Primary cns lymphoma is difficult to diagnose biology essay

Science, Biology

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Abstract:

INTRODUCTION: Primary CNS lymphoma is difficult to diagnose with conventional imaging modalities. Magnetic resonance proton spectroscopy , dynamic susceptibility contrast DSC perfusion and diffusion weighted images has been recently investigated as a problem-solving tool for evaluation of primary CNS lymphoma with favorable results. AIM OF THE WORK: To assess the value of advanced neuro-imaging (MR diffusion, perfusion and proton spectroscopy) in diagnosis of primary CNS lymphoma . PATIENTS AND METHODS: Five adult patients with suspected primary CNS lymphoma (as suggested by clinical or conventional imaging techniques) were prospectively studied Magnetic resonance proton spectroscopy , dynamic susceptibility contrast DSC perfusion and diffusion weighted images aiming to confirm the suspected diagnosis. The examinations were done on 1. 5T machines using diffusion weighted , dynamic susceptibility contrast perfusion and chemical shift CSI imaging sequences . RESULTS: Regarding the DWI. All patients show low ADC values ranging from 0. 61 to 0. 67x 10-3mm2 /sec with mean ADC value 0. 63 ± 0. 025(SD) x 10-3mm2 /sec , Regarding the DSC perfusion. The max rCBV ratios are ranging from 0. 23 to 1. 52 with mean ratio 1. 14 ± 0. 54(SD). Regarding the MRI spectroscopy. Cho/Cr ratios are ranging from 1. 9 to 63 with mean ratio 19. 16 ± 26 (SD) , Cho/NAA

ratios are ranging from 3. 7 to 50 with mean ratio 14. 8 ± 19. 8, NAA/Cr ratios are ranging from 0. 09 to 1. 6 with mean ratio 0. 72 ± 0. 59, NAA/Cho ratios are ranging from 0. 02 to 0. 3 with mean ratio 0. 19 ± 0. 1 Lactate peak was found in 3 cases. Lipid peak was found in 2 cases. Myo inositol peak was found in one case . CONCLUSIONS: Restricted diffusion , relative hypo perfusion, Increased Cho/Cr, Cho/NAA , Decreased NAA/Cho , NAA/Cr and presence of lactate or lipid peaks are consistent imaging finding in CNS lymphoma . Keywords: , Primary central nervous system lymphoma , Magnetic resonance imaging , Diffusion weighted images , Perfusion weighted images , Proton magnetic resonance spectroscopy . Abbreviations: Primary central nervous system lymphoma (PCNSL) , Chemical shift imaging (SCI) , Dynamic susceptibility contrast (DSC). Diffusion weighted images (DWI).

INTRODUCTION

Primary central nervous system (CNS) lymphoma is defined as isolated involvement of the cranio-spinal axis with absence of primary tumor elsewhere in the body. It is considered as a rare occurrence, primary lymphomatous disease of the CNS occurs in both immunocompetent and immunocompromised patients (1) , The role of imaging is not limited only to provide anatomic details. In this paper , the value of the advanced magnetic resonance imaging techniques, such as MR diffusion, perfusion imaging and MR proton spectroscopy, in the diagnosis of adult CNS lymphoma is discussed (2). PCNSL constitute between 1 and 6% of malignant tumors of the CNS (3, 4) and 3–5% of all extra-nodal non- Hodgkin’s lymphomas. The

incidence is 0. 5: 1, 000, 000 per year (5) . Because clinical and imaging features of PCNSL differ between immunocompromised and immunocompetent patients (6), this study is limited to the immunocompetent patients. Non-Hodgkin’s B-cell variant is the predominant type of CNS Lymphoma in the Immunocompetent patients (7). B-cell primary CNS lymphoma occurs mainly at age around 50 years and is more frequent in men. The most common presenting symptom at occurrence are altered mental status, headache, nausea, hemiparesis, cerebellar manifestations , cranial nerve palsies, and visual disturbances (7&8). CSF analysis diagnose about less than half of patients with B-cell primary CNS lymphoma (8) . Recently the increasing use of chemotherapy and chemoradiotherapy extends the survival of the patients (9) . However, histologic confirmation is required before starting therapy. Because lymphomatous lesions are large in size at their initial presentation and the use of steroids compromises the diagnostic yield of resection, stereotactic biopsy or CSF examination (10) . Identification of PCNSL by imaging criteria is mandatory to avoid steroid medication and to facilitate attempts at biopsy rather than resection which does not improve prognosis (11) . Primary CNS lymphoma may arise from any region of the brain however, the most common site of origin is deep hemispheric periventricular white matter. It can arise also from the Corpus callosum, cerebellum, orbits, and cranial nerves (12). In conventional MR imaging techniques . Most of the lymphomas appear hypo- or iso intense on T1-WI, variable signal intensities yet predominantly hypo intense on T2-WI and show avid enhancement after contrast administration (13) . The MR imaging findings of cerebral lymphomas are extremely variable and overlap

