

Primary Central Nervous System Lymphoma: Incorporating MRI in the Planning of Treatment Strategies

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ABSTRACT

Background: Primary lymphoma of the central nervous system is becoming increasingly encountered secondary to the acquired immune-deficiency disorders. MRI is rapidly evolving diagnostic tool in the management of the lymphomatous CNS primary infiltrates. **Methods and materials:** 40 patients of the National Cancer Institute of Cairo University were studied by medium and high power MRI machines before and after intra-venous contrast enhancement. **Results:** The cerebral lesions exhibited specific diagnostic criteria regarding the anatomical configuration, signal pattern, peri-focal oedema and response to steroids, such manifestations made. **Conclusion:** MRI a highly reliable tool in the management of the disease. The work proved that spinal cord primary lymphoma is a rare entity.

Key Words: Primary CNS lymphoma - MRI - Treatment strategies.

INTRODUCTION

Primary CNS lymphoma accounts for less than 5% of all primary brain tumors and approximately 1% to 2% of all lymphomas in immunocompetent patients [11].

The incidence of primary CNS lymphoma rises with age and has increased four times as rapidly as extra nodal non Hodgkin's lymphoma as a whole, although there is controversy as to whether this increase is entirely explained by acquired immune deficiency syndrome epidemic [4].

By definition primary CNS lymphoma is limited to the nervous system and has not metastasized there from a systemic site [13].

MRI scanning is the standard imaging technique for any patient with a cerebral neoplasm. The MRI of primary central nervous system lymphoma is usually quite distinctive and the

diagnosis may be suspected on the basis of radiographic appearance alone [10].

Aim of work:

This work is structured to establish MRI diagnostic criteria for primary central nervous system lymphoma in an attempt to shorten the pre-treatment time lapse and also to fix a place for MRI in planning different treatment strategies.

PATIENTS AND METHODS

The common pool of the study consisted of 40 patients investigated non-radiologically according to the treatment policy of the National Cancer Institute of Cairo University; all of them gave readings suggestive of primary central nervous system lymphoma. The diagnostic battery composed of CSF cytology, bone marrow biopsy and complete blood picture. Some patients were subjected to human immune deficiency virus detection tests.

37 patients were examined by MRI of the brain and 3 patients for spinal axis using medium power (0.5 Tesla) as well as high power (1.5 Tesla) systems.

The following imaging protocol was adopted:

- The pulse sequences used were conventional spin echo T1 and fast spin echo T1 as well as T2 weighted images.
- The three scanning planes were used; At least one plane was available in T1 as well as T2 weighted images.
- All the studies were performed before and after intravenous contrast administration. The contrast medium used was Gadolinium-DTPA and the dose was 0.2 mls/kg.

- The slice thickness for the brain studies was standardized as 7 mms while the slice gap was set up as 0.7 mm, in the spine studies it was 4 mm with a 0.4 mm slice gap.

The MRI findings were then collected, classified according to the lesions morphology and signal criteria.

RESULTS

- The general population of the work consisted of 40 patients; 28 males and 12 females the mean age value was 66 years.
- Sixty one lymphomatous lesions were detected in the general pool; 58 of them in the brain and only 3 in the spinal axis.
- Multiplicity was evident in 54% of the brain lesions while unifocal lesions represented 46% of the pool.
- The anatomical distribution of the lesions was as follows:

Table (1).

Anatomical distribution	Number of cases
Periventricular, cerebral hemispheres lesions	25
Corpus callosum lesions	11
Basal ganglia proper and centrum semiovale lesions	12
Cerebellar lesions	10
Spinal axis lesions	3
Total	61

- Regarding the size of the visualized brain lesions the following was elicited:

Table (2).

Size of the lesion	Number of lesions
Less than 2 cm	29
From 2 cm to 4 cm	24
Over 4 cm	5

The signal pattern of the visualized lesions was as follows compared to the healthy brain parenchyma:

Table (3).

Signal pattern	% of lesions
Hypo to isointense in T1 weighted images	97%
Iso to hypo intense in T2 weighted images	79%

The remaining percentage exhibited mixed pattern of signals in both T1 as well as T2 weighted images.

No signals indicative of hemorrhage or calcification within the lesions could be seen.

