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Cerebral malaria: susceptibility weighted MRI

Vinit Baliyan, Jeyaseelan Nadarajah, Atin Kumar*, Zohra Ahmad

Department of Radio Diagnosis, All India Institute of Medical Sciences, New Delhi-110029, India

PEER REVIEW

Peer reviewer

Bolni Marius Nagalo, Ph.D, Endicott College, School of Arts and Sciences, 376 Hale St. Beverly, MA 01915, America.
Tel: 978-232-5118
781-475-4539

Comments

This is a well written article with an interesting subject that SWI, a recent advance in the MRI, is very sensitive to microbleeds related to microangiopathy and it may provide additional information and improve the diagnostic accuracy of MRI in cerebral malaria.
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ABSTRACT

Cerebral malaria is one of the fatal complications of *Plasmodium falciparum* infection. Pathogenesis involves cerebral microangiopathy related to microvascular plugging by infected red blood cells. Conventional imaging with MRI and CT do not reveal anything specific in case of cerebral malaria. Susceptibility weighted imaging, a recent advance in the MRI, is very sensitive to microbleeds related to microangiopathy. Histopathological studies in cerebral malaria have revealed microbleeds in brain parenchyma secondary to microangiopathy. Susceptibility weighted imaging, being exquisitely sensitive to microbleeds may provide additional information and improve the diagnostic accuracy of MRI in cerebral malaria.

KEYWORDS

Cerebral malaria, MRI, Susceptibility weighted imaging

1. Introduction

Malaria is a worldwide health problem with 500 million cases per year and an annual mortality of more than 1 million. *Plasmodium falciparum* (*P. falciparum*) causes more severe diseases than the other *Plasmodium* species. One of the fatal complications of falciparum malaria is central nervous system involvement (malignant cerebral malaria). Pathogenesis of cerebral malaria involves cerebral microangiopathy related to microvascular plugging by the infected red blood cells (RBCs). CT and conventional MRI sequences do not reveal anything specific in cases of cerebral malaria, apart from some nonspecific white matter signal abnormalities. Susceptibility weighted imaging (SWI) is a recent advance in the field of MRI, which is sensitive to microbleeds related to cerebral microangiopathy. Here we present a case of cerebral malaria which revealed multiple punctuate microhemorrhages on SWI.

2. Case report

A 20 years old female patient presented with a history of fever and multiple episodes of seizure. The patient was unconscious at the time of admission. Signs of meningitis were negative. Fundoscopy revealed no papilledema. Cerebrospinal fluid was normal but revealed few RBCs. Serology was positive for falciparum and vivax malaria, and it was negative for *Leptospira*. CT scan at the time of admission was normal. Patient was treated with parentral

*Corresponding author: Dr. Atin Kumar, Additional Professor, Department of Radiodiagnosis, All India Institute of Medical Sciences, New Delhi-10029, India.
Tel: 09868398507
E-mail: dratinkumar@gmail.com

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antimalarial therapy. Subsequently, patient's clinical condition improved. The neurological examination still revealed quadriparesis (2/5) with right lateral rectus palsy. Hence, a MRI of brain was performed, which showed foci of T2 and FLAIR hyperintensity involving genu and splenium of corpus callosum, subthalamic region and frontal lobe (cingulate gyrus). SWI revealed microbleeds in corresponding regions including internal capsule, globus pallidi and grey white matter junction of bilateral cerebral hemispheres (Figure 1).

