Assessment with Magnetic Resonance Imaging and Spectroscopy in Lhermitte–Duclos Disease

Chen-Hao Wu[1], Jyh-Wen Chai[1,3,4,5], Chen-Hui Lee[2], Wen-Hsien Chen[1,3], Tan Lee[1], Clayton Chi-Cheng Chen[1,3]*

Departments of [1]Radiology and [2]Pathology, Taichung Veterans General Hospital, [3]Department of Radiological Technology, Central Taiwan University of Science and Technology, [4]Graduate Institute of Medical Technology, National Chung Hsing University, and [5]School of Medicine, China Medical University, Taichung, Taiwan, R.O.C.

Lhermitte–Duclos disease (LDD) is a rare benign lesion of uncertain pathogenesis characterized by distortion of the normal cerebellar laminar cytoarchitecture. We report a 22-year-old man admitted for injury sustained in a traffic accident with the incidental finding of a cerebellar mass. Magnetic resonance imaging (MRI) revealed a mass lesion within the right cerebellar hemisphere. The final diagnosis of LDD was made by obtaining a surgical specimen and identifying the characteristic appearance of the lesion by MRI study. The images showed the typical striated pattern of hyperintensity on T2-weighted images and corresponding hypointensity on T1-weighted images, as well as the typical absence of enhancement following gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA) administration. In addition, no disturbance of water diffusion on diffusion-weighted MRI, and associations of decreases in the *N*-acetylaspartate/creatine (NAA/Cr) and NAA/Choline (Cho) ratios with near normal values of Cho/Cr, as well as an obvious lactate peak gave supplemental information for diagnosis. [*J Chin Med Assoc* 2006;69(7):338–342]

Key Words: diffusion-weighted imaging, Lhermitte–Duclos disease, magnetic resonance imaging, magnetic resonance spectroscopy

Introduction

Lhermitte–Duclos disease (LDD) is a rare benign lesion of the cerebellum. The disease is characterized by a cerebellar mass composed of enlarged cerebellar folia containing abnormal ganglion cells. It usually presents in young and middle-aged adults, commonly with a symptom of intracranial hypertension and cerebellar signs. However, it may remain asymptomatic until incidentally discovered at autopsy or by imaging study for an unrelated condition.

We present a case of LDD and describe the magnetic resonance imaging (MRI) signal characteristics and magnetic resonance spectroscopy (MRS) to confirm the relatively benign hamartomatous nature of this lesion.

Case Report

A 22-year-old man was generally well before admission to a local hospital for the treatment of right lower limb fracture sustained in a traffic accident. He denied any previous experience of abnormal gait and visual or hearing impairment. On admission, neurologic examination revealed no evidence of focal sensory or motor dysfunction. Unfortunately, brain computed tomography (CT) for survey revealed a space-occupying lesion in the right cerebellar hemisphere. The patient was subsequently transferred to our hospital for preoperative MRI study. All MRI images were acquired at 1.5T (Sonata, Siemens Medical Systems, Germany). The multisequence and multiplanar images, including

*Correspondence to: Dr Clayton Chi-Cheng Chen, Department of Radiology, Taichung Veterans General Hospital, 160, Section 3, Taichung-Kang Road, Taichung 407, Taiwan, R.O.C.
E-mail: chenhaowu@mail.vghtc.gov.tw • Received: October 26, 2005 • Accepted: February 23, 2006

T1-weighted, T2-weighted, fluid-attenuated inversion recovery (FLAIR), and diffusion-weighted were obtained, followed by gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA) contrast administration intravenously. In addition, proton MRS was performed. Spectroscopic data were acquired from the patient's cerebellar abnormality using a single-voxel (8 mL), point-resolved (PRESS) technique (TR/TE/NEX: 1,500/135/2). Spectral postprocessing was performed using the software provided by the MR system manufacturer.

