Leukoencephalopathic changes on magnetic resonance imaging associated with a thermogenic dietary supplement (Thermatrim)

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Acute toxic leukoencephalopathy can be caused by exposure to many compounds. Reversibility has been described in some cases with prompt recognition and withdrawal of the offending agent. Its association with a thermogenic supplement has never been reported. We describe two such cases in young women taking a commercially available thermogenic dietary supplement who presented with acute neurologic deficits and a common magnetic resonance imaging pattern.

Due to the increasing prevalence of obesity in Western countries, the use of thermogenic dietary supplements is becoming more frequent. Toxic leukoencephalopathy may be caused by exposure to a wide variety of agents, including cranial irradiation, therapeutic agents, illicit drugs, and environmental toxins (1). Its association with a thermogenic supplement has not been reported. Such is the purpose of this report.

CASES

Pertinent findings for the two patients are summarized in Table 1. Magnetic resonance imaging (MRI) during the acute episode in both patients revealed extensive symmetric restricted diffusion involving the entire corpus callosum, the pons, and subcortical white matter with reduced apparent diffusion coefficient values. No abnormal enhancement was seen (Figures 1 to 3).

Both women were using the dietary thermogenic supplement Thermatrim for weight loss. The first patient had taken the supplement within the previous 2 months, and the second patient within the previous 3 weeks. They received supportive therapy and recovered within 2 to 5 days. Both patients had a benign clinical course with progressive clinical improvement and were discharged within the first week of admission. Two-month follow-up MRI of the first patient showed almost complete resolution of the findings.

DISCUSSION

Leukoencephalopathy describes the structural changes of cerebral white matter in which myelin suffers the most extensive damage (1). The neurological findings in acute toxic leukoencephalopathy can reverse with prompt recognition and with-

Table 1. Patient findings

Variable	Case 1	Case 2
Age (years)	19	17
Presenting symptoms		
Headache	+	+
Photophobia	+	0
Phonophobia	+	0
Blurred vision	0	+
Abnormal brain magnetic resonance imaging	+	+
Normal findings		
Physical examination	+	+
Neurological examination	+	+
Blood	+	+
Toxicology screening	+	+
Cerebrospinal fluid	+	+
Clinical recovery in 2 to 5 days	+	+

drawal of the offending agent (2). Definite findings on MRI to predict reversible versus irreversible and severe outcomes have not been determined.

Similar though less extensive findings have been described in the clinicoradiological syndrome of mild encephalitis/encephalopathy with reversible splenial and white matter lesions (MERS Type II). This entity presents in patients with clinically mild encephalopathy and reversible lesions involving the entire corpus callosum with bilateral extension into the subcortical white matter (3, 4). First reports described this rare entity in patients who had seizures with secondary generalization (5) and in patients with toxicity or drug sensitivity to antiepileptic

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Figure 1. MRI in Case 1. **(a)** Sagittal fast spin echo T2-weighted image demonstrates diffuse swelling and abnormal hyperintense signal of the entire corpus callosum (arrowheads). There is also abnormal hyperintensity of the pontine tegmentum (arrow). **(b)** Sagittal T1 contrast-enhanced image shows absence of abnormal enhancement. **(c)** Follow-up MRI fast spin echo T2-weighted image after 2 months shows resolution of the white matter changes.

drugs (6). Subsequently, this entity has widened its spectrum and has been associated with different clinical neurologic and nonneurologic conditions, including postinfectious disorder (7), rapid withdrawal of antiepileptic drugs (8), high-altitude

cerebral edema (9), and various metabolic disorders (hypoglycemia and hyponatremia) (10).

Due to the heterogeneous entities linked to mild encephalitis/encephalopathy with reversible splenial and white matter

Figure 2. Axial MRI in Case 1. **(a)** Fast spin echo T2-weighted imaging, diffusion-weighted imaging (b1000), and apparent diffusion coefficient (ADC) maps demonstrate abnormal T2 hyperintense signal intensity and matching restricted diffusion of the subcortical white matter (top row), corpus callosum (middle row), and the pontine tegmentum (bottom row), as indicated by the arrows. **(b)** Two-month follow-up imaging utilizing the same sequences shows near complete interval resolution of the white matter changes.

Figure 3. MRI in Case 2. Axial T2-weighted imaging shows abnormal T2 hyperintense signal (arrows) of the (a) subcortical white matter, (b) corpus callosum, and (c) pontine tegmentum. Diffusion-weighted (b1000) imaging and apparent diffusion coefficient (ADC) maps demonstrate restricted diffusion in the same distribution.

lesions, there is controversy regarding their pathogenesis. No unequivocal hypothesis has been formulated regarding the nature of the lesions. Several theories have been postulated, including intramyelinic edema due to transient disruption of energy metabolism, which may cause reversible myelin vacuolization (11), antiepileptic drug toxicity-induced reversible demyelination (12), alteration of the arginine-vasopressin system which may affect brain hydric content (13), and development of an inflammatory infiltrate with influx of inflammatory cells and molecules possibly combined with related cytotoxic edema (14).

The usage of thermogenic dietary supplements is widespread for augmentation in overall metabolism and “fat burning” in expectation to support weight loss by the consumer. Thermatrim is a thermogenic dietary supplement marketed via the Internet and available to the general public. Its contents profile states it contains garcinia cambogia, chromium picolinate, chitosan, equisetum arvense, momordica charantia, herbal sources of caffeine such as guarana, and other purported metabolic-supporting ingredients such as carnitine and *Ilex paraguariensis*, though there is a lack of information on the quantities of ingredients and other specific product information.

Thermogenic supplements have been associated with significant side effects, including anxiety, insomnia, cardiovascular disorders, and central nervous system stimulation, among others (15). However, these reports originate from isolated case reports due to the lack of forthcoming users experiencing said adverse effects.

This is the first time that reversible white matter lesions have been reported to be associated with a thermogenic dietary supplement. A larger series of patients needs to be studied to assess the specificity and correlation of these findings as a direct cause of acute leukoencephalopathy. Further product-specific research on thermogenic aids is needed to determine levels of effectiveness and safety for consumers.

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