

## Successful treatment of acquired idiopathic generalized anhidrosis

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Hypohidrosis and anhidrosis can be caused by various diseases. Diabetes mellitus, Sjögren syndrome, pure autonomic failure, Fabry disease, Ross syndrome, thyroid dysfunction, paraneoplastic autonomic dysfunction, and congenital absence of sweat glands are possible diagnoses.<sup>1</sup> A less common cause of hypohidrosis/anhidrosis is the acquired idiopathic generalized anhidrosis (AIGA). Until now, 64 cases of AIGA have been reported, 62 being Japanese.<sup>2</sup> We here report a European patient with AIGA.

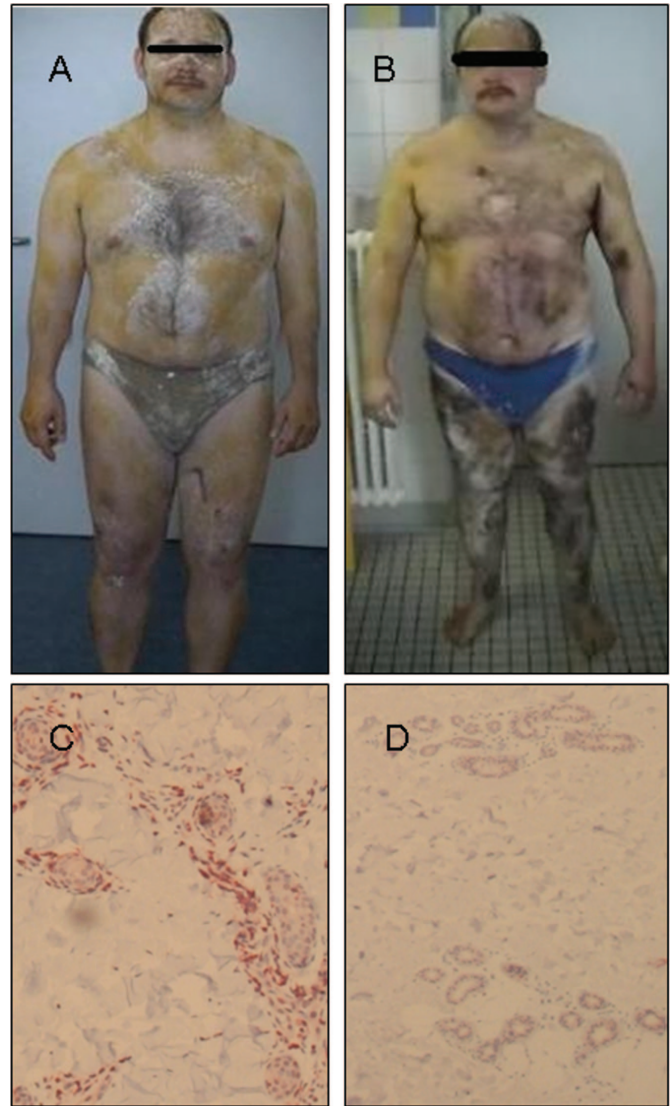
**Case report.** A 39-year-old white man presented with a 6-month history of progressive heat intolerance and lack of sweating except for the axillary zone and parts of his face. The patient also reported tachycardia and general fatigue. He had no history of dry mouth, dry eyes, concomitant sharp pain, or urticaria.

The patient's history and family history were unremarkable. The patient did not take any medications. Physical and neurologic examination including autonomic functional tests (heart rate variability, Valsalva maneuver, respiratory sinus arrhythmia, tilt table test) were normal. Axon reflex testing was not performed. The thermoregulatory as well as the pilocarpine sweating tests showed anhidrosis except for the axillary and periorbital zones (figure, A).

Cranial MRI, chest radiograph, and various laboratory tests (including anti-GM1 and anti-GQ1B antibodies, IgE level) revealed normal findings. A skin biopsy specimen from the sternum showed infiltration of sweat glands by CD3-positive lymphocytes (figure, C). Acquired idiopathic generalized anhidrosis was diagnosed, and methylprednisolone was administered (1,000 mg/day for 3 days IV followed by tapering oral doses for 2 weeks). One week after therapy initiation, the patient's sweat production improved. Two months later, the thermoregulatory sweating test was normal (figure, B). A repeated skin biopsy revealed no more CD3-positive lymphocyte infiltration (figure, D).

**Discussion.** AIGA is an uncommon cause of hypohidrosis/anhidrosis. Most of the reported cases were from Japan. Clinical features of AIGA are an acute or sudden onset of generalized anhidrosis with an onset early in life, the absence of other autonomic dysfunction, and a marked response to glucocorticoids. Concomitant sharp pain or cholinergic urticaria and elevated IgE levels have also been described in the majority of patients. These features were absent in our patient; however, the marked response to glucocorticoids and the histopathologic findings strongly support the diagnosis of AIGA.