MRI demonstrated a large mass lesion about 4.5 × 5 × 4.5 cm in the right cerebellar hemisphere. It was well circumscribed, with high signal intensity with respect to cerebellar white matter on FLAIR images (Figure 1A) and a striated pattern of high signal intensity on T2-weighted images (Figure 1B). The striations of the lesion were isointense to cerebellar gray matter on T2-weighted images and corresponded to the striated pattern with low signal intensity on T1-weighted images (Figure 1C). There was no obvious enhancement of the lesion following administration of GD-DTPA intravenously (Figure 1D). The mass appeared diffusely bright on diffusion-weighted images, whereas apparent diffusion coefficient (ADC) mapping revealed no restriction of water diffusion (Figure 2). Proton MRS showed an elevated lactate peak at 1.33 ppm, and association of decreased ratios in *N*-acetylaspartate/creatine (NAA/Cr) (1.2) and NAA/choline (Cho) (1.6), with near normal values of Cho/Cr (0.75) (Figure 3).

Because the patient was afraid of malignancy, subtotal resection of the tumor for tissue proof was

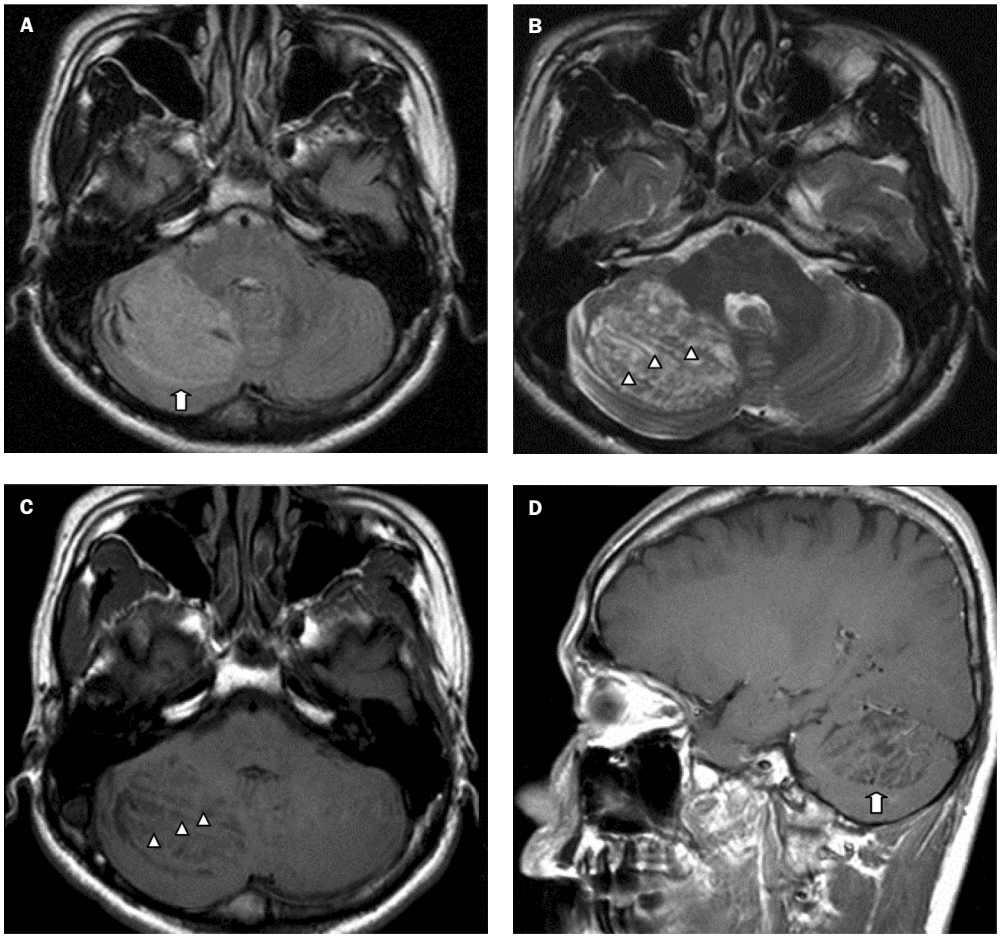

Figure 1. (A) Axial fluid-attenuated inversion recovery image [TR/TE/TI/NEX: 9,000/119/2,500/2] demonstrated a well-circumscribed mass about 4.5 × 5 × 4.5 cm in size in the right cerebellar hemisphere (arrow) with high signal intensity with respect to cerebellar white matter. (B) Axial T2-weighted image [TR/TE/NEX: 4,220/94/2] demonstrated a high signal intensity mass lesion with the characteristic striped appearance (arrowheads) in the right cerebellar hemisphere. (C) Axial T1-weighted image [TR/TE/NEX: 587/13/2] demonstrated a low signal intensity mass with multiple enlarged folia forming a characteristic striped appearance (arrow). (D) Sagittal T1-weighted image following administration of Gd-DTPA [TR/TE/NEX: 587/13/2]. A non-enhancing low signal intensity mass lesion (arrow) in the right cerebellar hemisphere was illustrated.