Three cases showed intra-lesional necrosis manifested as deep T1 hypointensity changing to hyperintense T2 pattern with no contrast uptake. All of the three cases were immunocompromised.

Regarding the contrast enhancement pattern of the lesions the following was detected:

Table (4).

Contrast enhancement behavior	Number of cases	% of brain lesions
Non enhancing	4	6.8%
Enhancing	54	93.1%

Table (5).

Pattern of contrast uptake	Number of cases	Percentage
Marked	41	76
Moderate	13	24
Homogenous	43	79.6
Heterogenous	12	22.2

The non-enhancing 4 cases were on steroid therapy prior to performing the MRI study.

Peri-lesional edema was present in 52 lesions; again the lack of edema was present in the patients under steroid therapy.

The extent of edema was as follows:

Extensive in 15 cases and moderate in 37 cases.

The 3 spinal axis lesions presented as dominantly isointense signal in T1 weighted images with mild signal elevation in the T2 sequences and moderate contrast enhancement of heterogeneous pattern.

One spinal axis case proved to be seedling from cerebral lesion while the other two were proved to be part of systemic non-Hodgkin's lymphoma.

No primary C.N.S. lymphoma of the spinal cord was encountered.



Fig. (1-A): Bilateral, hypointense basal ganglia lesions in T1 image.

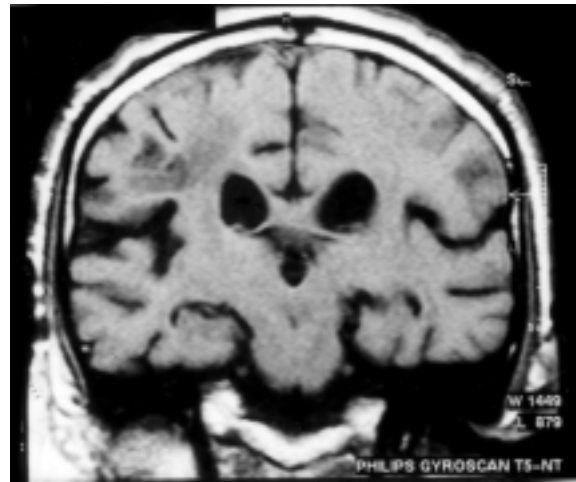


Fig. (2-A): Right frontal iso to hypointense lesion in T1 image.



Fig. (1-B): The lesions are isointense in the T2 image with hyperintense perifocal oedema.



Fig. (2-B): The lesion is isointense in the T2 image with bright perifocal oedema.



Fig. (1-C): Homogenous contrast uptake by the lesions more evidently on the right side.

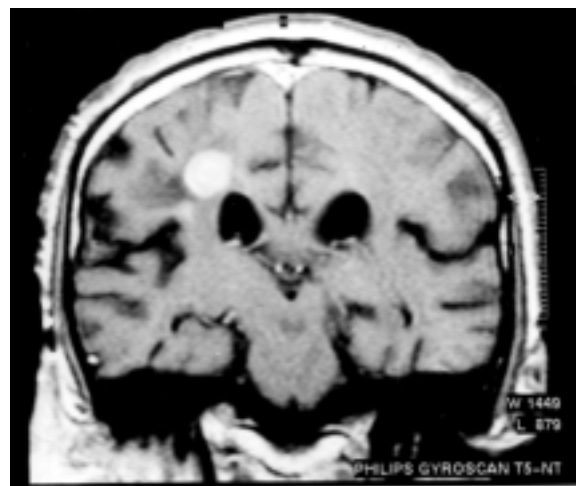


Fig. (2-C): The lesion exhibited strong homogenous contrast uptake.

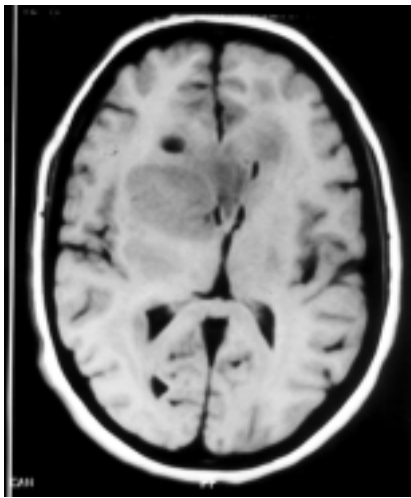


Fig. (3-A): Multiple iso to hypointense lesions in corpus callosum, basal ganglia, right thalamus and periventricular regions in T1 image.