with MR imaging findings of other intracranial tumors regarding the distribution , signal pattern and enhancement such as high grade gliomas, metastases or meningiomas. Therefore, the correct diagnosis of CNS lymphoma is difficult on conventional MRI (, 14) . DWI measures the diffusion of water molecules in biologic tissues; tumor diffusion is considered as a marker for tumor cellularity (15). Because CNS lymphomas are highly cellular tumors, diffusion restriction is one of their main features , making them appear hyper-intense on DWI and hypo-intense on ADC maps (16). Perfusion MR imaging visualize nutritive delivery of arterial blood to the capillary bed in the biologic tissue (tumors); with calculation of cerebral blood volume, cerebral blood flow, mean transit time, and time to peak, Cerebral lymphomas shows low rCBV values (17). MR spectroscopy obtains biochemical data from biologic tissue depending upon the chemical shift phenomena using protons (hydrogen) nuclei, In PCNSL proton MR spectroscopy show high Cho/Cr ratios and elevated lipid peaks (18&19) .

AIM OF THE WORK

To assess the value of advanced neuro-imaging (MR diffusion, perfusion and proton spectroscopy) in diagnosis of primary CNS lymphoma .

METHODS

Study PopulationBetween December 2011 and December 2012, patients who presented to the Neuro Surgery Unit in Alexandria Main University Hospital with suspected primary CNS lymphoma were referred to the Radio diagnosis Department for imaging assessment. Five adult patients (3 males & 2 females) age ranged from 27 to 82 years (median age 57 years) presenting

with one of the following clinical presentations. Focal neurological deficit, Neuropsychiatric symptoms , Increased intracranial pressure , seizures . The presence of specific attenuation or signal pattern as iso dense to hyper dense lesions on CT scan and iso intense to hypo intense lesions on T2-weighted MRI. Specific location. Central , Hemispheric or periventricular cerebral white matter , Frontal lobe , basal ganglia , brain stem or cerebellum also superficial location adjacent to the meninges. Enhancement pattern as homogeneous or ring-like enhancement are driving attention to further advanced neuro imaging evaluation. Imaging Techniques & analysisMR imaging was performed using a Siemens Avanto 1. 5 MR system with a standard head coil. Conventional MRI study was performed with conventional T2 [fast spin echo (FSE), fluid attenuated inversion recovery (FLAIR)] and T1 sequences, with the latter being used also after the intravenous administration of paramagnetic contrast material (gadobutrol, 0. 1 mmol/kg, Magnevist, Schering, Germany). Diffusion analysisThe DWI study was performed with a T2-weighted, echoplanar spin-echo sequence (TR 3, 400, TE 102, matrix 192×192, slice thickness 5 mm, gap 30%) with a duration of 120 s and b= 0, b= 500, and b= 1, 000. Isotropic maps of the ADC were calculated, and the lowest ADC was measured in the lesion core. Perfusion analysisThe PWI study was performed with a T2-weighted echo planar spin-echo sequence (TR 1. 480, TE 30, matrix 128×128, slice thickness 5 mm, gap 0, number of scans 50, IPAT2 Grappa 128 epi factor) with duration of 81 s. Nineteen images per second were acquired during the passage of a bolus of 0. 1 mmol/kg of gadobutrol, injected with an automatic injector at a flow velocity of 5 ml/s through an 18- to 20-gauge needle