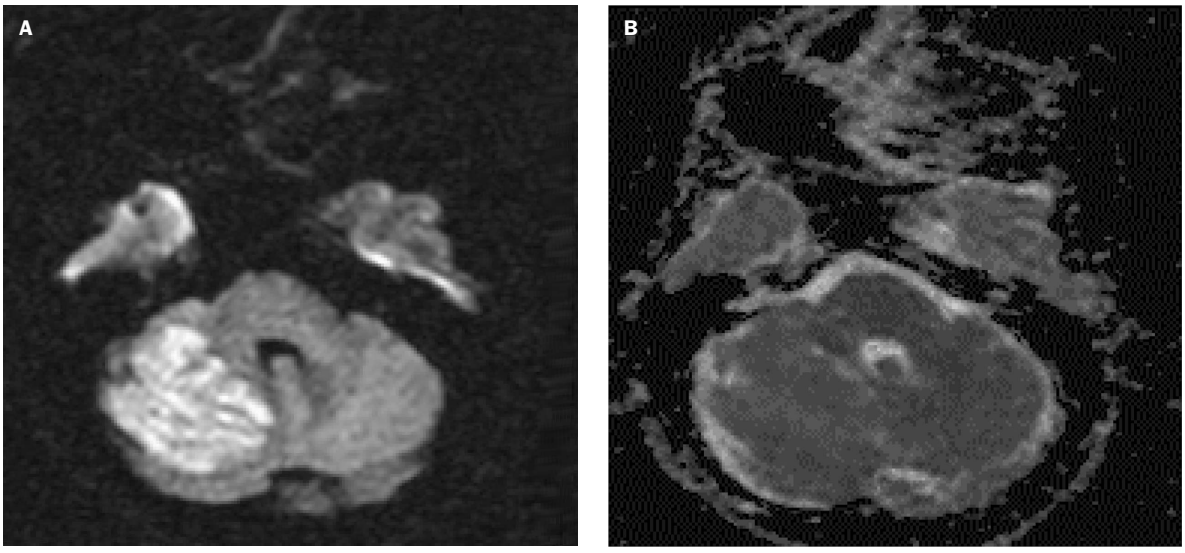

Figure 2. (A) Axial diffusion-weighted imaging performed using echoplanar sequence [TR/TE/NEX: 3,500/108/2, $b = 1{,}000$] demonstrated high signal intensity within the lesion. (B) On the corresponding apparent diffusion coefficient map, the lesion demonstrated no restriction of diffusion.