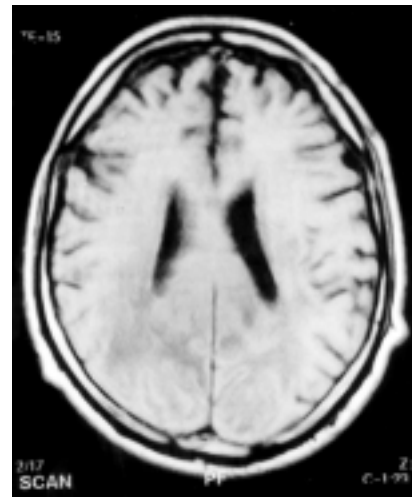


Fig. (4-A): Posterior body and splenium of corpus callosum iso to hypointense lesion with periventricular hypointensity in T1 image.

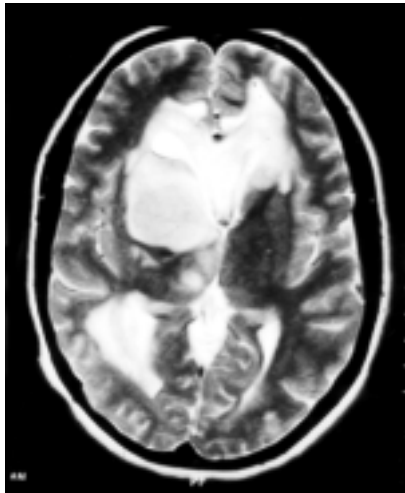


Fig. (3-B): The lesions appeared of moderate signal intensity compared to the bright signal of the perifocal oedema in T2 image.

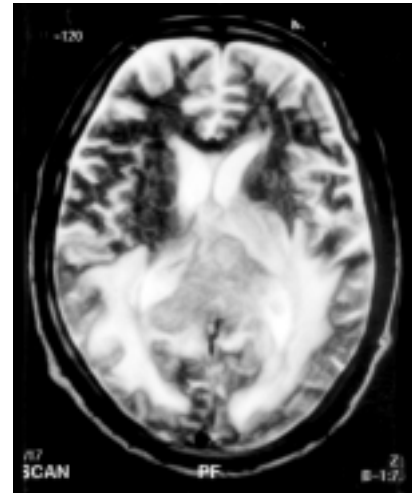


Fig. (4-B): The lesion is hypointense with bright oedema and trans ependymal C.S.F. Back flow in T2 image.

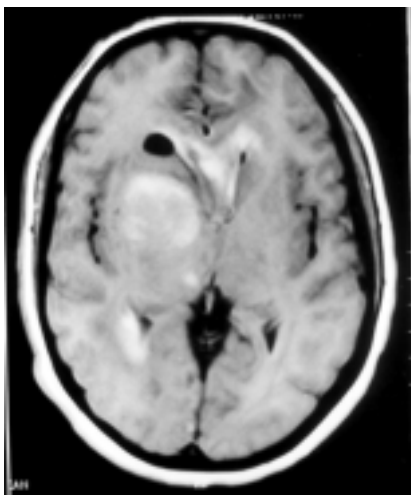


Fig. (3-C): The lesions exhibited homogenous contrast uptake.

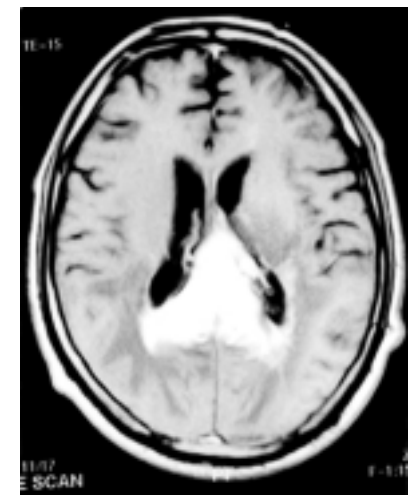


Fig. (4-C): Significant, homogenous contrast uptake by the lesion.

