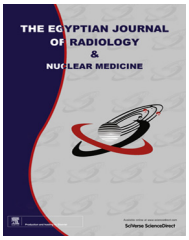
The Egyptian Journal of Radiology and Nuclear Medicine (2014) **45**, 1265–1274

Egyptian Society of Radiology and Nuclear Medicine

The Egyptian Journal of Radiology and Nuclear Medicine

www.elsevier.com/locate/ejrnm
www.sciencedirect.com



ORIGINAL ARTICLE

Brain MR imaging abnormalities in pediatric patients after allogeneic bone marrow transplantation

Sally Emad-Eldin [a,*], **Mohamed Abdel-Moeti** [b]

[a] *Diagnostic and Intervention Radiology Department, Cairo University Hospitals, Kasr Al-Ainy, Cairo, Egypt*
[b] *Oncology and Hematology Department, National Cancer Institute, Cairo University, Cairo, Egypt*

Received 14 June 2014; accepted 22 July 2014
Available online 15 August 2014

KEYWORDS

MRI brain;
CNS complications;
Children;
Allogenic BMT

Abstract *Objective:* Our aim was to analyze brain MRI findings in pediatric patients who developed neurologic complications after allogeneic bone marrow transplantation.
Materials and methods: This prospective study included 33 consecutive patients (age range from 3 to 18 years, mean 11.8 ± 5.1 years). They were referred to the MRI unit because of the neurological symptoms in the post transplant period. The underlying disorders included: non malignant hematological disorders (n = 20, 60.6%) and hematological malignancies (n = 13, 39.4%). Onset of the presentation of the complication in relation to the chronology of the transplant was identified in each patient (phase1: from days 0 to 30, phase 2: from days 30 to 100, and late phase after day 100).
Results: According to the MRI findings 6 patients (18.2%) showed normal examinations. Twenty-seven patients (81.8%) with positive MRI findings, are grouped into 7 main categories: posterior reversible encephalopathy syndrome (n = 16, 48.48%), intracranial hemorrhage (n = 2, 6.06%), cerebral venous sinus thrombosis (n = 1, 3.03%), CNS infection (n = 2, 6.06%), leukoencephalopathy (n = 5, 15.15%), mild atrophy (n = 11, 33.33%), CNS relapse (n = 1, 3.03%), with 9 patients having more than one diagnosis. Ten cases of PRES and 1 case of sinus thrombosis were detected in phase 1. Two cases of PRES and 2 cases of intracranial hemorrhage were detected in phase 2. Four cases of leukoencephalopathy, 4 cases of PRES, 2 cases of CNS infection, and 1 case of CNS relapse were detected in phase 3.

* Corresponding author. Address: Diagnostic and Intervention Radiology Department, Cairo University Hospitals, El-Manial, 11956 Cairo, Egypt. Tel.: +20 2 0106 1616935; fax: +20 02 23687673.
E-mail address: sallyemad@hotmail.com (S. Emad-Eldin).
Peer review under responsibility of Egyptian Society of Radiology and Nuclear Medicine.

http://dx.doi.org/10.1016/j.ejrnm.2014.07.005

Conclusion: CNS complications after allogenic BMT in pediatric patients could cause a significant clinical problem. MRI can provide early diagnosis and follow-up to monitor treatment changes. Knowing the onset of the presentation of the complication in relation to the chronology of the transplant is important as it provides significant guidance on which causes to consider.

1. Introduction

Bone marrow transplantation (BMT) is performed to restore hematologic and immunologic competence for a range of childhood hematologic malignancies (leukemia and malignant lymphoma), as well as to treat congenital conditions in which these functions are depressed or absent (1).

Before BMT, the patient is prepared with high doses of chemotherapy, frequently associated with total-body irradiation, to destroy the hematopoietic system and to suppress the immune system, especially T-cells, so that graft rejection is prevented. In addition in patients with hematological malignancies, the preparative regimen also serves to reduce the tumor burden (2). Such therapeutic regimens increase the risk of patient morbidity and mortality in both the short and long terms (1).

Complications in the post transplantation period are mostly related to hematopoietic and immune system aplasia and to the allo-reactivity of donor cells. Because preparative regimens destroy the recipient immune and hematopoietic systems, immunologic recovery depends on engraftment and proliferation of the infused stem cells (3).

The immune status of children after BMT can be divided into three phases: the pre-engraftment period (days 0–30), the post-engraftment period (days 30–100), and the late phase (after day 100). The timing of CNS complications that occur after BMT, as for complications in other organs, can be described with reference to these three phases of immune status (2).

The most common and clinically significant complications are infection, vascular disorders, therapy-induced cytotoxicity, graft versus-host disease (GVHD), and recurrence of preexisting diseases (3).

Early diagnosis is crucial to successful management and good prognosis, because CNS complications are potentially devastating. CT and MRI play an important role in early diagnosis, which maximizes the chance of prompt therapy for transplantation-related complications (3).

In the present study, we prospectively evaluated MRI findings in central nervous system complications in children after allogenic bone marrow transplantation with correlation from the onset of presentation to the post transplant period.

2. Material and methods

The study was approved by the hospital ethics committee. This prospective study included 33 consecutive patients who were referred to the MRI unit at our institution between July 2010 and December 2013 because of the neurological CNS symptoms that required MRI imaging evaluation after allogeneic BMT. There were 10 females and 23 males, ranging in age from 3 years to 18 years (mean 11.8 ± 5.1 years). All patients did allogenic BMT from HLA matched related donors.

The underlying disorders included: severe aplastic anemia (n = 7), Fanconi anemia (n = 4), beta thalassemia (n = 8), severe combined immunodeficiency (SCID) (n = 1), chronic myelogenous leukemia (n = 1), acute myelogenous leukemia (n = 4) and acute lymphocytic leukemia (n = 8) (Table 1).

