Functional imaging of a large demyelinating lesion☆

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Summary *Purpose.* To determine the metabolic characterization of a large solitary demyelinating lesion. *Methods.* Magnetic Resonance Spectroscopy (MRS) and Positron Emission Tomography (PET) studies with 2-deoxy-2-[F-18]fluoro-D-glucose (FDG), carbon-11-methionine (methionine) and carbon-11-choline (choline) were done on the demyelinating lesion. *Results.* The demyelinating lesion exhibited a low glucose uptake, prominent methionine uptake and a minimal choline uptake on the PET studies. MRS data revealed an increased choline to creatine (cho/cr) ratio and a decreased *N*-acetyl-aspartate to creatine (NAA/cr) ratio, which demonstrated a return to near normal ratios on follow-up study. *Conclusion.* The report summarizes the metabolic characteristics of a demyelinating plaque.

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INTRODUCTION

Brain lesions in multiple sclerosis (MS) may present as solitary mass lesions located in the white-matter and gray-white junction.[1] A typical clinical and radiographic features of large demyelinating plaques may lead to several erroneous differential diagnoses such as tumors, infection or demyelination from other causes.[2,3]

The diagnosis of MS, till recently, largely depended on the clinical course, which typically features an exacerbation and remission of multi-focal neurological deficits, electrophysiological tests, CSF analysis and imaging studies.[3] The advent of functional/metabolic imaging modalities such as magnetic resonance spectroscopy (MRS)[4–7] and positron emission tomography (PET) has revolutionized our concepts in many brain diseases, including MS.

We report an unusual case of multiple sclerosis presenting with subacute onset of focal neurological signs and a single, large enhancing lesion on the MRI. The lesion was further characterized using functional imaging modalities such as PET with different tracers (FDG, methionine, choline) and proton magnetic resonance spectroscopy (1H-MRS). We believe this is the first ever reported case of MS studied by methionine and choline PET imaging.

CASE REPORT

A 36-year-old lady presented with complaints of subacute (10 days) onset of dysarthria and right hemi-paresis. She had no neurological complaints prior to the present illness. She gave a history of mild hypertension for 2 years not requiring medication and was a chronic smoker. She had a family history for hypertension and diabetes.

Gadolinium enhanced magnetic resonance imaging (Gd-MRI) of the brain at the time of admission revealed a single enhancing 1.2×1.4 cm area of hyper-signal in the left corona radiata on T2-weighted images (Fig. 1). The differential diagnoses entertained were a low grade tumor vs a plaque of MS.

1H-MRS showed an increased peak of choline with a mean cho/cr ratio of 2.29 against a control of 1.79. The mean NAA peak was reduced with a mean NAA/cr ratio of 2.57 against 3.37 in the control. An elevated lactate peak was also noted (Fig. 2). The lesion volume was 2.6 cc. The findings on MRS strongly suggested a demyelinating pathology (Fig. 2).

A CSF analysis was then carried out to substantiate MS. CSF analysis showed no cells and an elevated protein of 65 mg%.

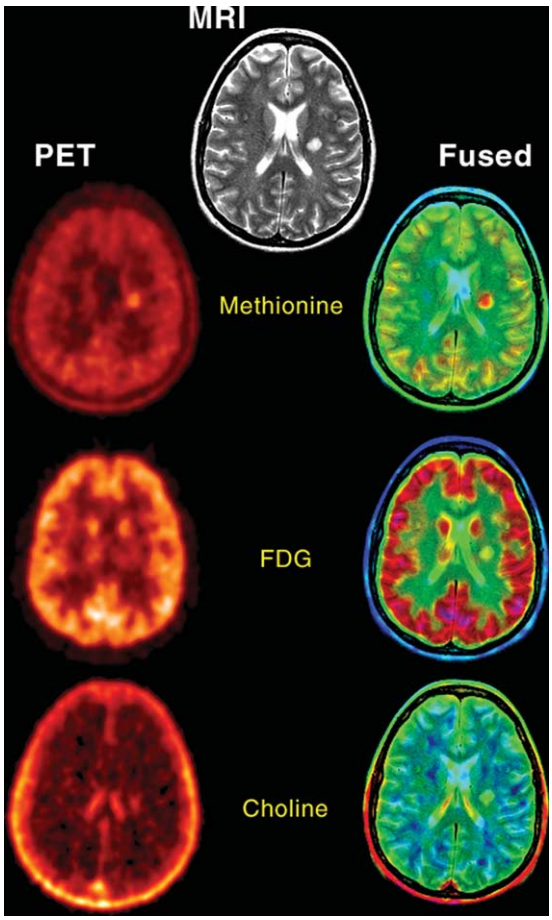

Fig. 1 Gd-MRI and the co-registered images of PET showing a single enhancing 1.2×1.4 cm area of hyper signal in the left corona radiata on T2-weighted images on the MRI of the brain; prominent methionine, mild glucose and choline uptake in the lesion.