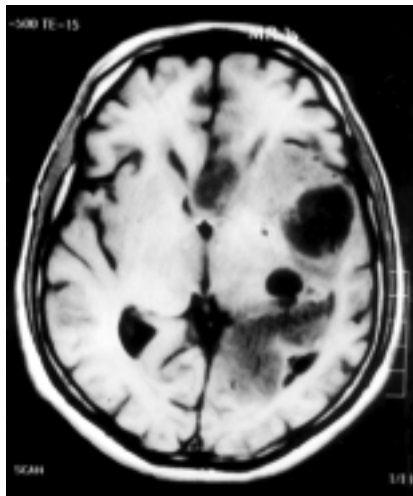


Fig. (5-A): Deeply hypointense lesions in corpus callosum, left temporal and deep occipital regions in immune-compromised patient in T1 image.

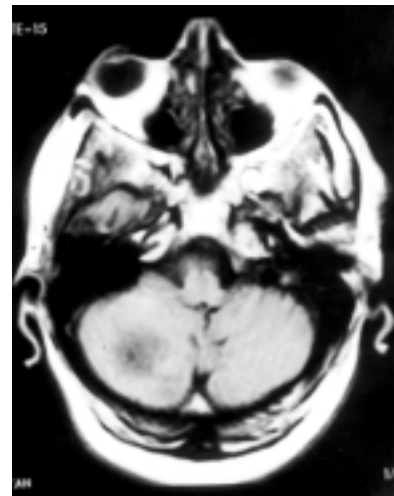


Fig. (6-A): Right cerebellar lesion in T1 image.

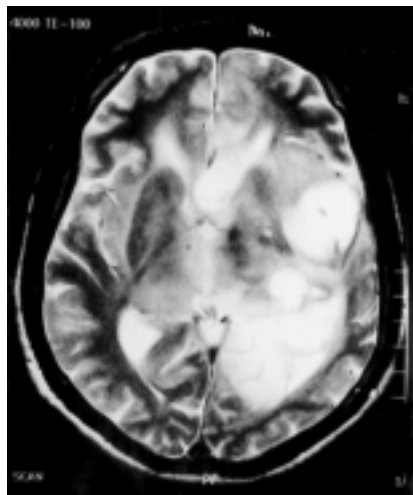


Fig. (5-B): The lesions changed to marked hyperintensity with limited oedema in T2 image denoting necrosis within the lesion.

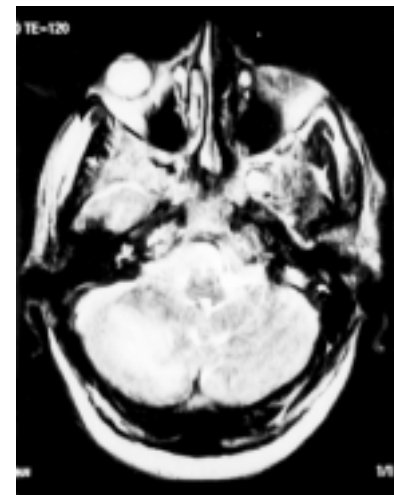


Fig. (6-B): The lesion became strongly hyperintense secondary to internal necrosis in T2 image.

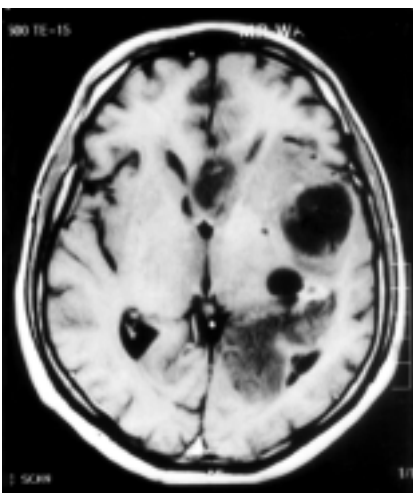


Fig. (5-C): Minimal, marginal contrast uptake around the lesions.