The neurological clinical symptoms that required MRI examination are presented in Table 2. Seizure was the most common presenting symptom in 11 patients (33.3%) followed by altered mental status in 8 patients (24.2%), visual disturbance in 6 patients (18.2%), severe headache in 5 patients (15.15%), motor weakness in 2 patients (6.1%), and paresthesia in 1 patient (3.03%). Onset of the presentation of the complication in relation to the chronology of the transplant was identified in each patient.

3. Methods

MR examinations were performed on two MRI machines: 3-T MR scanner (Gyroscan Intera, Philips medical systems, Netherlands) and 1.5 T MR scanner (Signa, General Electric, USA). MR imaging protocol included sagittal and axial T1WI, T2WI and FLAIR images in the axial plane. Contrast T1WI in axial, coronal and sagittal planes was obtained after injection of 0.1 mol Gadopentetate dimeglumine-DTPA (Magnevist; Schering, Berlin, Germany). Diffusion-weighted images (DWIs) and apparent diffusion coefficient (ADC) maps were obtained. Seventy-two MRI examinations were performed (9 patients had 1 study each; with 24 patients having more than 1 study: 18 patient had 2 studies; 1 patient had 3 studies; 4 patients had 4 studies and 1 patient had 6 studies). Follow-up MRI examinations were performed at variable intervals according to the patient clinical condition.

MRA and MRV examinations were performed in 7 patients due to clinical suspicion of vascular complications. Contrast enhanced studies were performed in all cases to exclude infection.

4. Conditioning regimen and preventive measures

The conditioning regimen for each patient depended on the underlying disease, type of donor and graft, and comorbidities.

GVHD prophylaxis consisted of Cyclosporin A (CsA) combined with one of the following: methotrexate or corticosteroid. The target serum concentration of CsA was 200 ng/mL.

All patients received antibacterial, antiviral and antifungal prophylaxis from the day of admission.

Table 1 Clinical indications of bone marrow transplantation in 33 children included in the study.

	Number	Percentage (%)
Acute myelogenous leukemia	4	12.12
Chronic myelogenous leukemia	1	3.03
Acute lymphocytic leukemia	8	24.24
Beta thalassemia	8	24.24
Severe aplastic anemia	7	21.21
Fanconi anemia	4	12.12
Severe combined immunodeficiency (SCID)	1	3.03

Table 2 Clinical presentations in 33 children after allogenic BMT.

Neurological symptoms	No	Percentage (%)
Seizures	11	33.30
Altered mental status	8	24.20
Visual disturbance	6	18.20
Severe headache	5	15.15
Motor weakness	2	6.06
Paresthesia	1	3.03

5. Results

The MRI diagnoses of the patients in relation to the chronology of BMT are demonstrated in Table 3. Among the 33 patients included in the study, 6 patients (18.2%) showed normal MRI brain findings, those patients presented with non repetitive neurological symptoms. Twenty-seven patients (81.8%) showed positive MRI findings, they were grouped into 7 main categories:

5.1. Calcineurin inhibitor (CNI)-induced toxicity

Sixteen patients were diagnosed as posterior reversible encephalopathy syndrome (PRES) associated with CNI-induced toxicity. The level of CsA at the onset of PRES presentation was reviewed, the serum level of CsA was slightly elevated in only 6/16 patients (37.5%). Hypertension associated with PRES was detected in 5/16 patients.

PRES lesions were identified in FLAIR images and their distribution in anatomical regions was made. The anatomical regions were identified as frontal, parietal, occipital and temporal lobes as well as corpus callosum, basal ganglia and cerebellum. Gadolinium enhancement was identified if any.

The most frequently affected regions on FLAIR were the parieto-occipital region in 3/16 (18.75%), posterior parietal lobes in 3/16 (18.75%), occipital lobes in 2/16 (12.5%). (Fig. 1) Thus 50% were in the posterior regions. Holo-hemispheric affection (involvement of the frontal, parietal, temporal and occipital regions) was detected in 7/16 (43.75%). (Fig. 2) Additional cerebellar affection was detected in 3/18 (18.75%), whereas basal ganglia and corpus callosum involvement were detected in 1/18 (6.25%) and 2/18 (12.5%) respectively.

Ten out of 16 cases (62.5%) diagnosed with PRES were detected in the early post transplant period (phase 1), whereas 2/16 cases (12.5%) were detected in phase 2 and 4/16 cases (25%) were detected in phase 3.

Contrast enhancement was detected in 2/16 (12.5%). The initial scan showed leptomeningeal enhancement which was resolved in follow up examinations.

Hemorrhagic changes were detected in 2/16 cases (12.5%). Initial MRI study showed minimal sulcal SAH in 1 case whereas in the other case, minute focal hemorrhage was detected in the follow up MRI examination (Fig. 3).

In follow up MRI, signal changes usually completely reverse in 15/16 cases (93.75%), with 1 case (6.25%) showing persistent signal changes. Recurrent PRES was found in 1 case (6.25%) who developed two episodes of PRES, 6 and 9 months after the first one. Two patients were initially diagnosed with PRES died due to acute GVHD.

5.2. Cerebrovascular hemorrhage

Intracranial hemorrhage was detected in 2 patients (6.06%). Parenchyma cerebral and cerebellar hematomas together with SAH were detected in one patient 40 days post transplant (phase 2) (Fig. 4). Follow up MRI done later showed resolution of the SAH and cerebellar hematomas, with decrease in the size of cerebral hematoma.

Intraventricular hemorrhage was detected in one patient 2 months post transplant (phase 2), this patient died within 24 h after hemorrhage detection.

Table 3 MRI findings in 33 children after allogenic BMT with their relation to the chronology of transplantation.

MRI findings	Phase 1 < 30 days	Phase 2 30–100 days	Phase 3 > 100 days	Total No[a]	%
Normal	5	1		6	18.20
Atrophy	3	1	7	11	33.33
PRES	10	2	4	16	48.48
Intracranial hemorrhage		2		2	6.06
Sinus thrombosis	1			1	3.03
Infection			2	2	6.06.
Leukoencephalopathy	1		4	5	15.15
Relapse			1	1	3.03

[a] Nine patients had more than one diagnosis.

