

The BiomolBiomed publishes an "Advanced Online" manuscript format as a free service to authors in order to expedite the dissemination of scientific findings to the research community as soon as possible after acceptance following peer review and corresponding modification (where appropriate). An "Advanced Online" manuscript is published online prior to copyediting, formatting for publication and author proofreading, but is nonetheless fully citable through its Digital Object Identifier (doi®). Nevertheless, this "Advanced Online" version is NOT the final version of the manuscript. When the final version of this paper is published within a definitive issue of the journal with copyediting, full pagination, etc., the final version will be accessible through the same doi and this "Advanced Online" version of the paper will disappear.

Neuroimaging in the diagnosis and treatment of cerebral

toxoplasmosis in children with severe β-thalassemia after

allo-HSCT

Supplementary content



Figure S1. Brain MRI images for the second lesion for Patient 1 upon presentation: The lesion in the right temporal lobe shows high signal intensity on T2-weighted imaging (T2) (F1) and T2- fluid attenuated inversion recovery (F2), with ring enhancement on post-contrast T1-weighted imaging (T1) (F3), surrounded by edema, and isointense on diffusion weighted imaging (DWI) (F4) and hyperintense on apparent diffusion coefficient (ADC) (F5).



Figure S2. Follow-up Brain MRI for Patient 1 after four months of treatment showing the left frontal lobe lesion being decreased in size and decreased associated edema. T2-weighted (G1), T2-fluid attenuation inversion recovery (FLAIR, G2), diffusion weighted imaging (DWI, G3) and post-contrast T1-weighted images (G4).



Figure S3. Follow-up brain MRI for Patient 3 after five months of treatment showing the lesions in the right cerebral peduncle and right temporal lobe being decreased in size and associated edema. H1: T1-weighted image, H2: T2-weighted image, H3: T2-fluid attenuation inversion recovery (FLAIR) image, H4: diffusion weighted imaging (DWI) image, H5: apparent diffusion coefficient (ADC) image, H6: post-contrast T1 image.

Table	S1 .	А	compre	hensive	review	of r	neuroimaging	g feature	s of	cerebral	toxoi	olasmosis i	in pa	atients	with an	d witho	ut trans	plantation.
			· · · ·										- I -					F

Number of	The site of the lesions	Number	Neuroimaging	Imaging findings		
patients		of lesions	examination		ces	
1	Left frontal lobe, right occipital lobe		T2, T2-FLAIR	An appearance of a target sign is observed in the left frontal lobe and right occipital lobe on T2 and T2-FLAIR sequences, with a three-layered signal pattern of low-		
				high-low, surrounded by edema signal in the lesion area.		
1	Basal ganglia, supratentorial and	multiple	T1, T2-FLAIR, DWI, T1	The lesion appears isointense on T1, and shows iso or high or peripheral low signal and central high signal on T2-FLAIR. Some lesions showed peripheral high	[2]	
	subtentorial brain parenchyma		enhanced scan	signal and internal low signal on DWI, while others demonstrate unrestricted diffusion. The T1 contrast-enhanced scan reveals annular enhancement of the lesion.		
2	Left basal ganglia, large cerebellum,	multiple	T2-FLAIR	Multiple irregular nodular and patchy areas of abnormal high signal intensity were detected on brain T2-FLAIR imaging, with some lesions demonstrating a target	[3]	
	thalamus			sign characterized by low-high-low three-layered signal intensity from the periphery to the center.		
1	Right basal ganglia, right internal	multiple	CT plain scan, T1, T2,	The CT scan reveals multiple discrete low-density areas in the right basal ganglia, right internal capsule, right hippocampus, bilateral thalamus, and left caudate	[4]	
	capsule, right hippocampus, left		T2-FLAIR, DWI, T1	nucleus. T2 and T2-FLAIR sequences demonstrate high signal lesions in the basal ganglia and left thalamus, with extensive high signal lesions also seen at the gray-		
	thalamus and left caudate nucleus		enhanced scan	white matter junction. T1 show high signal at the periphery and low signal at the center of some lesions, while DWI indicates high signal at the edges and low signal		
				at the center of certain lesions. Additionally, the T1 contrast-enhanced scan reveals annular of some lesions.		
14	Basal ganglia, large cerebellar	multiple	T1 enhanced scan, T2,	In 10 patients, there was ring and eccentric or central core enhancement on T1, or a target sign with low-high-low three-layered signal from the periphery to the	[5]	
	hemispheres		T2-FLAIR	center on T2 or T2-FLAIR, or both. In one patient, there was isolated T1 enhancement with a target sign, in four patients there was isolated T2/T2-FLAIR target		
				sign, and in five patients, both presentations were observed. Four patients did not exhibit of these features.		
10	Subcortical areas of frontal, parietal	multiple	T1, T2, T2-FLAIR, T1	The lesions predominantly demonstrate isointensity or hypointensity on T1. Different signal patterns are observed on T2: deep lesions exhibit high or heterogeneous	[6]	
	and temporal foramen (5 patients),		enhanced scan	signal, while 50% of superficial lesions show low signal, with 100% of the lesions surrounded by edema. T2-FLAIR reveals heterogeneous, isointense, hypointense,		
	midbrain (2 patients), cerebellum (1			or hyperintense patterns. All patients show enhancement on T1 contrast-enhanced imaging, predominantly in a ring-like fashion, with one patient displaying target-		
	patient), thalamus (1 patient)			like enhancement.		
27	Cerebral hemispheres, basal ganglia	multiple	CT plain and enhanced	CT: Most of the lesions demonstrate ring enhancement, with few showing homogeneous enhancement. In three patients, there were only multiple low-density lesions.	[7]	
	and cerebellum		scan, MRI enhanced	MRI examination revealed an increase in lesions, ring enhancement observed.		
			scan			
1	Right frontal and parietal lobes	multiple	T1 enhanced scan, T2	The T1 enhancement reveals lesions with ring enhancement and eccentric target-like enhancement, while T2 shows lesions with a low-high-low three-layered target	[8]	
				sign from the periphery to the center.		
6	Temporal lobe, parietal lobe,	Unknown	FDG PET/CT	Decreased radiotracer uptake in 6 patients of cerebral toxoplasmosis	[9]	
	cerebellum					
15	Unknown	Unknown	MRS	In 11 patients, the lesions showed elevated or significantly elevated Cho/Cr levels, 4 patients were normal with no low levels.	[10]	