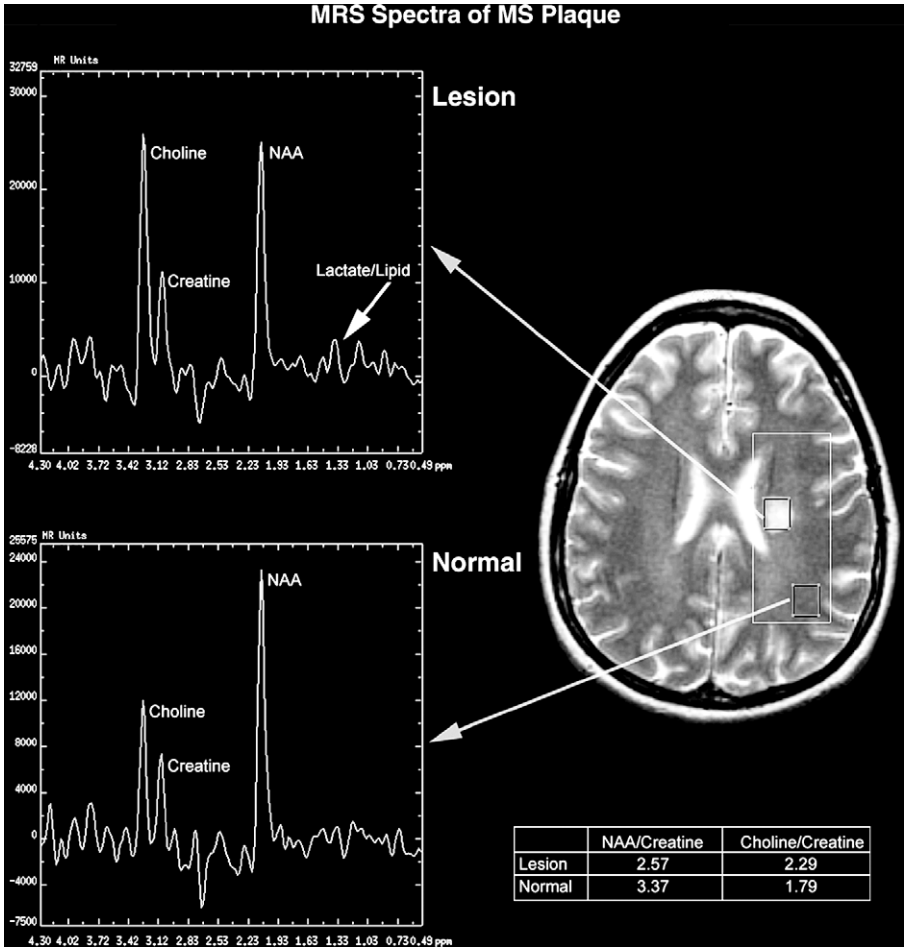

Fig. 2 1H-MRS image showing an increased peak of choline with a mean chol/cr ratio of 2.29 as against a control of 1.79 and a reduced NAA peak with a mean NAA/cr ratio of 2.57 as against 3.37 in the control.

There were no oligoclonal bands but myelin basic protein was positive.

Since the large size of the lesion provided an opportunity to determine the metabolic profile of the demyelinating lesion further, we categorized the lesion with FDG, 11C-MET and 11C-choline PET studies.

The glucose images demonstrated glucose uptake in the lesion which was more than white matter but much less than in cortical regions. The methionine study demonstrated a focal area of increased methionine uptake (35%) in the deep white matter of the left frontal parietal region corresponding to the enhancing abnormality noted on the MRI scan (Fig. 1). Choline PET imaging contrary to expectations revealed a mild focus of choline uptake, distinct from the surrounding normal brain tissue.