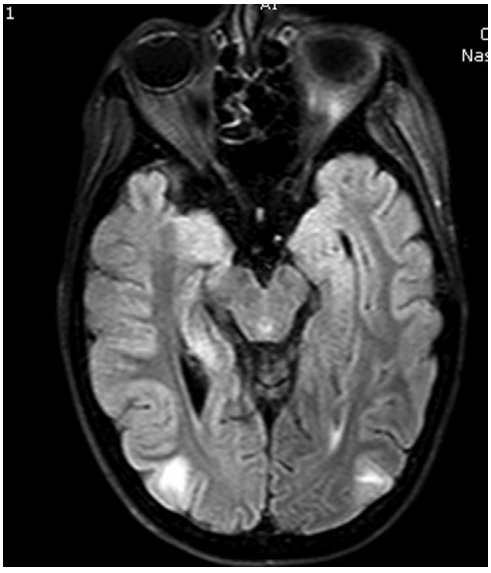


Fig. 1 Posterior reversible encephalopathy syndrome (PRES) in a 9 year-old male patient after BMT for beta thalassemia, presented with sudden seizure on day 25 post transplant. He had been treated with MTX and cyclosporine as prophylaxis from GVHD. Axial FLAIR MR image shows bilateral occipital cortical-subcortical abnormal hyperintense lesions. These imaging appearances are typically consistent with PRES.

5.3. Cerebral venous sinus thrombosis

Superior sagittal sinus (SSS) thrombosis was detected in one patient (3.03%), 5 days post transplant (phase 1). Recanalization of the occluded sinus was detected in follow up serial MRI done 5 and 22 days later.

5.4. Cerebral infection

In the current study 2 patients (6.06%) developed cerebral infection (one case of fungal aspergillosis (Fig. 5) and one case of toxoplasmosis (Fig. 6)). Both cases were diagnosed 6 months (phase 3) after BMT.

5.5. Leuko-encephalopathy

Leuko-encephalopathy was detected in 2 patients (6.06%) as an isolated finding, whereas it was detected in 3 patients (9.09%) combined with other diagnosis (PRES ($n = 1$), relapse ($n = 1$), and cerebral venous thrombosis ($n = 1$)).

The extent of the lesions was visually graded from 1 to 3 according to the US national Cancer Institute grading of leukoencephalopathy as grade 1: high focal periventricular, grade II: focal periventricular extending to the centrum semiovale, and grade III: confluent total white matter (4). According to this classification: 3 patients were classified as grade I, 1 patient as grade II and 1 patient as grade III (Fig. 7)

5.6. Mild brain atrophy

Isolated mild atrophic brain changes and volume loss were detected in 3 patients (3.03%), atrophic brain changes were detected in combination with 5 cases of leukoencephalopathy, and 3 cases of PRES.

5.7. CSN relapse

Relapse was diagnosed in one patient (3.03%) who did BMT for AML. The CNS relapse was detected 1 year after transplantation. MRI showed orbital and leptomeningeal soft tissue masses (Fig. 8). The relapsing disease showed a fluctuating

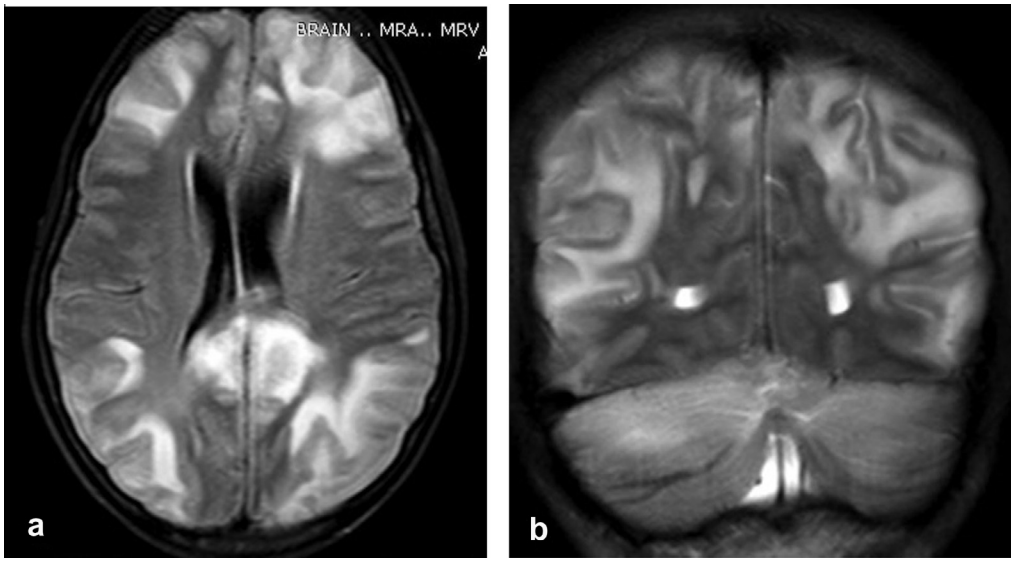


Fig. 2 Posterior reversible encephalopathy syndrome (PRES) in a 13 year-old male patient after BMT because of CML. He had been treated with MTX and cyclosporine as prophylaxis from GVHD. He experienced sudden onset of seizures and disturbed conscious level 6 months after BMT (a) Axial FLAIR and (b) Coronal T2WI show patchy hyperintense lesions at both frontal and parieto-occipital regions, splenium together with the cerebellum which is rarely seen. Although the lesions markedly regressed in follow up MRI examination done 2 weeks later, the patient died due to acute GVHD.

