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Imaging features of neurotoxoplasmosis: A multiparametric approach, with emphasis on susceptibility-weighted imaging☆

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ABSTRACT

Background: Neurotoxoplasmosis is a common opportunistic infection in HIV/AIDS patients. Imaging identification of neurotoxoplasmosis assists in timely treatment.
Purpose: To delineate the frequency of imaging abnormalities in patients with neurotoxoplasmosis on different MR sequences with a particular focus on SWI, and NCCT.
Material and methods: The PACS database was retroactively searched over a 5-year period for patients with neurotoxoplasmosis who underwent MRI with SWI. Included patients had imaging features of neurotoxoplasmosis based on consensus review by two neuroradiologists, a clinical diagnosis of neurotoxoplasmosis at the time of MRI, and diagnostic confirmation based on positive serum or CSF serology or histopathology; 15 patients were included. The number of abnormal foci with restricted diffusion, increased FLAIR signal, intrinsic T1 hyperintensity, abnormal enhancement (CE-T1WI), and intrinsic hyperdensity on CT were recorded.
Results: Intralesional susceptibility signal (ISS) foci on SWI were observed in 93.3% of patients with neurotoxoplasmosis (mean size 5.2 ± 3.8 mm). The average number of ISS foci was 3.9 per patient; 3/15 (20.0%) had a single ISS. Amongst other MR sequences, hyperintense FLAIR foci were the most common abnormalities observed (12.4 lesions/patient), followed by enhancing foci (8.2 lesions/patient), foci of restricted diffusion (7.1 lesions/patient), and intrinsic T1 hyperintense foci (3.4 lesions/patient). Abnormalities were least frequently observed on NCCT: abnormalities were identified in 5/15 (33.3%) patients, at a rate of 0.4 lesions/patient.
Conclusion: ISS foci are present in the vast majority of neurotoxoplasmosis patients, likely representing hemorrhage. The incidence and frequency of other abnormal foci are highest on FLAIR, and lowest on NCCT.

1. Introduction

Neurotoxoplasmosis has become a leading cerebral opportunistic infection in patients with HIV [1]. It is estimated that nearly 40% of the HIV-infected population will develop neurological manifestations during their lifetime, while over 75% are affected on autopsy [2–5]. In addition, one-third of patients with advanced immunosuppression may develop cerebral toxoplasmosis in a 12-month period [6].

The initial diagnosis of neurotoxoplasmosis is usually made empirically if multiple ring-enhancing lesions are present on brain MRI, serology is positive for Toxoplasma gondii in the CSF or blood, and subsequent clinico-radiological improvement after anti-toxoplasma therapy is observed. However, a shorter time to diagnosis is preferable in order to avoid the side effects of anti-toxoplasma medications, as well as to avoid treatment delays if the alternative scenario of tumor is present. Additionally, empiric diagnosis can be problematic because elevated serum IgG anti-toxoplasma titers are common in the general population in the absence of active disease [6–9]. While brain biopsy is the gold-standard for diagnosis, it is typically reserved for patients who are seronegative and have shown a lack of improvement after a two-week trial of empiric therapy [10]. Meanwhile, the use of steroids in tandem with anti-toxoplasma medications can falsely improve the neurological symptoms in patients thought to have cerebral toxoplasmosis, but who actually have PCNSL [11].

Already, a number of imaging features of neurotoxoplasmosis have been described. The process often appears as multifocal ring-enhancing

☆ Institutional Review Board (IRB) approval was obtained for this retrospective study.

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lesions in the cortex and periventricular white matter; when present, an "eccentric target sign" consistenting of an eccentric nodule along the rim of an enhancing lesion is considered pathognomonic [12]. However, to date only a few case reports have recently described abnormal signal within neurotoxoplasmosis lesions on CT or GRE T2*WI MRI [13,14]. SWI utilizes blood oxygenation level-dependent principles to detect susceptibility effects via the paramagnetic properties of hemorrhage, venous blood, or physiologic iron, as well as to identify calcium [15–19]. SWI has already proven to be much more sensitive than CT or conventional GRE T2*WI in the detection of cerebral hemorrhage [15,20]. Hence, the aim of this study was to identify the frequency of abnormal SWI foci in patients with neurotoxoplasmosis, as well as to delineate the frequency of abnormalities on other MR imaging sequences and non-contrast CT (NCCT).

2. Materials and methods

2.1. Patient selection and diagnosis

The institutional review board approved this retrospective study. During a 5-year period from 6/2010 to 6/2015, the electronic health records and PACS database were searched for patients with neurotoxoplasmosis who underwent SWI MRI at presentation. The inclusion criteria for neuroimaging review were: 1) a recent clinical diagnosis of neurotoxoplasmosis with a brain MRI with intravenous gadolinium contrast agent that utilized SWI, and 2) confirmation via either clinical improvement after therapy, positive serology, or histopathological diagnosis. Patients were excluded due to either: 1) lacking an MRI prior to therapy, or 2) suboptimal and/or non-diagnostic MRI secondary to motion or artifacts.

2.2. Diagnostic criteria

The etiologic workup of those patients ultimately determined to have neurotoxoplasmosis included detection of serum or CSF IgG +/− IgM antibodies against T. gondii. Despite T. gondii serology testing, a CSF analysis was also obtained at admission for exclusion of other less common CNS opportunistic organisms, including, but not limited to: JC virus, herpes simplex virus type 1 and 2, varicella zoster virus, Cryptococcus neoformans, and Mycobacterium tuberculosis.