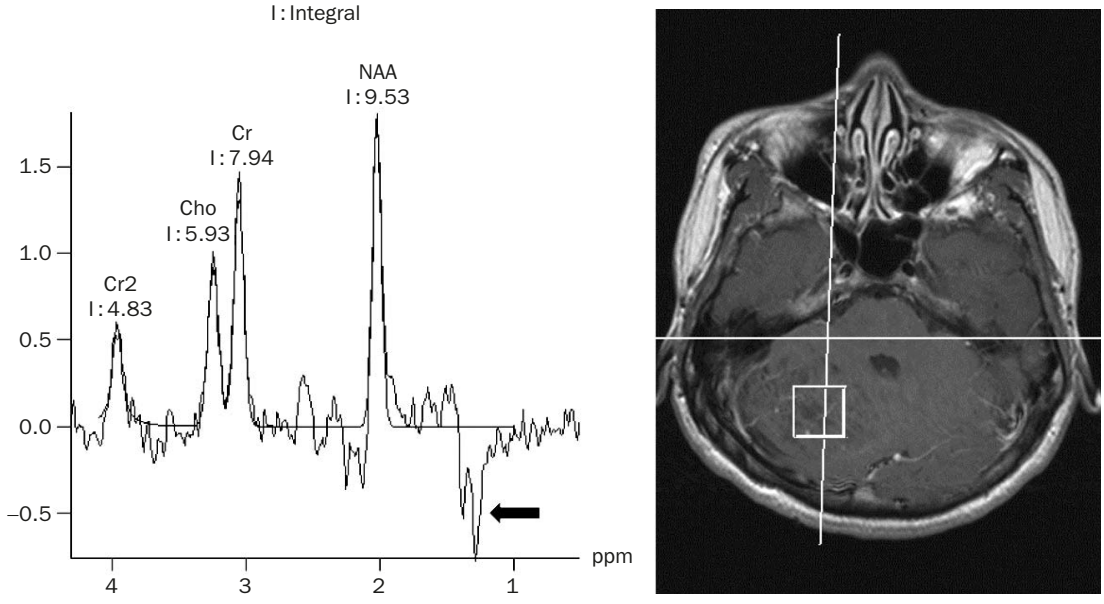

Figure 3. Magnetic resonance spectroscopy [single-voxel (8 mL), PRESS technique (TR/TE/NEX: 1,500/135/2)] showed elevation of lactate doublet at 1.33 ppm (arrow) and associations of decrease in the ratio of NAA/Cr (1.2) and NAA/Cho (1.6) with near normal values of Cho/Cr (0.75).

requested. After right paramedian suboccipital craniectomy was performed, moderate intracranial pressure was measured before the dura was opened. Upon opening of dura matter, a poorly-defined, whitish-brown mass lesion with hypovascularity extending throughout the right cerebellum was visualized. A specimen measuring about $2.5 \times 2 \times 0.5$ cm was taken out for histopathologic examination. On gross examination, the surgical specimen was characterized by thickening of the cerebellar cortex. On histopathologic examination of the tumor, we found that the granular layer had disappeared and was completely replaced by large ganglion-like neurons. Normal Purkinje's cells, between molecular layer and granular layer, were also absent (Figure 4). Those abnormal ganglion cells aggregated in the fibrillary matrix without any inflammation. After the pathologic diagnosis of LDD was made, a series of studies, including a more detailed

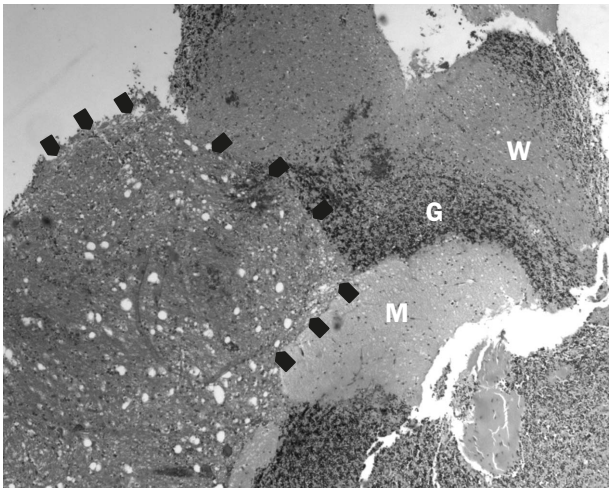

Figure 4. Photomicrograph of the fragmented brain tissue (hematoxylin and eosin stain, original magnification 40×) showed 3 visible layers of the normal cerebellum included the white matter (W), the granular layer (G), and the molecular layer (M) of gray matter. The thin Purkinje cell layer is between the granular layer and molecular layer. The tumor part (arrowheads) which should be the granular layer was replaced by a thick layer of abnormal ganglion cells.

physiologic examination to rule out Cowden disease, were performed. But no other skin or mucous membrane abnormality associated with Cowden disease or multiple hamartoma syndromes could be identified.

Discussion

In 1920, Lhermitte–Duclos described an unusual abnormality of the cerebellum, characterized by enlarged cerebellar folia, which contained circumscribed regions of abnormal ganglion cells. The authors originally described the lesion under the name of "ganglioneurome myélinique diffuse de l'écore cérébelleuse".[1] Subsequently, this disorder is now commonly classified as a diffuse ganglioneuroma of the cerebellar cortex,[2] (benign) hypertrophy of the cerebellum,[3] hamartoma of the cerebellum, gangliocytoma myelinicum diffusum of the cerebellar cortex, dysplastic gangliocytoma of the cerebellum, or simply LDD.