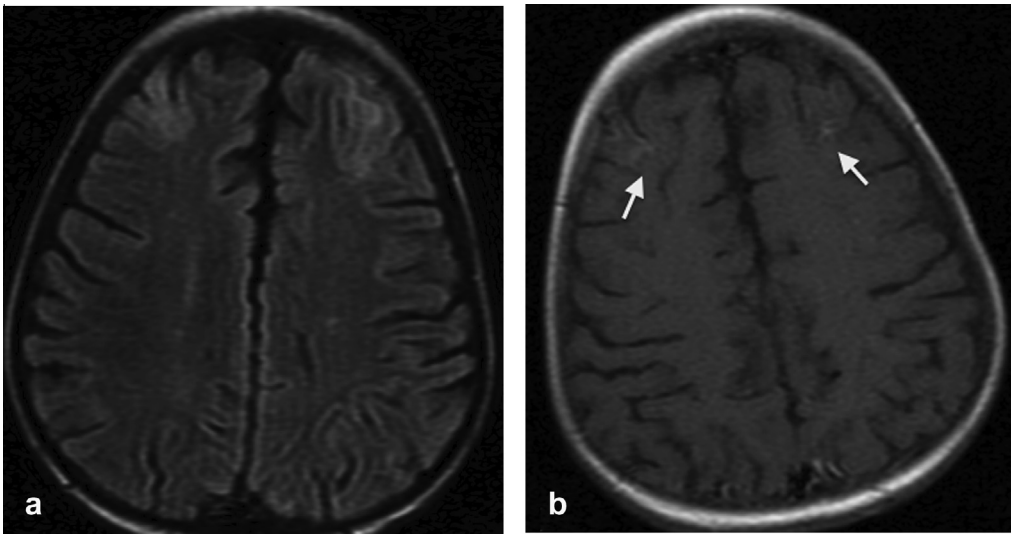


Fig. 3 Posterior reversible encephalopathy syndrome (PRES) in a 5-year-old boy after BMT because of beta thalassemia. He had been treated with CSA, steroid and MTX as prophylaxis of GVHD. He had been diagnosed with PRES on day 21 post transplant. Follow up MRI done 1 month later, showed residual areas of high T2 signal at both frontal regions (b) with tiny hemorrhagic foci of high T1 signal (c).

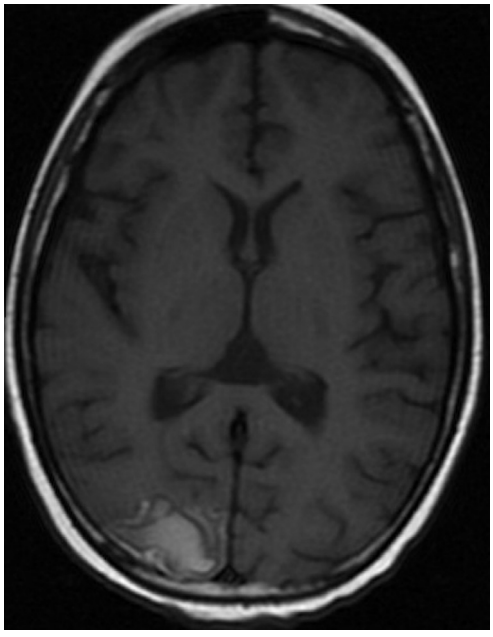


Fig. 4 Cerebral hemorrhage in an 8 year-old female patient after allogenic BMT for Fanconi anemia, presenting with a sudden seizure on day 40 post transplant. Axial T1WI shows small subacute hematoma at the right parietal region.

course of remission and exacerbation with the development of periventricular lesions in the follow up MRI done 2 years after the initial examination.

Out of the 33 patients with CNS complications, 5 patients (15.15%) died after BMT. The death of 3 patients was considered a direct result of CNS complications: intracranial hemorrhage in 2 patients and CNS infection in 1 patient. The remaining 2 patients died because of acute GVHD.

6. Discussion

CNS complications have been found more frequently in allogeneic stem cell transplantation than in autologous or syngeneic stem cell transplantation (3). The frequency of CNS involvement associated with BMT is reported to be 11–65% (90% at autopsy) of BMT recipients, and these CNS complications may be the main causes of death in 9–17% (1,5,6). Immediate and comprehensive diagnostic work-up, especially neuroimaging, is required to detect neurological events in any patients presenting with neurological symptoms (7). Thus early recognition of these complications with imaging and appropriate management will allow early intervention with immunotherapy or additional chemotherapy to improve the chance of survival (3).

In this study we presented different MRI imaging abnormalities of the central nervous system complications in pediatrics after allogeneic BMT. The findings of this study are in accordance with previous clinical studies (2,3,8) which demonstrated the effectiveness of MRI in early diagnosis of CNS complications in the post transplantation period after BMT.

To reach a proper diagnosis, it is essential for the radiologist to understand how imaging findings correlate with the clinical feature (2). On the other hand knowing the onset of the presentation of the complication in relation to the chronology of the transplant is important, as it was useful for narrowing the differential diagnosis (9).

In the current study CNI-induced neurotoxicity was the most common complication, as 16 patients (48.5%) were diagnosed with PRES. PRES is a clinico-neuro-radiologic disease entity represented by characteristic MR imaging findings of subcortical and cortical hyperintensity on T2WI, most often in the parieto-occipital lobes, accompanied by clinical neurologic alterations ranging from headache, altered mental status, seizures, and vision loss, to the loss of consciousness (10).