Abbreviations: CT=computed tomography; Cho=choline; Cr=creatine; DWI=diffusion-weighted imaging; FDG PET/CT=fluorodeoxyglucose positron emission tomography/computed tomography; FLAIR=fluid attenuated inversion recovery; Lip=lipid; MRI=magnetic resonance imaging; MRS=magnetic resonance spectroscopy; NA=N-acetylaspartate; T1=T1-weighted imaging; T2=T2 weighted imaging.

REFERENCES

- [1] ZAJAC-SPYCHALA O, PIECZONKA A, JANURA-SZYMANSKA J, JONCZYK-POTOCZNA K, WACHOWIAK J. Multiple Reactivations of Viral Infections Followed by Cerebral Toxoplasmosis After Allogeneic Hematopoietic Stem Cell Transplantation in an Adolescent With Ph(+) Acute Lymphoblastic Leukemia: A Case Report [J]. Transplant Proc, 2021, 53(4): 1355-9.10.1016/j.transproceed.2021.02.007
- [2] CORSINI C, ESQUER GARRIGOS Z, WELKER K M, THOENDEL M J. Toxoplasmosis-Associated Immune Reconstitution Inflammatory Syndrome in an Allogenic Hematopoietic Stem Cell Transplant Recipient [J]. Mayo Clin Proc, 2020, 95(4): 823-4.10.1016/j.mayocp.2020.01.019
- [3] 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: 17 yr experience in Fukuoka BMT group [J]. Eur J Haematol, 2007, 79(4): 317-21.10.1111/j.1600-0609.2007.00919.x
- [4] LEE G T, ANTELO F, MLIKOTIC A A. Best cases from the AFIP: cerebral toxoplasmosis [J]. Radiographics, 2009, 29(4): 1200-5.10.1148/rg.294085205
- [5] MASAMED R, MELEIS A, LEE E W, HATHOUT G M. Cerebral toxoplasmosis: case review and description of a new imaging sign [J]. Clin Radiol, 2009, 64(5): 560-3.10.1016/j.crad.2008.09.016
- [6] CAROLINA, DA, CUNHA, CORREIA, HELOÍSA, RAMOS, et al. Cerebral toxoplasmosis: unusual MRI finding [J]. Clinical Imaging, 2012, 36(5): 462-5
- [7] NAVIA B A, PETITO C K, GOLD J W, CHO E S, JORDAN B D, PRICE R W. Cerebral toxoplasmosis complicating the acquired immune deficiency syndrome: clinical and neuropathological findings in 27 patients [J]. Ann Neurol, 1986, 19(3): 224-38.10.1002/ana.410190303
- [8] KUMAR G G, MAHADEVAN A, GURUPRASAD A S, KOVOOR J M, SATISHCHANDRA P, NATH A, et al. Eccentric target sign in cerebral toxoplasmosis: neuropathological correlate to the imaging feature [J]. J Magn Reson Imaging, 2010, 31(6): 1469-72.10.1002/jmri.22192
- [9] WESTWOOD T D, HOGAN C, JULYAN P J, COUTTS G, BONINGTON S, CARRINGTON B, et al. Utility of FDG-PETCT and magnetic resonance spectroscopy in differentiating between cerebral lymphoma and non-malignant CNS lesions in HIV-infected patients [J]. Eur J Radiol, 2013, 82(8): e374-9.10.1016/j.ejrad.2013.03.008
- [10] CHINN R J, WILKINSON I D, HALL-CRAGGS M A, PALEY M N, MILLER R F, KENDALL B E, et al. Toxoplasmosis and primary central nervous system lymphoma in HIV infection: diagnosis with MR spectroscopy [J]. Radiology, 1995, 197(3): 649-54.10.1148/radiology.197.3.7480733