In the vast majority of cases, LDD manifests in adulthood (usually in the 3rd or 4th decade of life), but the age at presentation may vary from birth to the 6th decade. Patients with LDD may become symptomatic because of the mass effect from the lesion, with resultant intracranial hypertension, and cerebellar signs and symptoms. But LDD may remain asymptomatic until incidentally discovered at autopsy or in an imaging study for an unrelated condition. The disease is typically unilateral; however, LDD may extend into the vermis or, more rarely, into the contralateral hemisphere. Grossly, the tumor appearance is that of expanded cerebellar folia that efface the sulci.[4,5] The histopathologic characteristics include a thick layer of abnormal ganglion cells replacing the granular layer of the cerebellar cortex, a thick hypermyelinated marginal layer, and a thin Purkinje's cell layer with thinning of medullary white matter. Numerous associated abnormalities have been described in patients with LDD. These include megalocephaly, microgyria, spongioblastomas, peritheliomas, hydromyelia, partial gigantism, hemangiomas, polydactyly, macroglossia, and leontiasis ossea.[6] Coexistence of Cowden disease or multiple hamartoma syndromes, an autosomal dominant disorder of the skin and mucous membranes, with LDD has been described,[7] suggesting that this constellation of diseases represents a phakomatosis. In this syndrome, thyroid disorders are also common, and malignancies of the breast, colon and adnexa may also occur.[4]

The neuroimaging feature of LDD on unenhanced CT is hypoattenuating but may occasionally be isoattenuating in posterior fossa. Due to the inherent beam-hardening artifacts in the posterior fossa with CT, MRI is certainly the imaging modality of choice. On T1-weighted images, the striations have been described as hypointense and isointense, respectively, to cerebellar gray matter.[8] On T2-weighted images, the lesions are well circumscribed and have a unique striated pattern consisting of alternating bands of high signal intensity and normal signal intensity relative to cerebellar gray matter.[9] The majority of lesions appear very mild or with no enhancement following administration of intravenous Gd-DTPA. The lack of contrast enhancement suggests insignificant disturbances of the blood-brain barrier and/or absence of extracellular edema. The characteristic non-enhancing gyriform patterns correspond to the enlargement of cerebellar cortical folia. The enlarged folia lose their secondary foldings and asymmetrically widen the affected cerebellar hemisphere.[10] Kulkantrakorn et al[4] reported that the high signal intensity band seen on T2-weighted images corresponded to the inner molecular layer and the granular cell layer. Loss of central white matter within the folia also contributed to this appearance. The outer portion of the folia consisting of the outer molecular layer and leptomeninges within effaced sulci created the band isointense to cerebellar gray matter on T2-weighted images. On diffusion-weighted images, the lesion was characterized by higher signal intensities on diffusion-weighted images from T2 shine-through

effect, whereas ADC mapping showed no disturbance of water diffusion.[9] Two prior reports of 3 cases[9,11] demonstrated the same characteristics of diffuse-weighted images and ADC maps as our case. They presumed that this might be due to hypercellularity with diffuse replacement of the granular and Pukinje cell layers with ganglion cells and dense collections of axons throughout the molecular layer.[11]

Spectral peaks obtained from normal parenchyma include those that represent NAA-containing compounds (at 2.02 ppm), Cr (at 3.0 ppm), and Cho (at 3.2 ppm). The other peak, lactate, usually not detected in normal parenchyma, appears as a doublet (at 1.3 ppm). Nagaraja et al[12] reported that NAA/Cr and NAA/Cho ratios in LDD represent a decrease in the concentration of NAA, which could be attributed to a lack of neuronal architecture (a hallmark of hamartoma) and/or the presence of embryonic neural tissue, which fails to express NAA. If Cr is taken as an internal standard, the near normal values of Cho/Cr ratios in LDD indicate a lack of cell turnover or proliferation, and the pathology is unlikely to be tumorous. These results are in favor of "benign" hamartoma rather than a tumor.[12] In other cerebral neoplasia, a decrease in NAA or NAA/Cr ratio associated with an increase in Cho or Cho/Cr ratio is often reported.[13] This combination has also been described in cerebellar tumors.[14] On the other hand, decreased Cho/Cr ratios are not observed in cerebral malignant tumors, where increases in Cho levels are associated with enhanced membrane turnover. Lactate, normally undetectable in brain, accumulate in cysts, necrotic tissue, or within active tumors because of the high rate of glycolysis. Hence, the lactate peak suggests altered anaerobic metabolism. Klisch et al[9] and Nagaraja et al[12] considered that the elevated lactate level is due to an abnormal high glucose metabolism with the LDD, rather than representing high lactate level in cystic or necrotic components of LDD. Combined with the histopathologic findings of no necrotic areas within the LDD lesion, the elevated lactate levels do not represent cell death. Therefore, LDD has some characteristics of tumors such as decreased NAA and increased lactate, but not increased levels of Cho. In 1 of the 2 prior studies, Klisch et al[9] also mentioned decreased myoinositol/Cr ratio, and this finding was associated with astrocyte marker or cell volume regularity. They described that this peak could be visualized on shot TE MRS sequence, not on long TE as in our routine protocol.[15]

