Enteropathy-associated T-cell lymphoma with initial manifestation in the CNS

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We report a patient with asymptomatic celiac disease who developed an enteropathy-associated T-cell lymphoma (EATCL) with primary manifestation in the CNS. A previously healthy 56-year-old woman was admitted after a 6-week history of depression, headache, and progressive cognitive decline. Her medical history was unremarkable, except for celiac disease diagnosed in 1992, which, upon gluten-free diet, resolved rapidly and remained asymptomatic. Clinically, she was disoriented and somnolent and had sensorimotor aphasia, apraxia, and acalculia. The remaining neurologic state was unremarkable. Full blood count and chemistry were within the normal range. The anti-gliadin IgA (IgA 21 kU/L) and IgG (IgG 127 kU/L) titers were elevated (normal IgA < 20 kU/L, IgG < 20 kU/L), and anti-endomysium IgA was negative. Cranial MRI showed multiple subcortical and periventricular, partially gadolinium-enhancing lesions, without leptomeningeal involvement (figure, A and B). CSF contained 39 cells (normal <4.7; 98% lymphocytes) and elevated protein with 0.8 g/L (normal <0.48 g/L). Cytologic analysis failed to detect malignant cells. A stereotactic brain biopsy on the right prefrontal region revealed white matter diffusely infiltrated by pleomorphic atypical lymphoid cells, which were immunoactive for CD2, CD3, CD7, CD8, CD30, CD56, and T cell internal antigen-1 (TIA-1) and negative for CD4, CD5, and CD20 (see the figure, C through E). A diagnosis of peripheral T-cell lymphoma of the brain with cytotoxic phenotype was made. Upon whole-body CT scan, no evidence of an extracranial manifestation of the lymphoma was found. Under chemotherapy (dexamethasone and six cycles of methotrexate 4,000 mg/m², followed by leucovorin rescue), her deficits resolved completely. Ten weeks later, she became again symptomatic with grand mal seizures resulting from CNS involvement.2 There is one report3 of a 70-year-old man presenting with grand mal seizures resulting from CNS involvement in recurrent disseminated EATCL. A second patient has been reported4 presenting with cognitive decline and personality changes caused by EATCL, which was manifesting as primary CNS lymphoma according to stereotactic brain biopsy. In contrast to that report, we confirm the intestinal involvement by molecular methods and already establish intra vitam the diagnosis of cryptogenic T-cell lymphoma of the duodenum. Whereas there is a clear association between celiac disease and EATCL, the evolution of the disease remains unpredictable. In some patients, a period of refractory celiac disease with clonal proliferation of intraepithelial lymphocytes precedes EATCL. Such a course of disease was demonstrated at the molecular level in at least one patient.5 It is tempting to speculate that chronic stimulation of gut-sensitive T cells, even without clinical symptoms of sprue, may lead to clonal selection and finally to malignant transformation.

In summary, any extraintestinal manifestation—particularly in the brain—of a T-cell non-Hodgkin’s lymphoma in a patient with established celiac disease should be considered as a possible manifestation of a cryptogenic EATCL, even if the enteropathy is clinically asymptomatic. This results in important implications for the clinical management of such patients as the prognosis of overt EATCL is generally very poor.

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References


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Clinical/Scientific Notes
Guillain–Barré syndrome (GBS) is characterized by acute, motor-predominant neuropathy frequently preceded by infection. *Campylobacter jejuni* enteritis is involved in about one-third of patients. Molecular mimicry between *C. jejuni* and gangliosides can lead to the production of serum anti-ganglioside antibodies, which may cause neuropathies.

A literature search revealed only one report describing a family with *C. jejuni* enteritis, in which GBS developed in one of three affected members. That report implicated anti-ganglioside antibody as the cause of GBS. We now describe a second such family in which additional factors as well as anti-ganglioside antibodies may have contributed to the GBS onset.

Two brothers, 16 and 19 years old, had diarrhea of 3-days' duration. A week after the onset, the younger brother had severe tetraparesis. Neurologic and electrophysiologic findings were consistent with a diagnosis of axonal GBS. Blood specimens were obtained from the two brothers on the fourth day after the GBS onset. The brothers were sero-positive for anti-*.C. jejuni* antibody. Anti-ganglioside antibodies were examined as described previously, using GM1, GM2, GM3, GD1a, GD1b, GalNAc-GD1a, GD3, GT1b, and GQ1b as antigens. IV immunoglobulin therapy produced prompt marked improvement in the patient's condition. The elder brother had no signs or symptoms suggestive of GBS. The serum was strongly positive for anti-GD1a IgG antibody (1:320), confirmed to react with GD1a on thin-layer chromatography (figure). Anti-ganglioside antibody titers for both brothers decreased to 1:40 3 months after the disease onset.