cannula, followed by 20 ml of saline solution. Post processing was performed with a dedicated software package (Syngo neuro perfusion evaluation). Color maps of the cerebral blood volume were generated, and the mean value of the maximum regional cerebral blood volume (rCBV) was calculated by placing the region of interest in the peripheral solid areas showing the highest intensity of color. Data were then compared with those of the normal-appearing contralateral white matter and expressed as a ratio of rCBV [ratio = rCBV (lesion)/rCBV (contralateral white matter)]. Spectroscopy analysisMR spectroscopy multi-voxel 2D CSI was performed with an echo time of intermediate TE (135) (TR 1, 500, FOV 160 mm, acquisition time 7 min 34 s) to evaluate the levels of choline (Cho), creatine (Cr), N-acetyl aspartate (NAA), lactate and lipids. also we acquired data at short TE (30) to evaluate myoinositol (MI). Using a Point Resolved Spectroscopy (PRESS) sequences. The volume of interest size and position were determined by examining the MR images in all three dimensions (Sagittal, Coronal & Transverse planes), with the aim is include the largest portion of the tumor, peri-lesional area together with normal contra-lateral brain within the region of interest as much as we can and to exclude subcutaneous fat and regions with large variations in magnetic susceptibility. Appropriate automatic shimming & water suppression were achieved by using 4-8- HZ line width, 1-khz spectral width & the automated software developed by the manufacture spectroscopic data. Pathological analysisThe diagnoses were confirmed by pathology. Routinely processed paraffin-embedded tissues were cut and stained with the conventional H&E stain and reticulin stain. Sections on coated slides were submitted to immunohistochemistry for CD20, CD3,

pancytokeratin and S-100. Both the primary antibody and the detection kit were purchased from Lab Vision Corporation (Neo Markers, USA). Immunohistochemical staining was performed using an avidin-biotinylated immunoperoxidase methodology.

RESULTS

Patients demographic and conventional MRI imaging data are demonstrated in table 1, Advanced MRI imaging data are demonstrated in table 2. Conventional MRI showed central location of the lesion for 4 patient and peripheral cortical and sub cortical location with central extension for 1 patient (Table-1; case 3) (Fig-1D) , Multiple lesions are noted in 4 patients (Fig-2) , Single lesion is noted in 1 patient (Table 1; case 2) (Fig-3) , Low signal intensity to grey matter within the lesions in T2 weighted images found in 3 patients , T2 iso intense signals found in 1 patient (Table-1; case 3), High T2 signal intensity found in 1 patient (Table-1; case 4), Intense enhancement noted in 4 patients (Fig- 3A), moderate rim enhancement noted in 1 patient (Table -1; case 5) . Advanced neuro-imaging data. Regarding the diffusion weighted images and ADC values. All patients show low ADC values (Figs -1C, 2A, 3B) ranging from 0. 61 to 0. 67 x 10-3mm2 /sec with mean ADC value 0. 63 ± 0. 025(SD) x 10-3mm2 /sec (table 2; case 1&3). For the central lesions the range of ADC values is form 0. 61 to 0. 65 x 10-3mm2 /sec with mean ADC value 0. 625 ± 0. 017 x 10-3mm2 /sec, Slightly higher ADC value is noted for the peripheral lesion 0. 67 x 10-3mm2 /sec (Table- 2; case 3). Regarding the perfusion weighted images. The maximum relative CBV ratio in all patients is summarized in table 2 . The

rCBV ratios are ranging from 0. 23 to 1. 52 with mean. rCVB ratio 1. 14 ± 0. 54(SD) (table- 2 ; case 2&5) (Fig-1A) , perfusion is decreased with max. rCVB Below 1. 2 in 2 cases (case 1&2) , Relatively increased max. rCBV in 3 cases (case 3, 4&5) (Figs -2B, 3C). Regarding the MRI spectroscopy. All the metabolic ratios are summarized in table 2. Cho/Cr ratios are fluctuating, ranging from 1. 9 up to 63 with mean ratio 19. 16 ± 26 (SD) , showing very high values in case (1&2) 24 and 63 respectively (Fig 2 C). Cho/NAA ratios are also ranging from 3. 7 to 50 with mean ratio 14. 8 ± 19. 8 Showing very high values in case (1&2) 50 and 10 respectively (Figs 1B, 3D) . NAA/Cr ratios ranged from 0. 09 to 1. 6 with mean ratio 0. 72 ± 0. 59, NAA/Cho ratios ranged from 0. 02 to 0. 3 with mean ratio 0. 19 ± 0. 1, Lactate peak is found in 3 cases (case 1, 3&5) (Fig 2D). Lipid peak was found in 2 cases (case 1&3) . Myo inositol peak is found in one case (case 5).