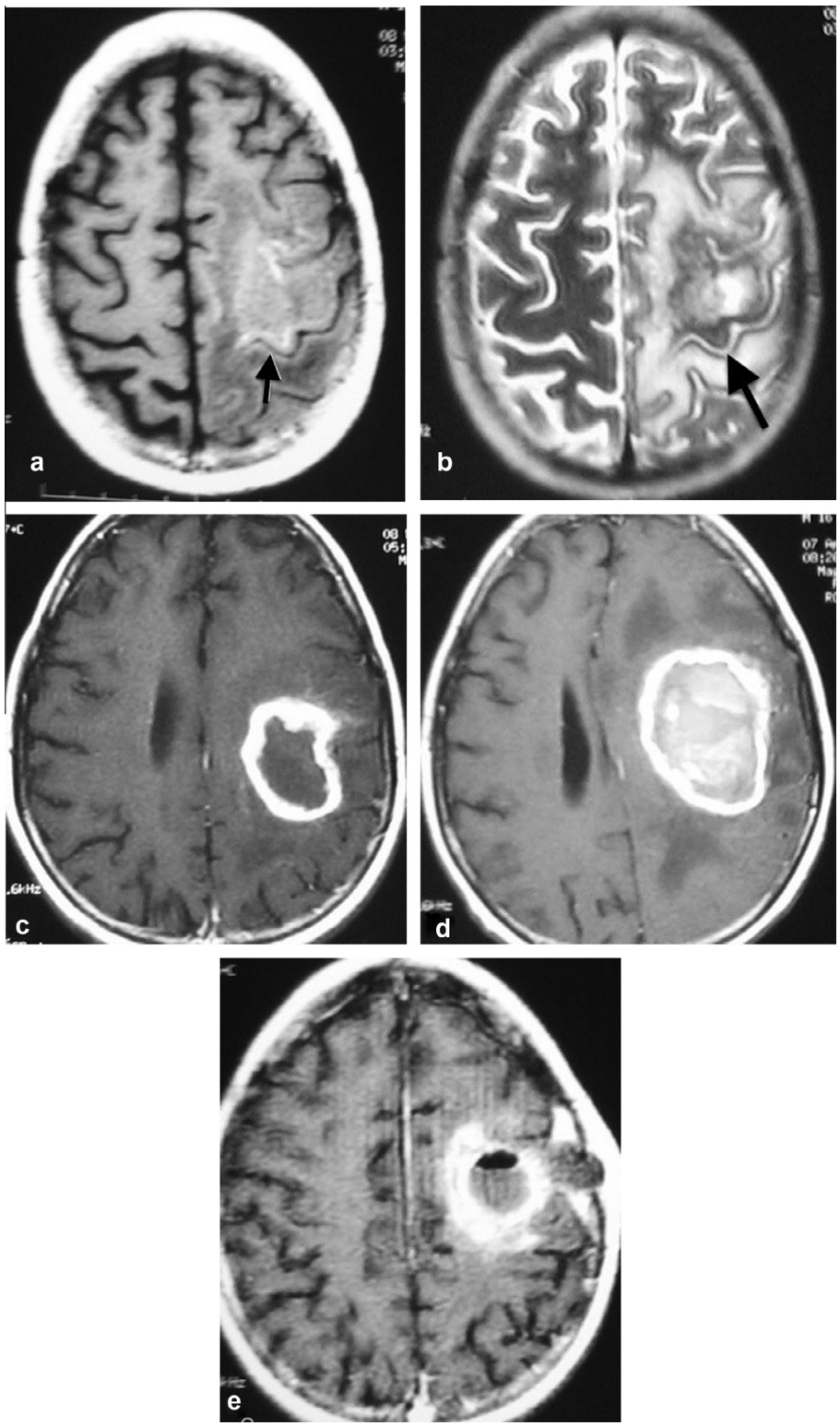


Fig. 5 Cerebral aspergillosis in a 16 year-old-boy after BMT due to severe aplastic anemia. He presented with headache and altered mental status 4 months post transplant. Three serial MRI studies were obtained. (a) and (b) Axial T1 and T2WI show left parietal irregular shaped lesion with a peripheral rim of high T1 and low T2 signal. (c) Post contrast axial T1WI shows marginal enhancement of the lesion. Brain MR imaging was repeated 30 days after the initial study (d), which shows progression of the lesion with increase in its size, surrounding edema and newly depicted midline shift. The core of the lesions shows high T1 signal denoting hemorrhage. Stereotactic drainage with intra-lesional administration of Amphotericin B was performed. A third MR imaging study was obtained 57 days after the initial study (e) shows shrinkage size of the lesion, with intralesional air, likely sequel of previous intervention. Despite aggressive antimicrobial treatment, the patient died of complication 6 months after the initial diagnosis of aspergillosis.

In this study most cases diagnosed with PRES (62.5%) were detected early in the post transplant period (phase1), with 37.5% detected in phases 2 and 3. Similarly Dhar and Human, have reported that although drug toxicity tends to occur early, yet it may occur at any point while the patient is on immunosuppressant therapy (9).

MRI examinations showed typical features of PRES and less commonly affected regions such as cerebellum and basal ganglia, with the most frequently affected areas of the brain being the posterior regions. This was in accordance with the findings of previous studies (11–13).

Atypical MR imaging appearances which include contrast enhancement and hemorrhage were detected in 4/16 patients (25%). Gyral and leptomeningeal enhancement was previously reported, and this was interpreted as leakage due to direct endothelial injury causing blood–brain barrier breakdown (12,13). Hefzy and his colleagues previously described three distinct types of hemorrhage, including focal minute hemorrhages, larger more typical focal hematomas, and sulcal-based subarachnoid hemorrhage (14).

The level of CsA at the onset of PRES presentation was reviewed, the serum level of CsA was slightly elevated in only 6/16 patients (37.5%). This was supported by the previous findings of Koh et al. (7) and Weber et al. (8). The lack of direct correlation between CsA level and CsA induced neurotoxicity was perviously described (15).

Although hypertension is a risk factor for PRES, yet blood pressure may be normal in some cases, particularly in the settings of chemotherapy, and immunosuppressive therapy (10). This is strongly supported by our data, as only few cases who presented with PRES are associated with hypertension.

GVHD was the primary cause of death in 2 patients initially diagnosed with PRES. This was in accordance with the previous studies (7,11,16). The discontinuation of CNI administration may cause poor prevention and management of GVHD resulting in significant mortality due to GVHD. Thus decisions on the changes in the immunosuppressive agent should be made carefully in order to balance the control of GVHD and the management of CNI-associated neurotoxicity (7).

Cerebral venous sinus thrombosis should be considered in the differential diagnosis when neurological symptoms occur following BMT (17). In our study 1 case (3.03%) complained of headache on day 5 post transplant, and MRV showed thrombosis of the superior sagittal sinus, which recanalized in the follow up studies. For the diagnosis of venous thrombosis, the combination of MR imaging with MRV is now the method of choice because of its capability to reveal a lack of flow in the cerebral veins even with the absence of typical findings of brain infarcts (18). Whereas the thrombus is easily recognizable in the subacute phase, it can be mistaken for flowing blood in the acute phase, but MRV will demonstrate the absence of flow (10).