In conclusion, patients with LDD may demonstrate the typical striated pattern of hyperintensity on T2-weighted images and corresponding hypointensity on T1-weighted images, as well as the typical absence of enhancement following Gd-DTPA administration. In addition, the lack of restricted diffusion on diffusion-weighted MRI, and associations of decreases in the NAA/Cr and NAA/Cho ratios with near normal values of Cho/Cr, as well as an obvious lactate peak may suggest a benign hamartoma.

References

1. Lhermitte J, Duclos P. Sur un ganglioneurome diffuse du cortex du cervelet. *Bull Assoc Fr Etud Cancer* 1920;9:99–107.
2. Hallervorden J. Über die hamartome (ganglioneurome) des kleinhirns. *Deutsch Z Nervenheilk* 1959;179:531–63.
3. Duncan D, Snodgrass SR. Diffuse hypertrophy of the cerebellar cortex (myelinated neurocytoma). *Arch Neurol Psychiatr* 1943;50:667–84.
4. Kulkantrakorn K, Awwad EE, Levy B, Selhorst JB, Cole HO, Leake D, Gussler JR, et al. MRI in Lhermitte–Duclos disease. *Neurology* 1997;48:725–31.
5. Nowak DA, Trost HA. Lhermitte–Duclos disease (dysplastic cerebellar gangliocytoma): a malformation, hamartoma, or neoplasm? *Acta Neurol Sand* 2002;105:137–45.
6. Ambler M, Pogacar S, Sidman R. Lhermitte–Duclos disease (granule cell hypertrophy of the cerebellum): pathological analysis of the first familial cases. *J Neuropathol Exp Neurol* 1969;28:622–47.
7. Padberg GW, Schot JD, Vielvoye GJ, Bots GT, de Beer FC. Lhermitte–Duclos disease and Cowden disease: a single phakomatosis. *Ann Neurol* 1991;29:517–23.
8. Carter J, Merren M, Swann K. Preoperative diagnosis of Lhermitte–Duclos disease by magnetic resonance imaging: case report. *J Neurosurg* 1989;70:135–7.
9. Klisch J, Jeungling F, Spreer J, Koch D, Thiel T, Buchert M, Arnold S, et al. Lhermitte–Duclos disease: assessment with MR imaging, positron emission tomography, single-photon emission CT, and MR spectroscopy. *Am J Neuroradiol* 2001;22:824–30.
10. Robinson S, Cohen A. Cowden diseases and Lhermitte–Duclos disease: characterization of a new phakomatosis. *Neurosurgery* 2000;46:371–83.
11. Gul M, Mahanad I, Elias R. Diffusion-weighted MRI in Lhermitte–Duclos disease: report of two cases. *Neuroradiology* 2004;46:351–4.
12. Nagaraja S, Powell T, Griffiths PD, Wilkinson ID. MR imaging and spectroscopy in Lhermitte–Duclos disease. *Neuroradiology* 2004;46:355–8.
13. Howe FA, Barton SJ, Cudlip SA, Stubbs M, Saunders DE, Murphy M. Metabolic profiles of human brain tumors using quantitative *in vivo* 1H magnetic resonance spectroscopy. *Magn Reson Med* 2003;49:223–32.
14. Wang Z, Sutton LN, Cnaan A, Haselgrove JC, Rorke LB, Zhao H, Bilaniuk LT, et al. Proton MR spectroscopy of pediatric cerebellar tumors. *AJNR Am J Neuroradiol* 1995;16:1821–33.
15. Lara A, Romeu C. *MR Spectroscopy of the Brain*. Philadelphia: Lippincott Williams & Wilkins, 2004:4–5.