DISCUSSION

Primary CNS lymphoma is rare aggressive neoplasm with increased incidence in both immunocompetent and immunocompromised patients (1). The initial diagnosis of CNS lymphoma is difficult by conventional MRI imaging . However, the correct diagnosis of CNS lymphoma and proper differentiation from other intracranial mass lesions such as high grade gliomas, metastases, or meningiomas is important, because the management and prognosis is different (20). Primary CNS lymphoma is restricted in DWI reflecting high cellularity , and they appear hyper intense on DWI and hypo intense on ADC maps (21). PCNSL lesions show more diffusion restriction and lower ADC values than high-grade gliomas and

metastases (22) , other lesions appears with high signal intensity in DWI are acute ischemic stroke, pyogenic brain abscesses, high-grade gliomas, and some metastases. (22) . Perfusion MR imaging with relative cerebral blood volume (rCBV) ratio is crucial for diagnosis of PCNS lymphomas , Mean relative CBV measured in tumor tissue and showing relatively lower values in lymphomas than in other brain tumors. This characteristic finding may differentiate glioblastomas and metastases from lymphomas (23) . The MR spectrum in PCNSL is variable with presence of multiple zones of transitions between normal and tumor tissues. MR spectra with PCNSL show decreased NAA/Cho , NAA/Cr and increased Cho/Cr and ratios; in some patients Cho was the only observable metabolite , others show depleted NAA. Several patients had lactate, lipid, or both within the evaluated voxels (18). Our results revealed that the rate of water diffusion of CNS lymphomas, as represented by ADC values, was significantly low , ADC values ranging from 0. 61 to 0. 67 x 10-3mm2 /sec with mean ADC value 0. 63 ± 0. 025 x 10-3mm2 /sec , In a study by Guo et al. (24) , The mean ADC of CNS lymphoma was 0. 87 ± 0. 27 × 10−3 mm2/s, whereas the mean ADC of high grade astrocytoma was 1. 21 ± 0. 35 × 10−3 mm2/s. Results of other studies (25) on this issue have revealed even higher ADCs, up to 1. 37 ± 0. 52 × 10–3 mm2/s. These findings were also consistent with our results of diffusion weighted MR images and ADC maps analyses . Lymphomas were hyperintense to gray matter on diffusion-weighted images and isointense to hypointense on ADC maps, findings that were consistent with lower diffusivity (24) . In this study, the results showed that the maximum rCBV ratios were less than 1. 2 in 2 patients and more than 1. 2 in other 3 patients. These results (mean value:

1. 14 ±0. 54) are similar to the previous reports (mean value: 1. 10–2. 48) (25) . These findings are different from other tumors such as high grade gliomas (mean value: 4. 03–7. 32) or metastasis (mean value: 4. 68–5. 27) or meningiomas (mean value: 8. 02–10. 58) with high max. rCBV ratios (26) . Sugahara et al. reported that cerebral lymphomas had a tendency to have low rCBV values in 1999 (28) . Hakyemez et al (27). reported that the rCBV ratios of high grade gliomas were higher than those of lymphomas in 2006. Avid enhancement without higher rCBV ratios in lymphoma is due to blood brain barrier destruction without neovascularization in contrast to the marked contrast enhancement with increased vascularity in high grade gliomas (26). In this study MR spectra with PCNSL consisted of increased Cho/Cr with mean ratio 19. 16 ± 26 , Cho/NAA mean ratio 14. 8 ±19. 8 and decreased NAA/Cho with mean ratio 0. 19 ± 0. 1 and NAA/Cr with mean ratio 0. 72 ±0. 59, high lipid and lactate peaks , unexpected finding with presence of myo inositol peak in 1 patient ; These ratios are similar to the few patients reported with PCNSL and elevated lipid and Cho ratios may help in differentiate between glioma and lymphoma (18&29). The increase in Cho likely results from the high mitotic activity, rapid cell turnover and the dense cellularity of these lesions (29). The lipid signals arise from fatty acyl moieties released during membrane breakdown (30). The spectral patterns seen in PCNSL is similar to glioblastoma multiform. However, increasing ratios of Cho/Cr or decreasing NAA/Cho and NAA/Cr in PCNSL is related to tumor progression and possibly increased aggressiveness but not increased tumor grade (31).

CONCLUSION

Advanced MR imaging techniques have identified characteristic findings in CNS lymphoma that may aid in the differentiation of CNS lymphomas from other CNS lesions. Restricted diffusion. Relative hypo perfusion, Increased Cho/Cr, Cho/NAA , Decreased NAA/Cho , NAA/Cr and Presence of lactate and lipid peaks are consistent imaging findings in CNS lymphoma.