In this study, MRI accurately detected extra-axial and parenchyma hemorrhage in 2 cases (6.06%). Cerebrovascular disease occurs in 3.8–8.8% of BMT recipients (more than 50% at autopsy), mostly during the first or second phase after BMT (1,6,19). Subdural hemorrhage is most common, reflecting thrombocytopenia. Intraparenchymal hemorrhage, subarachnoid hemorrhage, and infarction may also develop (2).

Another complication after BMT is infectious disease. The use of more potent and effective immunosuppressive regimens have reduced the risk of graft rejection but increased the susceptibility of transplant recipients to a variety of opportunistic CNS infections (9).

In imaging of brain abscess post BMT, ring enhancement is often absent reflecting the deficiency of the inflammatory response caused by severely immunocompromised status, whereas in less severe immunocompromised status, there may be ring like enhancement (2). Nishiguchi et al., have suggested that brain abscess should be considered in the diagnosis of hypodense cerebral parenchymal lesion, even if there are minimal mass effect and negligible enhancement (3). However in our series the 2 patients who diagnosed with CNS infection (6.06%), showed marginal enhancement of the brain lesions.

Aspergillosis is the most common CNS infection after BMT, especially during the first and second phases.(2) Early diagnosis of invasive aspergillosis in immunocompromised patient remains a major challenge (8). The organism is rarely cultured from cerebrospinal fluid, so the clinical diagnosis of cerebral aspergillosis can be difficult (2). Although typical MRI findings have been described, appearance of cerebral lesions may be too late for a successful treatment. Thus, the diagnosis is usually delayed (8).

In this study one patient suffered from cerebral aspergillosis, the diagnosis was ultimately made by the typical MRI findings as the lesion showed a central core of hypointense T1 signal, with a rim of high T1 and low T2 signal. This was in accordance with the previous findings of Weber et al. (8). Shortened T1 relaxation times and the zones of low signal intensity at the periphery of the lesion on T2WI are attributed to the presence of iron, manganese, and magnesium in the fungal concretions (20,21). However Tempkin and his colleagues attributed these findings to areas of hemorrhage (22).

Previous clinical studies have suggested that clinicians should exclude the presence of coexisting pulmonary or sinus infections (23–25). In our case, CT examinations of the chest and sinuses were performed to exclude pulmonary and sinus aspergillosis, yet they were negative.

Cerebral toxoplasmosis is considered a rare but fatal complication after BMT (25). It is usually seen after engraftment in the early post transplantation period (8). Ionita et al., previously reported that toxoplasma encephalitis complicating BMT, a lack of enhancement is occasionally encountered for small nodular lesions or sometimes may be masked by T1 shortening due to hemorrhagic transformation in larger lesions (26). In this study there was one case of toxoplasmosis manifested as wide spread cerebellar and cerebral lesions, primarily at the gray white matter interface and basal ganglia, with minimal hemorrhagic signal in few lesions. MRI promoted early diagnosis of the lesions, with the patient stabilized and survived after responding to proper antimicrobial treatment.

Among our patients, we had 5 cases (15.5%) diagnosed with leukoencephalopathy, associated with mild atrophy and volume loss. They received methotrexate in their conditioning regimen, with total body irradiation (TBI) performed in 3 of them who were initially diagnosed with ALL before BMT.

The prevalence of leukoencephalopathy post BMT is ranging from 16 to 69%. Neurological symptoms may or may not be present (2). Prophylactic chemotherapy using MTX can cause leukoencephalopathy. The dose of intravenous MTX correlates with the incidence of leukoencephalopathy, regardless of the history of radiation therapy (27). In addition radiation therapy can produce white matter lesions, the possible