There are three subgroups of AIGA<sup>1</sup>: The idiopathic pure sudomotoric failure (IPSF), sudomotoric neuropathy, and sweat gland failure. Most cases of AIGA seem to represent IPSF, as in the case of our patient. Typical histopathologic findings here include CD3-positive lymphocyte infiltrations of the sweat glands<sup>3</sup> and occlusion of proximal coiled ducts,<sup>4</sup> whereas CD3-positive lymphocyte infiltration seems to be a hallmark of IPSF. Although the etiology of AIGA is still unclear, immunologic mechanisms contribute to the disease. The facts that IPSF as a subgroup of AIGA is associated with CD3-positive lymphocyte infiltration of sweat glands and that CD3 plays an important role in the induction of cell-mediated disorders support this hypothesis. This may also explain the improvement in sweat function with corticosteroids in 78% of patients with AIGA.<sup>2</sup> A deficit in the muscarinic cholinergic receptor in eccrine sweat glands or interference in transmission of acetylcholine to cholinergic receptors is supposed to be involved in the pathogenesis of IPSF. This might explain the persisting sweat production of the axilla, as seen in our patient. Sweat glands of the axilla are apocrine glands and are supposed to be under adrenergic control.<sup>2</sup> Another explanation would be the early stage of the disease in our patient, with not all sweat glands already being involved. The possibility that the CD3 cells might be directed to some parts of the eccrine sweat gland itself has to be considered as well.



**Figure.** (A) Thermoregulatory sweating tests on admission (note missing blue color for anhidrotic areas). (B) Thermoregulatory sweating test after steroid treatment (note blue color for improved sweating, especially of trunk and legs). (C) Skin biopsy (CD3 stain) on admission (note lymphocyte infiltrations of the sweat glands). (D) Skin biopsy (CD3 stain) after steroid treatment.

In cases of progressive hypohidrosis/anhidrosis with no other pathologic findings, the diagnosis of AIGA should be considered. In most cases, steroid pulse therapy is effective.

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## Occult celiac disease presenting as epilepsy and MRI changes that responded to gluten-free diet

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Andre Lagrange, MD, PhD

Celiac disease (CD), an autoimmune disorder involving hypersensitivity to gluten, has been associated with many neurologic manifestations, most commonly ataxia and neuropathy.<sup>1-3</sup> We report contrast-enhancing brain lesions and epilepsy in a patient with previously occult CD that responded to a gluten-free diet (GFD).

**Case report.** A 30-year-old, previously healthy man presented with a 2-year history of headaches and refractory seizures with postictal right hemiparesis and aphasia. He also had a constant milder hemiparesis. A brain MRI revealed multiple contrast-enhancing lesions involving white and gray matter. Serologic testing was unrevealing. A brain biopsy showed inflammation with reactive gliosis but no microglial nodules. There was also endothelial proliferation, without vasculitis. Special stains for periodic acid-Schiff, Gomori methenamine silver, Steiner, herpes simplex virus 1 and 2, amoeba, and encephalitis panel were all negative, as were CSF cultures for viral, bacterial, and fungal organisms. Despite treatment with glucocorticoids and multiple antiepileptic drugs, his seizures persisted, and subsequent MRI over the following 10 months found the appearance and disappearance of new lesions. He then presented to our clinic for a second opinion. Past medical, family, and social history were noncontributory; a systems review revealed no fever or weight loss, but he did have chronic constipation and rash, which were exacerbated during times of increased seizures. Physical examination showed a well-nourished man with excoriated erythematous papules over his elbows, knees, and buttocks; his general medical examination was otherwise unremarkable. Neurologic examination revealed word-finding difficulty and right-sided weakness. An extensive evaluation for infectious, neoplastic, and inflammatory etiologies was negative. Notable negative studies included HIV, vitamin B<sub>12</sub> and E levels, screens for collagen vascular disease, serum and CSF angiotensin-converting enzyme levels, CSF cell counts, oligoclonal banding, IgG index, cytology, and flow cytometry. CT angiogram showed no evidence for vasculitis or cerebral calcifications. Although he denied diarrhea, the patient's gastrointestinal complaints and rash prompted an evaluation for celiac disease. Antigliadin IgG and IgA antibodies as well as anti-transglutaminase and anti-endomysial antibodies were all markedly elevated. Small bowel biopsy was diagnostic of CD, and a skin biopsy was consistent with dermatitis herpetiformis. Staining of his previous cerebral biopsy for anti-transglutaminase antibodies was not available. Despite our

recommendations, he refused a repeat brain biopsy to further exclude malignancy. He was instead treated with a GFD and antiepileptic medication. He has been strictly compliant with the diet and has been seizure-free for nearly 2 years, although the hemiparesis and cognitive difficulties persist. Abnormal antibody levels have normalized, as is expected with GFD compliance,<sup>4</sup> and the contrast-enhancing brain lesions have all resolved without recurrence (figure).