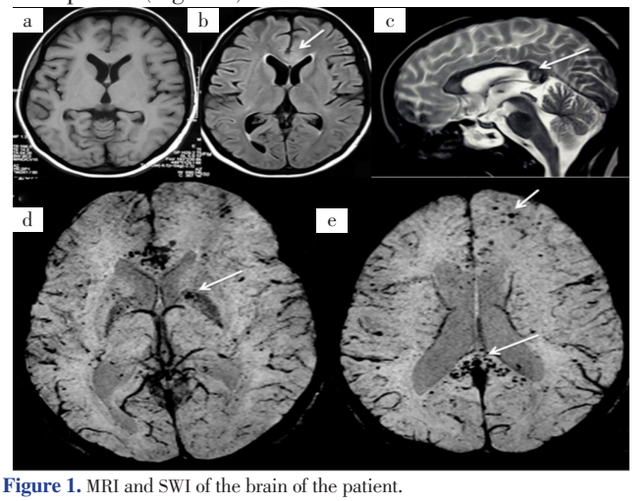

Figure 1. MRI and SWI of the brain of the patient.
a: T1 W images were unremarkable; b and c: Axial FLAIR and Sagittal T2 Weighted MR images show subtle hyperintense foci in the genu and splenium of corpus callosum and cingulate gyrus; d and e: Axial SWI images show punctuate microbleeds having more diffuse distribution; especially in corpus callosum, internal capsules and grey white junction in bilateral cerebral hemispheres.

3. Discussion

Cerebral malaria occurs in approximately 2% of patients infected by *P. falciparum*, especially in children. The neurologic manifestations are nonspecific due to the diffuse involvement. Transient extrapyramidal and neuropsychiatric manifestations as well as isolated cerebellar ataxia may occur, but localizing signs are rare[1]. It may lead to coma and approximately one third of patients die.

P. falciparum causes more severe disease than other *Plasmodium* species. Greater pathogenicity of *P. falciparum* is a result of its ability to make the infected red cells to clump together in form of rosettes and to stick to endothelial cells, which leads to microvasculature blockage[2]. Ischemia caused by hypoperfusion is responsible for the manifestations of cerebral malaria. Autopsy studies on patients died of cerebral malaria are highly variable and have demonstrated diffuse cerebral edema with multiple petechial hemorrhages diffusely scattered in the brain[3,4]. Histopathologic findings have revealed ring hemorrhages around the smaller blood vessels, parasitized RBCs in the intracranial vessels and Durck granulomas. Durck granulomas are aggregates of parasitized RBCs, inflammatory cells, and necrotic tissue that seen in the perivascular region[3,4].

SWI is based on the fact that signals from substances with different magnetic susceptibilities dephase at long echo times. SWI uses this phase information that originates from magnetic susceptibility differences to generate a unique contrast. SWI provides excellent contrast between gray and white matter, iron-laden tissues, venous blood vessels and other tissues with susceptibilities different from the background. SWI is the most sensitive sequence to detect microbleed[5,6].

There are few studies on neuroimaging findings in cerebral malaria. Potchen *et al.* described neuroimaging findings in children with retinopathy confirmed cerebral malaria[7]. In their study, they have reported diffuse cerebral and isolated deep grey matter nuclei edema and cerebral infraction in multiple large vessel territory on CT. Millan *et al.* reported hemorrhage and infarction in a patient with cerebral malaria by using conventional imaging on MRI[8]. One recently published large series by Potchen *et al.* described basal ganglia as the most common site of involvement in children with cerebral malaria[9]. Cordoliani *et al.* reported findings like brain swelling, infarcts and white matter lesions on conventional sequences[10]. Nickerson *et al.* also reported diffuse petechial hemorrhages throughout the gray-white matter junction, corpus callosum, and internal capsules on SWI as well as edema in the posterior limbs of the bilateral internal capsules[11]. These findings are similar to the findings in our patient. Focal T2 hyperintensities involving the corpus callosum, could represent the oedema due to ischemia following microvascular plugging by clumped infected RBCs. The cerebral microhemorrhages seen on SWI could represent the histopathological finding of ring microhemorrhages.

In conclusion, the patients with cerebral malaria show cerebral microbleeds on histopathological analysis but lack findings on CT and conventional MRI, apart from diffuse brain swelling and focal T2 hyperintensities in some patients. SWI, being exquisitely sensitive to microbleeds, may provide additional information and improve the diagnostic accuracy of MRI in cerebral malaria as well.

Conflict of interest statement

We declare that we have no conflict of interest.

Comments

Background

Cerebral malaria is a rare but potentially fatal complication of infection with *P. falciparum*. It can be seen in approximately 1%-2% of patients with acute *P. falciparum* infection. MRI and CT do not reveal anything specific in case of cerebral malaria. SWI, a recent advance in the MRI, is very sensitive to microbleeds related to microangiopathy. SWI also provide additional information and improve the diagnostic accuracy of MRI in cerebral malaria.