Following the CSF and the 1H-MRS report, the patient was diagnosed to have a demyelinating disease and was started on a short course of high dose steroids (1000 mg of solumedrol/i.v/day/3 days) followed by oral steroids tapered over the next 10 days. She improved rapidly and recovered fully with no residual neurological deficit over the next 10 days.

A repeat MRI scan done three weeks later showed a mild decrease in the initial hyperintense lesion in the left corona radiata. However, two other lesions were now seen. On the flair sequence in the white matter. This lent further credence to primary demyelinating plaques as the etiology. Repeat MRS study showed a decrease in the ratios closer to normal (NAA/cr: 2.53 vs 2.9 and cho/cr: 2.26 vs 2.1) (Table 1).

Table 1

	Initial study		Repeat study	
	NAA/cr	**Cho/cr**	**NAA/cr**	**Cho/cr**
Patient	2.57	2.29	2.53	2.26
Control	3.37	1.79	2.9	2.1

DISCUSSION

Imaging studies in MS usually reveal multiple small plaques ranging from a few millimeters to 16 mm in size. However, MS sometimes presents as a large solitary mass lesion that is indistinguishable from a brain tumor. Multiple sclerosis simulating a single mass lesion has been described in the literature.

Acute plaques are characterized by edema and some demyelination, while chronic plaques are characterized by gliosis, and to some extent, neuronal loss. There have been several studies of MRS in MS.[4–7] Acute plaques can show an increase of choline (Cho), lactate (Lac), and mobile lipid peaks (products of myelin breakdown). The increase of Choline signal is due to the release of phosphocholine and glycerolphosphocholine during active demyelination. In MS plaques, ^{1}H MRS has shown a reversible decrease of NAA, which suggests axonal damage and/or impairment. We found a relatively decreased NAA/cr ratio and an elevated cho/cr ratio in the lesion. This agrees well with reports in the literature. An elevated lactate peak represented inflammation.

MRS investigations have been further validated from the positive biopsy results in tumors with high in vivo choline peak.[7,8] Low grade gliomas in contrast are characterized by low NAA, strongly elevated choline and inositol and variable lactate levels.

The most widely used PET ligand for mapping the glucose metabolism in the brain is FDG. The amount of intracellular FDG is proportionate to the rate of glucose transport and intracellular phosphorylation. Very few studies have to date evaluated the MS lesions with FDG PET.[9,10] The few that were done have shown inconsistent results. Bakshi et al.[9] studied the regional glucose metabolism prospectively in MS using a high resolution FDG PET. When compared with controls, MS subjects demonstrated a 9% reduction in total brain glucose metabolism. The hypo-metabolism was widespread, including the cerebral cortex, sub-cortical nuclei, supratentorial white matter and infratentorial structures. Schiepers et al.[8] reported glucose metabolism by PET in 13 patients with MS. In most cases of stable MS, large lesions have a relatively increased glucose utilization. Active lesions in acute MS are also hyper metabolic. The quantitative cerebral abnormalities detected by FDG PET may serve as a marker of disease activity aiding in understanding the pathophysiological expression and therapeutic response of MS. The degree of glucose uptake may simply indicate the temporal stage of the demyelinating plaque. A very minimally increased glucose uptake was noted in our case, which was consistent with an inflammatory lesion.

Methionine is used to evaluate amino acid uptake and protein synthesis providing an indicator of tumor viability. There is little uptake of methionine into normal brain tissue. Accumulation of methionine into malignant cells is thought to be due to amino acid metabolism and incorporation of amino acid into protein fractions. Recent studies have suggested that the accumulation of methionine may also reflect amino acid active transport. Methionine uptake has also been seen at certain stages of non-tumor CNS diseases. This would imply uptake of the tracer as a result of the disruption of the blood–brain barrier as well as metabolic incorporation. There are reports in the literature of frontal hypertrophic cranial pachymeningitis revealed with methionine PET imaging. The thickened dura mater where the tracer accumulated was composed of inflammatory cells. Methionine uptake has also been seen in cases of brain abscess, hematoma, radiation necrosis and infarct.[10–12] The mechanisms of increased methionine uptake in inflammatory lesions are still unclear. There are no reports of methionine uptake in lesions of MS to date. The increased methionine uptake in the lesion implies once again the presence of inflammation.