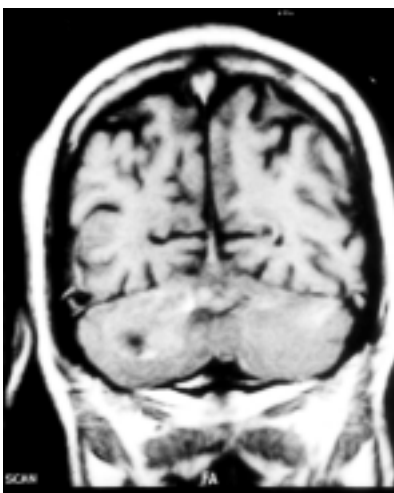


Fig. (6-C): Marginal contrast uptake by the lesion.

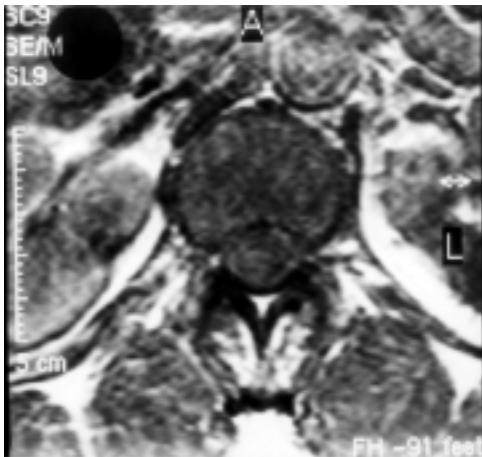


Fig. (7-A): Intradural abnormal hypointense lesion in T1 image.



Fig. (7-B): The lesion showed contrast uptake extending as high as lower dorsal region in a post contrast study.

DISCUSSION

The theme of this discussion will pivot around the inherent MRI criteria of primary central nervous system lymphoma as well as if such imaging profile could be influenced by iatrogenic and immunological factors in an attempt to reduce the pre-treatment period as well as help establishing the role of MRI in the treatment strategies of such an increasingly evolving neoplastic entity.

Primary central nervous system lymphoma is defined as lymphoma limited to the cranial-spinal axis without systemic disease. An increasing incidence of this disease has been seen among patients with immunodeficiency syndrome and among other immunocompromised persons [2].

In our work the common pool of patients contained three immune-compromised patients; one of them proved to be human immune deficiency virus positive while the other two had performed renal transplant surgery and were under immune suppression therapy.

To establish a characteristic MRI profile of central system lymphoma a battery of items should be addressed regarding the anatomical configuration of the diagnosed lesions and their signal patterns.

The classical imaging findings of parenchymal lymphoma include masses, which involve the deep gray matter structures, periventricular region and corpus callosum [6].

Multiplicity is very common and has been noted in up to one-half of cases [15].

In this study the incidence of multiple lesions was more than that of the unifocal being 54% for the former and 46% for the latter. The localization of the cerebral lesions was of dominant deep periventricular distribution scoring 40.9%, the corpus callosum lesions scored 18%, the basal ganglia 19.6% while the cerebellar lesions represented 16.3% of the brain lesions, the remaining score was that of the spinal axis lesions representing about 4.9% of the lesions.

Buhring et al. [1], found that cerebral parenchymal infiltration with lymphoma represented about 31% of their work, while corpus callosum scored 15%, basal ganglia 15%, cerebellum 14% while the spine cases scored about 1% of the sample.

In our work we could not detect intra-cranial lepto-meningeal lymphomatous infiltrates, while Buhring et al., scored 7% lepto-meningeal affection in their work.

In metastatic lymphoma of the central nervous system it is exceptional for parenchymal masses to occur without leptomeningeal involvement [15].

This point may help in the differentiation between primary and secondary central nervous system lymphoma.

Trying to set up specific MRI signal pattern to the central nervous system lymphoma may represent a crucial point in the differential diagnosis of the disease.

In this study the lymphomatous infiltrations exhibited hypo to isointense signal compared to the healthy brain parenchyma in the T1 weighted images in 97% of the lesions while 79% of the lesions became iso to hypointense in the T2 sequences.

In the work of Johnson et al., 100% of the lesions exhibited iso to hypointense signal pattern in the T1 images while 53% were iso to hypointense in the T2 weighted sequences; subsequently we can now adopt a guide line regarding the signal pattern as we expect all the lesions to be iso to hypointense in the T1 images with no gross signal increase in the T2 weighted sequences, this finding can help in differentiating the lymphomatous infiltrations from other parenchymal space occupying lesions like gliomas.