Research frontiers

Conventional imaging with MRI and CT do not reveal anything specific in case of cerebral malaria. SWI (MRI) is very sensitive to microbleeds related to microangiopathy. Histological studies in case of cerebral malaria have revealed microbleeds in brain parenchyma. Therefore, the use of SWI might drastically improve the diagnostic accuracy of MRI in cerebral malaria.

Related reports

In the study of Nickerson *et al.* (2009), SWI has been shown to be helpful in the detection of small hemorrhages in various conditions (diffuse axonal injury, coagulopathy, neoplasms, and neurodegenerative disorders). He concluded that, in the future, SWI may play a significant role in the detection of small hemorrhagic lesions that are not detectable by conventional MRI or CT scan.

Innovations & breakthroughs

This study aimed to present a case of cerebral malaria which revealed multiple punctuate microhemorrhages on SWI. The report showed that because of the sensitive to microbleeds of SWI, it may provide additional information and improve the diagnostic accuracy of MRI in cerebral malaria as well.

Applications

SWI may play a significant role in the detection of small hemorrhagic lesions and improve the diagnostic accuracy of MRI in cerebral malaria.

Peer review

This is a well written article with an interesting subject that SWI, a recent advance in the MRI, is very sensitive to microbleeds related to microangiopathy and it may provide additional information and improve the diagnostic accuracy of MRI in cerebral malaria.

References

[1] Marsden PD, Bruce-Chwatt LJ. Cerebral malaria. *Contemp Neurol Ser* 1975; **12**: 29-44.

[2] Haldar K, Murphy SC, Milner DA, Taylor TE. Malaria: mechanisms of erythrocytic infection and pathological correlates of severe disease. *Annu Rev Pathol* 2007; **2**: 217-249.

[3] Dorovini-Zis K, Schmidt K, Huynh H, Fu W, Whitten RO, Milner D, et al. The neuropathology of fatal cerebral malaria in Malawian children. *Am J Pathol* 2011; **178**(5): 2146-2158.

[4] Patankar TF, Karnad DR, Shetty PG, Desai AP, Prasad SR. Adult cerebral malaria: prognostic importance of imaging findings and correlation with postmortem findings. *Radiology* 2002; **224**(3): 811-816.

[5] Haacke EM, Xu Y, Cheng YC, Reichenbach JR. Susceptibility weighted imaging (SWI). *Magn Reson Med* 2004; **52**(3): 612-618.

[6] Nandigam RNK, Viswanathan A, Delgado P, Skehan ME, Smith EE, Rosand J. MR imaging detection of cerebral microbleeds: effect of susceptibility-weighted imaging, section thickness, and field strength. *AJNR Am J Neuroradiol* 2009; **30**(2): 338-343.

[7] Potchen MJ, Birbeck GL, Demarco JK, Kampondeni SD, Beare N, Molyneux ME, et al. Neuroimaging findings in children with retinopathy-confirmed cerebral malaria. *Eur J Radiol* 2010; **74**(1): 262-268.

[8] Millan JM, San Millan JM, Muñoz M, Navas E, Lopez-Velez R. CNS complications in acute malaria: MR findings. *AJNR Am J Neuroradiol* 1993; **14**(2): 493-494.

[9] Potchen MJ, Kampondeni SD, Seydel KB, Birbeck GL, Hammond CA, Bradley WG, et al. Acute brain MRI findings in 120 Malawian children with cerebral malaria: new insights into an ancient disease. *AJNR Am J Neuroradiol* 2012; **33**(9): 1740-1746.

[10] Cordoliani YS, Sarrazin JL, Felten D, Caumes E, Lévêque C, Fisch A. MR of cerebral malaria. *AJNR Am J Neuroradiol* 1998; **19**(5): 871-874.

[11] Nickerson JP, Tong KA, Raghavan R. Imaging cerebral malaria with a susceptibility-weighted MR sequence. *AJNR Am J Neuroradiol* 2009; **30**(6): e85-e86.