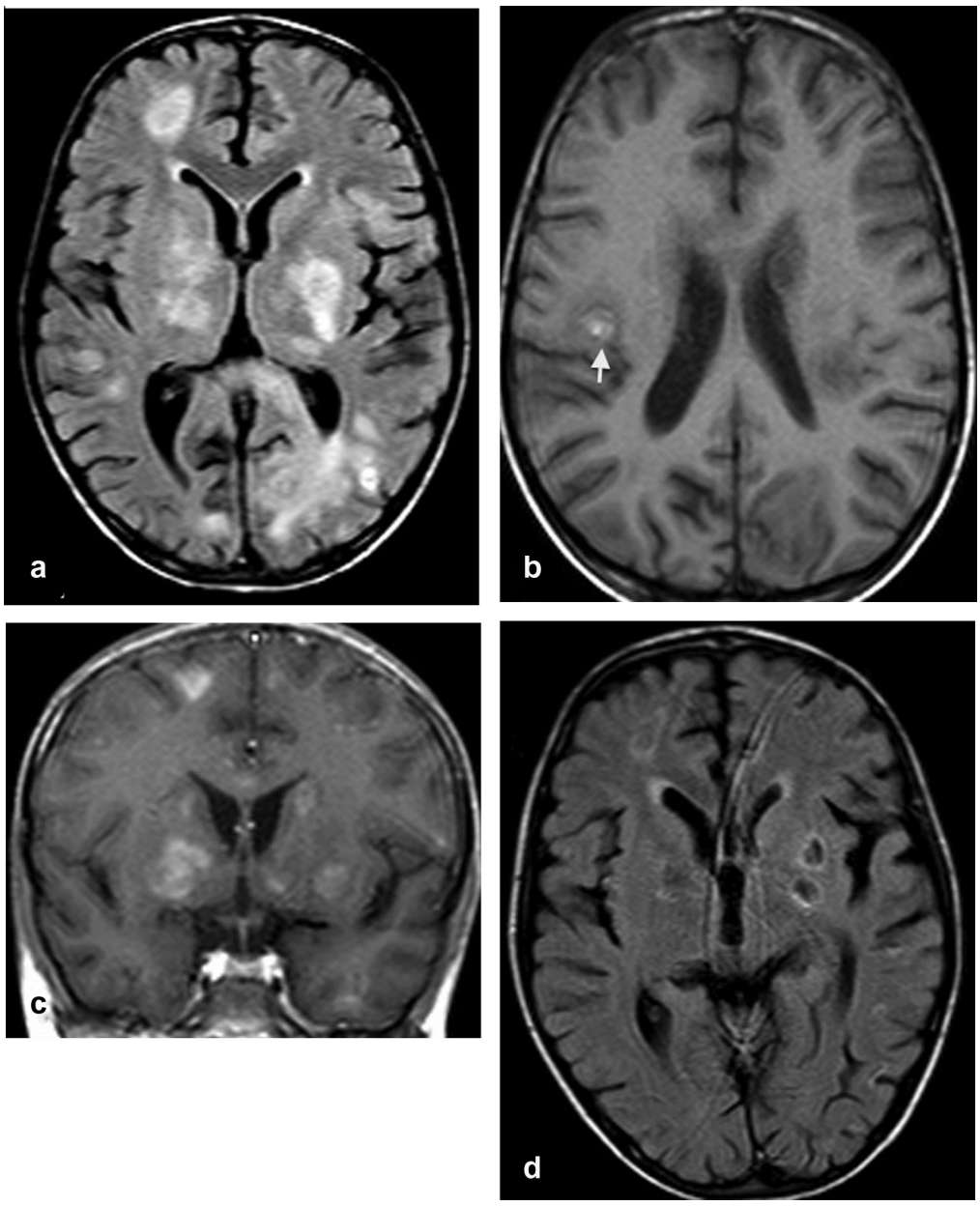


Fig. 6 Cerebral toxoplasmosis in a 7-year-old male patient after BMT due to severe aplastic anemia. He presented with altered mental status 6 months post transplant (a) axial FLAIR image shows bilateral basal ganglia and gray matter–white matter interface hyperintense lesions. (b) Axial T1WI shows small hemorrhagic signal in a right temporal lesion. (c) Coronal T1WI post contrast MR image shows marginal enhancement of the lesions. Follow up MRI done 2 months later and axial FLAIR image (d) shows regression of the lesions after proper antimicrobial treatment.

mechanisms of radiation injury are alterations of the microvasculature within the brain and damage to the oligodendrocytes that produce myelin, which result in an increase in brain water with a loss of brain tissue (10).

In this study one patient who did BMT for ALL, was diagnosed with extramedullary CNS relapse one year post transplant, the case showed intra-orbital, and leptomeningeal lesions, with no associated medullary relapse.

The relapse of acute leukemia is less frequent after allogeneic than after autologous BMT and this is due to the graft-versus-leukemia (GVL) effect that occurs after allogeneic BMT (28). However there is a relative higher frequency of extramedullay relapse of acute leukemia than medullary relapse. This is due to the GVL effect in extramedullary sites of the body which may not be as effective as in the bone marrow (28).

In conclusion, CNS complications after allogenic BMT in pediatric patients could cause a significant clinical problem in the post transplant period. To begin proper treatment as early as possible, accurate diagnosis is important. MRI can provide early diagnosis and follow-up to monitor treatment changes. Knowing the onset of the presentation of the

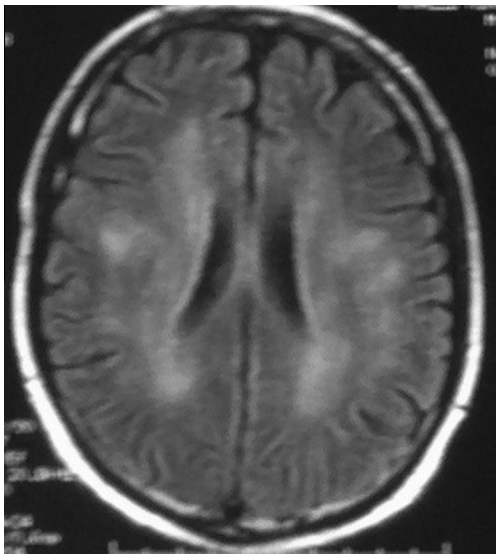


Fig. 7 Leukoencephalopathy in an 18-year-old male patient after allogenic BMT for AML. Axial FLAIR image shows extensive bilateral areas of abnormal signal intensity involving the white matter that are due to the previous combination of chemotherapy and radiation therapy.

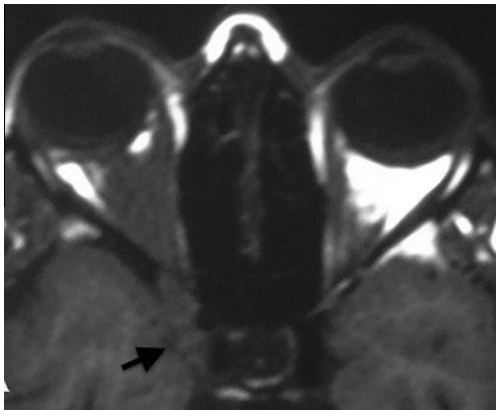


Fig. 8 CNS relapse in an 18-year-old female patient 1 year after allogenic BMT for ALL. (a) Axial T1WI shows right orbital soft tissue mass causing mild proptosis of the right eye globe, with associated small right parasellar extra-axial leptomeningeal lesion.

complication in relation to the chronology of the transplant is important as it provides significant guidance on which causes to consider.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgments

The authors would like to thank Dr. Mahmoud El-Sayed, Hematology and Bone marrow Transplant Unit, Naser Institute for Research and Treatment, Cairo for his assistance in clinical information.

