Published in final edited form as:

Neuroradiology. 2019 January ; 61(1): 13–15. doi:10.1007/s00234-018-2128-8.

“Pseudo” T1-weighted appearance of the brain on FLAIR: unmasking the extent of gray matter involvement on susceptibility-weighted imaging in chronic toluene abuse

Charlie Chia-Tsong Hsu¹, E. Mark Haacke², Chinthaka Heyn^{3,4}, Kosuke Kato¹, Trevor William Watkins⁵, Timo Krings⁶

¹Department of Medical Imaging, Gold Coast University Hospital, 1 Hospital Blvd, Southport, Queensland 4215, Australia

²Departments of Radiology and Biomedical Engineering, Wayne State University, Detroit, MI, USA

³Department of Medical Imaging, Sunnybrook Health Sciences Centre and University of Toronto, Toronto, ON, Canada

⁴Physical Sciences, Sunnybrook Research Institute, Toronto, ON, Canada

⁵Department of Medical Imaging, Princess Alexandra Hospital, Brisbane, Queensland, Australia

⁶Joint Department of Medical Imaging, Toronto Western Hospital and University Health Network, Toronto, ON, Canada

Dear Editor-in-Chief,

Toluene is a readily accessible neurotoxic organic solvent present in paints, inks, glues, and thinners. Chronic toluene abuse through inhalation causes progressive debilitating neurologic complications including cognitive impairment, cerebellar, and extrapyramidal symptoms [1, 2]. White matter involvement is perhaps the most well-recognized radiologic feature of chronic toluene abuse. White matter lesions are localized to the periventricular region in early stages and become more confluent with subsequent involvement of the subcortical U-fibers [3, 4]. The extent of white matter involvement on MRI correlates with the severity of cognitive impairment [1, 2]. Less emphasized radiologic findings of toluene abuse are the involvement of cortical and central gray matter (basal ganglia and thalami) which manifests as low-signal intensity on the T2-weighted spin echo or T2*-weighted gradient echo (GRE) sequences [3–6]. A causal relationship between the white and gray matter signal alterations can be difficult to elucidate, although available evidence favors axonopathy over myelin injury.

Charlie Chia-Tsong Hsu, charlie.ct.hsu@gmail.com.

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

We present a case of a 27-year-old female patient with a long history of paint and glue inhalation abuse. The magnetic resonance imaging (MRI) brain T2 fluid attenuation inversion recovery (FLAIR) sequence showed striking confluent high-signal intensity of the subcortical and deep white matter and low signal in cortex and central gray matter (globus pallidus, thalami, and dentate nuclei) with generalized brain volume loss (Fig. 1, left panel). The diffuse FLAIR signal alteration of the brain was dramatic with reversal of the normal tissue contrast between the gray and white matter giving a “pseudo” T1-weighted appearance (Fig. 1, right panel). A susceptibility-weighted imaging (SWI) sequence was crucial to unmask the extensive low-signal intensity in the cortex and central gray matter (Fig. 1, left panel). The conventional T2-weighted sequence underestimated the extent of the susceptibility signal in both the central and cortical gray matter which was exquisitely depicted in this illustrated case. We also show the brain of a normal subject using MRI to highlight the difference in tissue contrast on the T2 FLAIR, T1-weighted, and SWI sequences (Fig. 1, right panel).

Chronic toluene abusers have reduced gray matter volumes relative to healthy controls in various regions of the brain but specifically in the frontal and parietal cortices [7]. Clinically, chronic toluene abuse patients who exhibit this pattern of specific atrophy frequently show greater cognitive deficits [7]. Quantitative MR spectroscopy studies revealed significant reduction in N-acetylaspartate (NAA)/creatine (Cr) and elevation in myo-inositol (ml)/Cr in the cerebellum and centrum semiovale of chronic toluene abusers [8]. Alteration in these metabolite ratios was significantly higher with a longer duration of abuse. Cho/Cr ratios were not significantly elevated [8]. Selective reduction of NAA and an increased level of ml in white matter supports the theory that axonopathy and gliosis are the main pathophysiologic mechanisms [8].

The pathogenesis of toluene encephalopathy is yet to be fully elucidated. Toluene accumulation leads to white matter injury causing impaired axonal iron transport which has been postulated to result in a gradual accumulation of iron in the cortex and deep gray matter. Although this has yet to be confirmed on histological examination, other neurodegenerative disorders with similar radiologic findings due to postulated axonal disruption of iron transport from the neuronal disease have been histologically confirmed to show iron deposition on Prussian blue staining [9, 10]. Postmortem examination of chronic toluene abusers revealed pattern-specific atrophy in the cerebral cortex, basal ganglia, and cerebellum [1, 11]. Selectively, neuronal loss in the second, third, and sixth layers of the parietal cortex and the cerebellar Purkinje cells were the most pronounced [1, 11]. Histopathological analysis of chronic toluene abusers has shown axonal degeneration in the periventricular and deep white matter of the cerebral cortex as the dominant feature, and although demyelination was present this is considered to be a secondary process [1, 11].

