoplasms, infarcts, demyelinating disease, encephalitis, cystic gliomas and in non-pyogenic abscesses including toxoplasmosis¹⁵.

Other peaks, indicative of abnormal tissue were identified. Both patients showed amino-acid signals at 0.9 ppm, seen in many brain abscesses and assigned to valine, leucine, and isoleucine, considered representing accumulated end-products of proteolysis caused by proteolytic enzymes secreted by microorganisms or polymorphonuclear leukocytes in pus, or both¹⁶⁻²². Patient 2, infected by an anaerobe facultative bacteria, presented acetate and succinate, considered being the end products of homolactic and heterolactic fermentation and key markers of bacterial infection²³⁻²⁵. Other infectious diseases as cysticercosis may also display succinate elevation²⁶.

Garg et al.¹, in an *in vivo* and *in vitro* study of 75 patients with brain abscess, also demonstrated differences in MRS according to bacterial etiology. Succinate and/or acetate were present in anaerobic infection. Latter, Lai et al.²⁷ showed the same findings in MRS performed in low and high magnetic fields²⁸. These metabolite resonances are probably the result of enhanced glycolysis and the fermentative pathways for energy generation⁴.

Results of studies focused on bacterial metabolism suggest that glycolysis is the universal cycle, irrespective of the aerobic or anaerobic nature of the bacteria. The pyruvate from glycolysis may enter into the tricarboxylic acid cycle in aerobes and in facultative anaerobes in the presence of oxygen. Alternatively, the pyruvate may follow the anaerobic fermentative route in anaerobes, where it may undergo carboxylation to form succinate via oxaloacetate, malate, and fumarate; and part of the pyruvate also forms acetate. The involvement of alternative anaerobic pathways for energy demands during acetate and succinate production by anaerobic bacteria may cause the appearance of these resonances in anaerobic abscesses. On the other side, the absence of acetate and succinate in the spectra of the patients with aerobes and facultative anaerobes can be explained by the fact that the pyruvate from glycolysis follows the tricarboxylic acid cycle. Although succinate is one of the intermediate metabolites of the tricarboxylic acid cycle it does not accumulate during its formation and immediately

transforms to the next intermediate compound. This phenomenon could result in the absence of succinate in the spectra of aerobe²⁹. Succinate was also earlier described as a marker for anaerobic infections in clinical samples at gas liquid chromatography²⁵.

Beyond MRS represents a potential tool for non-invasive diagnosis of brain abscesses, it might be useful for evaluating changes after treatment. With effectiveness of antibiotic therapy, a decreasing of these abnormal peaks, produced by infectious organism and intense host inflammatory reaction, and the lactate signal persists³⁰, besides the changes in signal and retraction of lesion at conventional MRI.

In conclusion, MRS coupled with structural MRI and DWI and MRS is effective and promising not only to diagnosing but also to explore the etiology of bacterial abscesses. In addition, it also may be a powerful tool to control the response to the treatment.

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