References

(1) Levine DS, Navarro OM, Chaudry G, Doyle JJ, Blaser SI. Imaging the complications of bone marrow transplantation in children. Radiographics 2007;27(2):307–24.
(2) Yoshida S, Hayakawa K, Yamamoto A, Kuroda H, Imashuku S. The central nervous system complications of bone marrow transplantation in children. Eur Radiol 2008;18(10):2048–59.
(3) Nishiguchi T, Mochizuki K, Shakudo M, Takeshita1 T, Hino M, Inoue Y. CNS complications of hematopoietic stem cell transplantation. AJR 2009;192:1003–11.
(4) Won SC, Kwon SY, Han JW, Choi SY, Lyu CJ. Posterior reversible encephalopathy syndrome in childhood with hematologic/oncologic diseases. J Pediatr Hematol Oncol 2009;31(7):505–8.
(5) Uckan D, Cetin M, Yigitkanli I, Rezcan I, Tuncer M, Karasimav D, et al. Life-threatening neurological complications after bone marrow transplantation in children. Bone Marrow Transplant 2005;35:71–6.
(6) Sostak P, Padovan CS, Yousry TA, Ledderose G, Kolb HJ, Staube A. Prospective evaluation of neurological complications after allogenic bone marrow transplantation. Neurology 2003;60:842–8.
(7) Koh KN, Park M, Kim BE, Im HJ, Seo JJ. Early central nervous system complications after allogeneic hematopoietic stem cell transplantation in children. Korean J Hematol 2010;45:164–70.
(8) Weber C, Schaper J, Tibussek D, Adams O, MacKenzie CR, Dilloo D, et al. Diagnostic and therapeutic implications of neurological complications following paediatric haematopoietic stem cell transplantation. Bone Marrow Transpl 2008;41(3):253–9.
(9) Dhar R, Human T. Central nervous system complications after transplantation. Neurol Clin 2011;29:943–72.
(10) Vazquez E, Delgado I, Sanchez-Montanez A, Barber I, Sanchez-Toledo J, Enriquez G. Side effects of oncologic therapies in the pediatric central nervous system: update on neuroimaging findings. Radiographics 2011;31(4):1123–39.
(11) Siegal D, Keller A, Xu W, Bhuta S, Kim DH, Kuruvilla J, et al. Central nervous system complications after allogeneic hematopoietic stem cell transplantation: incidence, manifestations, and clinical significance. Biol Blood Marrow Transplant 2007;13:1369–79.
(12) Kastrup O, Schlamann M, Moenninoghoff C, Forsting M, Goericke S. Posterior reversible encephalopathy syndrome: the spectrum of MR imaging patterns. Clin Neuroradiol; 2014 [Epub ahead of print].
(13) McKinney AM, Short J, Truwit CL, McKinney ZJ, Kozak OS, SantaCruz KS, et al. Posterior reversible encephalopathy syndrome: incidence of atypical regions of involvement and imaging findings. Am J Neuroradiol 2007;189:904–12.
(14) Hefzy HM, Bartynski WS, Boardman JF, Lacomis D. Hemorrhage in posterior reversible encephalopathy syndrome: imaging and clinical features. Am J Neuroradiol 2009;30:1371–9.
(15) Trullemans F, Grignard F, Van Camp B, Schots R. Clinical findings and magnetic resonance imaging in severe cyclosporine-related neurotoxicity after allogeneic bone marrow transplantation. Eur J Haematol 2001;67:94–9.
(16) Chohan R, Vij R, Adkins D, et al. Long-term outcomes of allogeneic stem cell transplant recipients after calcineurin inhibitor – induced neurotoxicity. Br J Haematol 2003;123:110–3.
(17) Harvey CJ, Peniket AJ, Miszkiel K, Patterson K, Goldstone AH, Mackinnon S, et al. MR angiographic diagnosis of cerebral venous sinus thrombosis following allogeneic bone marrow transplantation. Bone Marrow Transplant 2000;25(7):791–5.
(18) Vázquez E, Lucaya J, Castellote A, Piqueras J, Sainz P, Olivé T, et al. Neuroimaging in pediatric leukemia and lymphoma: differential diagnosis. Radiographics 2002;22(6):1411–28.

(19) Bleggi-Torres LF, Medeiros BC, Werner B, et al. Neuropathological findings after bone marrow transplantation: an autopsy study of 180 cases. Bone Marrow Transplant 2000;25:301–7.
(20) Zinreich SJ, Kennedy DW, Malat J, Curtin HD, Epstein JI, Huff LC, et al. Fungal sinusitis: diagnosis with CT and MR imaging. Radiology 1988;169:439–44.
(21) Almutairi BM, Nguyen TB, Jansen GH, Asseri AH. AFIP archives best cases from the AFIP. Invasive aspergillosis of the brain: radiologic-pathologic correlation. Radiographics 2009;29:375–9.
(22) Tempkin AD, Sobonya RE, Seeger JF, Oh ES. Cerebral aspergillosis: radiologic and pathologic findings. Radiographics 2006;26:1239–42.
(23) Ruhnke M, Kofla G, Otto K, Schwartz S. CNS aspergillosis: recognition, diagnosis and management. CNS Drugs 2007;21:659–76.
(24) Rubio-Agusti I, Bataller L. Neurologic complications of hematopoietic stem cell transplantation. Eur Assoc Neuro Oncol Mag 2012;2(2):78–83.
(25) Matsuo Y, Takeishi S, Miyamoto T, Nonami A, Kikushige Y, Kunisaki Y, et al. Toxoplasmosis encephalitis following severe graft-vs.-host disease after allogeneic hematopoietic stem cell transplantation: 17yr experience in Fukuoka BMT group. Eur J Haematol 2007;79(4):317–21.
(26) Ionita C, Wasay M, Balos L, Bakshi R. MR imaging in toxoplasmosis encephalitis after bone marrow transplantation: paucity of enhancement despite fulminant disease. Am J Neuroradiol 2004;25(2):270–3.
(27) Reddick WE, Glass JO, Helton KJ, Langston JW, Xiong X, Wu S, et al. Prevalence of leukoencephalopathy in children treated for acute lymphoblastic leukemia with high-dose methotrexate. Am J Neuroradiol 2005;26:1263–9.
(28) Lee K-H, Lee J-H, Kim S, Lee J-S, Kim S-H, Kim W-K. Acute leukaemia high frequency of extramedullary relapse of acute leukemia after allogeneic bone marrow transplantation. Bone Marrow Transplant 2000;26(2):147–52.