No signal indicative of hemorrhage or calcification could be detected in our study. Jack et al. [6], stated that lymphomatous masses do not calcify and hemorrhage is distinctly uncommon on imaging studies.

The use of intravenous contrast enhanced MRI studies in the assessment of central nervous system lymphomas added a lot to our diagnostic yield regarding the evaluation of the detected lymphomatous lesions.

Contrast enhancement by the lymphomatous lesions in our work was evident as 93.4% of the lesions exhibited contrast uptake; those lesions that did not enhance were under steroid therapy. 76% of the enhancing lesions showed marked contrast uptake, 24% revealed moderate enhancement. 80% of the enhancement patterns were homogenous and 20% were heterogeneous. A specific curvilinear marginal contrast uptake was seen in the immune-compromised patients.

Buhring et al. [1], stated that 100% of their cases enhanced after the intravenous injection of Gadolinium-DTPA, the same was scored by Floris et al. [3], in addition the latter authors

stated that 74% of the lesions enhanced markedly, 26% moderately enhanced with 80% homogenous contrast uptake.

Three cases encountered in this study with evident tumoral necrosis and subsequently limited contrast uptake of marginal pattern; all such cases were immune-compromised. Lehrke et al. [9], stated that central necroses were frequent in HIV-positive patients but rare in HIV-negative patients.

Ring enhancement is more commonly associated with immune-compromised patients [12].

Peri-lesional interstitial edema represents an important point in the diagnosis of intra-cranial space occupying lesions; in our work perilesional edema was detected in 52 cerebral lesions scoring 89.6% of the encountered cerebral lesions. The degree of edema was extensive in 28% of cases and moderate in 72%; the lack of edema was seen in all the cases under steroid therapy. Floris et al. [3], scored 74% perilesional edema in their study.

Recognizing primary C.N.S. lymphoma by imaging criteria is essential to avoid steroid medication and to facilitate attempts to biopsy rather than resection, which does not improve prognosis [14].

The incidence of medullary cord lymphoma has been estimated as 1% of primary C.N.S. lymphoma. Very few cases have been reported in the literature. However, spinal cord lymphoma may occur and must therefore be included in the differential diagnosis of spinal cord neoplasm. Neither characteristic nor specific imaging findings of this disease have been established [7].

In our work three intra dural spinal axis lesions were diagnosed; non of them was primary lymphoma. One case was seedling from brain lesion while the other two cases were part of systemic lymphoma.

Conclusion:

The incidence of primary lymphoma of the central nervous system had witnessed significant increase in the last decade due to the evolving immune-deficiency disorders.

MRI represents a potent diagnostic tool in the diagnosis of primary lymphoma of the central nervous system.

In our work we were able to structure guide lines regarding the behavior of primary central nervous system lymphoma in the magnetic resonance images that could be summed up as follows:

A- Morphology of the lesions:

- Central nervous system parenchymal lymphomatous infiltrates are dominantly multiple and less commonly uni-focal.
- Deep periventricular location of the cerebral parenchyma lesions is a major diagnostic criterion.
- Infratentorial lesions are less common than those of supra-tentorial compartment.
- Lepto meningeal disease is a sign of secondary and not primary lymphoma of the central nervous system.
- Primary lymphoma of the spinal cord is rare.

B- MRI signal pattern of the lesions:

- Primary cerebral parenchymal lymphomatous infiltrates appear of hypo intense T1 signal pattern with no significant signal increase in the T2 weighted images compared to the healthy brain parenchyma.
- Moderate interstitial perifocal parenchymal edema is always present. The use of steroids blocks the development of interstitial edema and subsequently its MRI presentation.
- Primary central nervous system lymphoma does not calcify and hemorrhage is not a diagnostic criterion.

C- Contrast enhancement patterns:

- Untreated primary cerebral lymphoma in immune-competent patients enhance homogeneously.
- Parenchymal infiltrates in immune - compromised patients exhibit marginal contrast uptake due to the intra-lesional necrosis.

Guided by the previously mentioned MRI criteria of central nervous system primary lymphoma, a quick diagnosis of the disease is within reach hence shortening the pre-treatment time lapse.

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