Choline is a precursor for cellular membranes and acetylcholine synthesis. Various neuropathologies including degenerative diseases and tumors impact choline metabolism.[13] Studies using choline PET consistently gave high uptake images of the tumors surrounded by background of very low activity. Since increased choline turn over is expected in demyelinating disorders, it is logical to expect an increased choline uptake on PET study. Unlike the high uptake seen in tumors, we found a very faint uptake of choline in our patient. Once again, this may represent a stable plaque with relatively decreased rate of on-going demyelination. Since this is the first ever report of choline PET in a demyelinating lesion, we have not compared with different stages or types of MS lesions. It would certainly be interesting to study various demyelinating pathologies with choline PET.

The above report therefore sums up the metabolic characterization of a demyelinating lesion. The demyelinating plaque in our case exhibited a low glucose uptake, prominent methionine uptake and a minimal choline uptake on the PET studies. MRS data showed an increased cho/cr ratio and a decreased NAA/cr ratio, which demonstrated a return to near normal ratios on follow-up study.

REFERENCES

1. Kurihara N, Takahashi S, Furuta A, Higano S, Matsumoto K, Tobita M, et al. MR imaging of multiple sclerosis simulating brain tumor. Clin Imaging 1996; 20(3): 171–177.
2. Friedman DI. Multiple sclerosis simulating a mass lesion. J Neuroophthalmol 2000; 20(3): 147–153.
3. Annesley-Williams D, Farrell MA, Staunton H, Brett FM. Acute demyelinaton, neuropathological diagnosis, and clinical evolution. J Neuropathol Exp Neurol 2000; 59(6): 477–489.
4. Simone IL, Tortorella C, Federico F. The contribution of (1)H-magnetic resonance spectroscopy in defining the pathophysiology of multiple sclerosis. Ital J Neurol Sci 1999; 20(5): S241–S245.
5. Van Walderveen MA, Barkhof F, Pouwels PJ, van Schijndel RA, Polman CH, Castelijns JA. Neuronal damage in T1- hypointense multiple sclerosis lesions demonstrated *in vivo* using proton magnetic resonance spectroscopy. Ann Neurol 1999; 46(1): 79–87.
6. Bonavita S, Di Salle F, Tedeschi G. Proton MRS in neurological disorders. Eur J Radiol 1999; 30: 125–131.
7. Lee PL, Gonzalez RG. Magnetic resonance spectroscopy of brain tumors. Curr Opin Oncol 2000; 12(3): 199–204.
8. Schiepers C, Van Kecke P, Vandenberghe R, Van Oostende S, Dupont P, Demaerel P, et al. Positron emission tomography, magnetic resonance imaging and proton NMR spectroscopy of white matter in multiple sclerosis. Mult Scler 1997; 3(1): 8–17.
9. Bakshi R, Miletich RS, Kinkel PR, Emmet ML, Kinkel WR. High-resolution fluorodeoxyglucose positron emission tomography shows both global and regional cerebral hypometabolism in multiple sclerosis. J Neuroimag 1998; 8(4): 228–234.
10. Dethy S, Manto M, Kentos A, Konopnicki D, Pirotte B, Goldman S, et al. PET findings in a brain abscess associated with a silent atrial septal defect. Clin Neurol Neurosurg 1995; 97(4): 349–353.
11. Dethy S, Goldman S, Blecis S, Luxen A, Levivier M, Hilderbrand J. Carbon 11-methionine and fluorine – 18-FDG – PET study in brain hematoma. J Nucl Med 1994; 35: 1162–1166.
12. Jacobs A. Amino acid uptake in ischemically compromised brain tissue. Stroke 1995; 26: 1859–1866.
13. Shinoura N, Nishijima M, Hara T, Haisa T, Yamamoto H, Fujii K, et al. Brain tumors: detection with C-11 choline PET. Radiology 1997; 202(2): 497–503.

Aqueduct stenosis—?Benign

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Summary 'Benign' aqueduct stenosis is a common cause of hydrocephalus in the paediatric population and is frequently treated by endoscopic third ventriculostomy. Occasionally, aqueduct stenosis can be a prelude to the development of other pathology, as is seen in these two cases of pineal tumours developing in patients whose hydrocephalus was successfully treated with endoscopic third ventriculostomy. The case histories are presented, along with the recommendation for increased radiological screening of patients with this usually 'benign' presentation.

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