Brain iron quantification is an emerging diagnostic tool in the evaluation of neurodegenerative diseases. MRI techniques for quantifying iron content include mapping of T2, T2*, T2', phase and magnetic susceptibility of the tissue [12]. Utilizing tissue susceptibility for iron quantification is most advantageous as it is not dependent on imaging parameters such as main field strength, echo time, or orientation-like phase [12]. An approximate linear relationship between susceptibility and iron content has been investigated

in vivo and postmortem analysis but interpreting the susceptibility values would depend on the quantitative method and reconstruction parameters [12].

Quantitative analysis of the SWI sequence was not performed in our case; nevertheless, SWI offers invaluable diagnostic value in unmasking the extent of the neurotoxic effects of toluene. The observed low-signal intensity on SWI in the cortical and central gray matter could be attributed to extensive iron deposition but we must emphasize that a relative increase in T2 and T2* effect of the white matter also contributes to the observed darkening of the gray matter structures. We speculate both iron deposition and the relative change in the brain tissue signal intensity ultimately lead to the peculiar “pseudo” T1-weighted appearance of the FLAIR sequence in our patient with a history of chronic toluene abuse.

Funding

No funding was received for this study.

References

1. Rosenberg NL, Kleinschmidt-DeMasters BK, Davis KA, Dreisbach JN, Hormes JT, Filley CM (1988) Toluene abuse causes diffuse central nervous system white matter changes. *Ann Neurol* 23:611–614 [PubMed: 3408242]
2. Filley CM, Halliday W, Kleinschmidt-DeMasters BK (2004) The effects of toluene on the central nervous system. *J Neuropathol Exp Neurol* 63:1–12 [PubMed: 14748556]
3. Caldemeyer KS, Armstrong SW, George KK, Moran CC, Pascuzzi RM (1996) The spectrum of neuroimaging abnormalities in solvent abuse and their clinical correlation. *J Neuroimaging* 6:167–173 [PubMed: 8704292]
4. Aydin K, Sencer S, Demir T, Ogel K, Tunaci A, Minareci O (2002) Cranial MR findings in chronic toluene abuse by inhalation. *AJNR Am J Neuroradiol* 23:1173–1179 [PubMed: 12169477]
5. Ohnuma A, Kimura I, Saso S (1995) MRI in chronic paint-thinner intoxication. *Neuroradiology* 37:445–446 [PubMed: 7477852]
6. Kamran S, Bakshi R (1998) MRI in chronic toluene abuse: low signal in the cerebral cortex on T2-weighted images. *Neuroradiology* 40: 519–521 [PubMed: 9763341]
7. Aydin K, Kircan S, Sarwar S, Okur O, Balaban E (2009) Smaller gray matter volumes in frontal and parietal cortices of solvent abusers correlate with cognitive deficits. *AJNR Am J Neuroradiol* 30:1922–1928 [PubMed: 19643925]
8. Aydin K, Sencer S, Ogel K, Gencellac H, Demir T, Minareci O (2003) Single-voxel proton MR spectroscopy in toluene abuse. *Magn Reson Imaging* 21:777–785 [PubMed: 14559343]
9. Thomas M, Jankovic J (2004) Neurodegenerative disease and iron storage in the brain. *Curr Opin Neurol* 17:437–442 [PubMed: 15247539]
10. Mills E, Dong X, Wang F, Xu H (2010) Mechanisms of brain iron transport: insight into neurodegeneration and CNS disorders. *Future Med Chem* 2:51–64 [PubMed: 20161623]
11. Escobar A, Aruffo C (1980) Chronic thinner intoxication: clinico-pathologic report of a human case. *J Neurol Neurosurg Psychiatry* 43:986–994 [PubMed: 7441282]
12. Ghassaban K, Liu S, Jiang C, Haacke EM (2018) Quantifying iron content in magnetic resonance imaging. *NeuroImage*. 10.1016/j.neuroimage.2018.04.047

CHRONIC TOLUENE INHALATION ABUSE

NORMAL CONTROL

Fig. 1.

MRI of the brain of a chronic toluene inhalation abuse patient (left panel). FLAIR images (a–c) shows diffuse high-signal intensity of the cerebral and cerebellar white matter (white arrows) and symmetric low-signal intensity of the basal ganglia (arrow heads) and cortex resulting in striking reversal of normal gray-white matter signal contrast producing a “pseudo” T1-weighted appearance. Actual T1-weighted images show diffuse increased signal intensity of the cerebral and cerebellar white matter. SWI images (g–i) revealed extensive symmetric cortical and central gray matter (arrow heads) iron deposition. MRI brain of an age-matched control subject (right panel) showing the normal tissue contrast of the supratentorial brain on FLAIR (a), T1-weighted (b), and SWI (c) images