Brain MRI were interpreted via consensus of a neuroradiology fellow (GMC) and a staff neuroradiologist with > 10 years' experience (AMM). To assess the frequency of brain lesions in patients with neurotoxoplasmosis, the readers documented the frequency of neuroimaging findings by manually counting the number of lesions on the following sequences at initial presentation: 1) SWI, 2) FLAIR, 3) DWI, 4) noncontrast T1WI, 5) CE-T1WI, and 6) NCCT. The maximum number of lesions was recorded as 20, even if greater. Each sequence was reviewed in conjunction with FLAIR, which was considered the standard for the presence or absence of a lesion. Regarding SWI, both the axial 2mm-thick and reformatted minimum intensity projections (8–10 mm thickness) were reviewed in conjunction with filtered-phase maps in order to distinguish paramagnetic (e.g. ferritin, hemosiderin) from diamagnetic (e.g. calcification) substances. Intralesional susceptibility signal (ISS) foci were defined as blooming signal on susceptibility-weighted images corresponding with abnormal foci on other sequences. ISS were excluded if the pattern and distribution of the hemorrhagic foci had imaging characteristics of vasculopathy-related microhemorrhages as multiple scattered punctate foci or confluent patchy subcortical and periventricular signal changes on FLAIR images, rather than ill-defined toxoplasmosis lesions surrounded by perilesional edema. In addition, the abnormalities within FLAIR-positive lesions on the following imaging sequences were noted: 1) the number of enhancing lesions on CE-T1WI, 2) the number of foci of reduced diffusion on DWI and ADC images, 3) the number of hyperintense foci on noncontrast T1WI, and 4) the number of hyperdense foci on NCCT. Size of ISS was recorded in mm; size and characteristics of abnormal foci on other sequences was not collected.

MR examinations were acquired on both 3T ((Tim Trio; Siemens Healthcare, Erlangen, Germany) with the following sequence parameters: TR 27 ms, TE 20 ms, flip angle 15°, bandwidth 250 kHz, matrix size 256 × 134, thickness 2 mm, parallel factor = 2, and acquisition time of about 2.5 min) and 1.5T ((Avanto; Siemens Healthcare, Erlangen, Germany) with the following sequence parameters: TR 49 ms, TE 40 ms, flip angle 15°, bandwidth 80 kHz, matrix size 256 × 157, slice thickness 2.5 mm, parallel factor = 2, and an acquisition time of about 3 min) scanners, being obtained on four different scanner models over the study period. CT imaging was completed on either a 64 multidetector scanner (Sensation, Siemens Healthcare, Erlangen, Germany), or a dual-source 256 slice scanner (Definition Flash, Siemens Healthcare, Erlangen, Germany). Regarding postcontrast CE-T1WI MRI, the intravenous gadolinium-based contrast utilized was gadobutrol, with a weight-based bolus of 0.1 mL/kg (0.1 mmol/kg, maximum of 10 mL total), and a 5-min delay prior to T1WI acquisition. Each sequence was obtained in multiple planes at 5 mm axial thickness, with the exclusion of SWI, which was reconstructed at 2 mm. The DWI gradient strength was b = 1000 s/mm^2.

3. Results

3.1. Patient population

The electronic health records and PACS database searches yielded 32 patients with toxoplasmosis who underwent contrast enhanced MRI with SWI; 17 were excluded from imaging review due to SWI not being performed (n = 9), a lack of clinical or MRI followup (n = 7), or motion degradation during the MRI that precluded interpretation (n = 1). Ultimately, 15 patients (13 males) were included for imaging review (mean age 44 years, range 34–51). All 17 patients were immunocompromised with HIV/AIDS. Every patient had CD-4 T-cell count levels < 50 cells/uL (mean: 7.2 cells/uL; range 1.3–26.0). Average time to followup was 15 months for MRI, and 20 months for clinical followup.

3.2. Clinical followup

Three patients underwent biopsy; two of these patients had improvement on an MRI within 2 weeks of initiating anti-toxoplasma therapy, while the third had cerebellar enhancing lesions that did not improve until nearly 2 months after starting anti-toxoplasma therapy (Table 1). None of the patients expired prior to the resolution of their

Table 1
MR, CT, and clinical data on 15 patients with neurotoxoplasmosis. HIV+ indicates infected patients wit low CD4 counts (below 50 uL). MR indictes the magnet strength used at the time of the study acquisition.

No./Sex/Age(y)	FLAIR	CE-T1WI	DWI	SWI	T1WI	CT	HIV+	Biopsy	MR
01/M/34	20	20	30	3	0	1	Y	Y	3.0T
02/M/46	20	20	20	5	0	1	Y	N	3.0T
03/M/35	20	20	12	4	16	0	Y	N	3.0T
04/M/44	20	20	7	20	0	0	Y	N	3.0T
05/M/37	20	20	5	1	9	1	Y	N	1.5T
06/F/40	20	5	20	2	1	0	Y	N	3.0T
07/M/40	20	4	3	3	11	0	Y	N	1.5T
08/M/42	20	0	11	10	9	0	Y	Y	3.0T
09/F/50	10	1	0	0	1	1	Y	N	1.5T
10/M/48	5	5	1	4	2	0	Y	N	3.0T
11/M/50	5	2	2	1	0	2	Y	N	3.0T
12/M/50	2	2	2	2	1	0	Y	N	3.0T
13/M/39	2	2	0	2	0	0	Y	N	3.0T
14/M/51	1	1	1	1	1	0	Y	N	1.5T
15/M/43	1	1	1	1	0	0	Y	N	1.5T