**Discussion.** Our patient with new-onset epilepsy and contrast-enhancing brain lesions meets the serologic and pathologic diagnostic criteria for CD. Furthermore, initiation of a GFD resulted in the clinical and radiologic resolution of the brain lesions, suggesting that the neurologic symptoms and CD were causally related.

Gastrointestinal involvement of CD may produce malabsorption and some of the neurologic manifestations of CD may be due to vitamin deficiencies.<sup>5</sup> However, these data have not been reproducible or conclusive. Moreover, the patient appeared well nourished, and serum albumin, hemoglobin, and vitamins E and B<sub>12</sub> were all normal. To our knowledge, there is only one other report of relapsing and remitting contrast-enhancing MRI lesions associated with CD.<sup>2</sup> However, that patient had exclusively white matter lesions, also had oligoclonal bands in the CSF, and responded to glucocorticoids but not a GFD. It is therefore difficult to distinguish those findings from coincident multiple sclerosis in a patient with CD. In contrast, our patient's cortical involvement and seizures would be distinctly unusual for multiple sclerosis. The protracted, nearly year-long course would argue against an alternative diagnosis of acute disseminated encephalomyelitis. Finally, the contrast-enhancing white and gray matter lesions are not consistent with MRI changes due to frequent seizures.

Several series have associated CD with epilepsy,<sup>3,5</sup> including a child with CD whose refractory epilepsy responded to a GFD.<sup>6</sup> Nonetheless, other than those rare CD cases involving cerebral calcification, the potential link between CD and epilepsy remains elusive. Moreover, the pathophysiologic basis of neurologic disease and CD, if one exists, is unknown. However, recent work<sup>7</sup> has found deposition of anti-transglutaminase antibodies in the cerebral vessels and brain tissue of patients with gluten ataxia, thereby suggesting that the antibodies themselves may contribute to the neurologic complications of CD.

Our case of GFD-responsive CD, epilepsy, and brain MRI lesions supports the idea that CD may involve the CNS and expands the repertoire of possible neurologic complications associated with CD. Further investigation into the relationship between CD and epilepsy is warranted.

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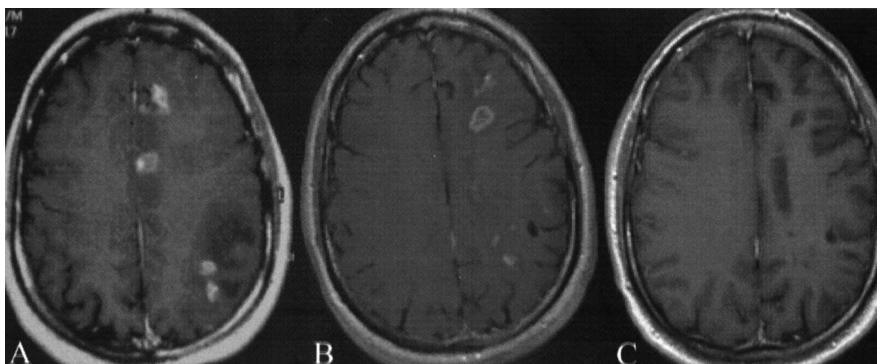


Figure. (A) T1 image showing contrast-enhancing gray and white matter lesions. (B) T1 image 2 years later, showing new contrast-enhancing lesions. (C) T1 image after 12 months on gluten-free diet, showing resolution of prior contrast-enhancing regions and no new lesions.

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## Correction

### **There is nothing staid about STARD: Progress in the reporting of diagnostic accuracy studies**

In the editorial “There is nothing staid about STARD: Progress in the reporting of diagnostic accuracy studies” by Karen C. Johnston and Robert G. Holloway (*Neurology* 2006;67:740–741), accompanying the article “The quality of diagnostic accuracy studies since the STARD statement: Has it improved?” by Smidt et al. (*Neurology* 2006;67:792–797), the pre-STARD vs post-STARD comparison was stated to be significant but the data provided demonstrated a statistically insignificant difference. The authors wish to correct the statement and apologize for the error.

## Correction

### **CSF tau protein: A new prognostic marker for Guillain-Barré syndrome**

In the Brief Communication “CSF tau protein: A new prognostic marker for Guillain-Barré syndrome” by K. Jin et al. (*Neurology* 2006;67:1470–1472), the units of CSF tau protein should be pg/mL instead of ng/mL in table 1, table 2, and figure. The authors regret these errors.

## Correction

### **Correspondence: Neuropsychological deficits in long-term frequent cannabis users**

In the reply from authors Lambros Messinis and Panagiotis Papatathanasopoulos in the Correspondence concerning “Neuropsychological deficits in long-term frequent cannabis users” (*Neurology* 2006;67:1902), the second respondent’s first name and surname are transposed. The author’s name is Panagiotis Papatathanasopoulos.

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## Correction

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