

Steroid-Responsive Encephalopathy Associated With Autoimmune Thyroiditis

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Background: Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT), often termed *Hashimoto encephalopathy*, is a poorly understood and often misdiagnosed entity.

Objective: To characterize the clinical, laboratory, and radiologic findings in patients with SREAT to potentially improve recognition of this treatable entity.

Design: Retrospective analysis of clinical features and diagnostic test data.

Setting: Two affiliated tertiary care referral institutions.

Patients: Twenty consecutive (6 male) patients diagnosed as having SREAT from 1995 to 2003.

Main Outcome Measures: Clinical features and ancillary test findings associated with SREAT.

Results: The median age at disease onset was 56 years (range, 27-84 years). The most frequent clinical features were tremor in 16 (80%), transient aphasia in 16 (80%), myoclonus in 13 (65%), gait ataxia in 13 (65%), seizures in 12 (60%), and sleep abnormalities in 11 (55%). All patients were assigned an alternative misdiagnosis at

presentation, most commonly viral encephalitis (n=5), Creutzfeldt-Jakob disease (n=3), or a degenerative dementia (n=4). The most frequent laboratory abnormalities were increased liver enzyme levels in 11, increased serum sensitive thyroid-stimulating hormone levels in 11, and increased erythrocyte sedimentation rate in 5. In only 5 patients (25%) did cerebrospinal fluid abnormalities suggest an inflammatory process. Magnetic resonance imaging abnormalities believed to be related to the encephalopathy were present in 5 patients (26%).

Conclusions: The clinical, laboratory, and radiologic findings associated with SREAT are more varied than previously reported. Misdiagnosis at presentation is common. This treatable syndrome should be considered even if the serum sensitive thyroid-stimulating hormone level and erythrocyte sedimentation rate are normal, the cerebrospinal fluid profile does not suggest an inflammatory process, and neuroimaging results are normal. Until the pathophysiologic mechanism of this and other autoimmune encephalopathies is better characterized, we believe that descriptive terms that reflect an association rather than causation are most appropriate for this syndrome.

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NEUROLOGISTS ARE OFTEN consulted to evaluate patients with acute or subacute encephalopathy. The differential diagnosis for encephalopathy is wide, but the clinical features and findings on blood, cerebrospinal fluid (CSF), electroencephalography (EEG), and neuroimaging studies often (but not always) lead to an accurate diagnosis. Once infectious causes are excluded, an autoimmune or inflammatory process may be suspected on the basis of inflammatory and autoimmune markers in the serum and CSF and meningeal and parenchymal abnormalities on magnetic resonance imaging (MRI) of the brain.

Autoimmune encephalopathy may take many forms, including paraneoplastic or idiopathic limbic encephalitis, that are de-

finied by characteristic serologic and neuroimaging abnormalities.^{1,2} Idiopathic autoimmune encephalopathy is also often defined on the basis of a clinical response to steroids. Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT), often referred to as *Hashimoto encephalopathy*, was initially described by Brain et al.³ Although high serum levels of thyroperoxidase (TPO) antibody, formerly known as antimicrosomal antibody, are often found in patients with SREAT, this organ-specific autoantibody is a serologic marker for the common condition of autoimmune (Hashimoto) thyroiditis and a common marker of autoimmunity in most autoimmune neurologic disorders.^{4,5} A direct causal relationship between thyroid antibodies and encephalopathy is unlikely.⁶ Numerous case re-

Table 1. Clinical Findings in 20 Patients With Steroid-Responsive Encephalopathy Associated With Autoimmune Thyroiditis

Abnormal Clinical Finding	No. (%) of Patients
Cognitive impairment and behavioral changes	20 (100)
Fluctuating symptoms	19 (95)
Transient aphasia	16 (80)
Tremor	16 (80)
Myoclonus	13 (65)
Ataxia or gait disorder	13 (65)
Seizures	12 (60)
Generalized	10 (50)
Partial	7 (35)
Both	5 (25)
Sleep disturbance	11 (55)
Hypersomnolence	8 (40)
Insomnia	3 (15)
Headache	10 (50)
Lateralized motor or sensory deficits	5 (25)
Psychosis or paranoia	5 (25)

Table 2. Initial Clinical Diagnoses in 20 Patients With Steroid-Responsive Encephalopathy Associated With Autoimmune Thyroiditis

Initial Clinical Diagnosis	No. (%) of Patients
Viral encephalitis	5 (25)
Creutzfeldt-Jakob disease	3 (15)
Stroke or transient ischemic attack	3 (15)
Alzheimer disease	3 (15)
Migraine	2 (10)
Lewy body dementia	1 (5)
Psychosis	1 (5)
Metabolic encephalopathy	1 (5)
Delirium	1 (5)

ports, small series, and an excellent recent literature review⁷⁻¹¹ have characterized this entity further. Nevertheless, many uncertainties regarding the condition persist, including the spectrum of clinical findings, the associated laboratory and radiologic findings, the clinical significance of the quantitative level of TPO antibody, the criteria required for diagnosis, the appropriate terms for the condition, and the typical outcome of steroid treatment. The literature thus far has not provided sufficient data on these challenging issues to aid the diagnosis of this disorder and guide its management. We sought to address some of these issues by analyzing data on a series of patients in whom the diagnosis of SREAT was made at Mayo Clinic Rochester (in Minnesota) and Mayo Clinic Scottsdale (in Arizona) during an 8-year period.

METHODS

This retrospective study was reviewed and approved by the Mayo Clinic institutional review board. The authors identified consecutive patients in whom a diagnosis of SREAT was made at Mayo Clinic Rochester or Mayo Clinic Scottsdale between November 1995 and July 2003. For the purpose of this study, the diagnosis

of SREAT required fulfillment of the following criteria: (1) encephalopathy manifested by cognitive impairment and 1 or more of the following: neuropsychiatric features (eg, hallucinations, delusions, or paranoia), myoclonus, generalized tonic-clonic or partial seizures, or focal neurologic deficits; (2) presence of serum thyroid antibody (TPO or microsomal); (3) euthyroid status (serum sensitive thyroid-stimulating hormone [TSH], 0.3-5.0 mIU/L or mild hypothyroidism (serum sensitive TSH, 5.1-20.0 mIU/L) that would not account for encephalopathy; (4) no evidence in blood, urine, or CSF analyses of an infectious, toxic, metabolic, or neoplastic process; (5) no serologic evidence of the neuronal voltage-gated calcium channel, voltage-gated potassium channel, or other currently recognized paraneoplastic autoantibodies to indicate another diagnosis; (6) no findings on neuroimaging studies indicating vascular, neoplastic, or other structural lesions to explain the encephalopathy; and (7) complete or near-complete return to the patient's neurologic baseline status following corticosteroid treatment. This last criterion was specifically required because our primary aim was to identify patients who responded to treatment and then characterize their clinical, laboratory, and radiologic features. These criteria are similar to those previously published,^{6,7,12} except that we required the absence of voltage-gated calcium and potassium channels and other paraneoplastic autoantibodies for inclusion in this analysis.

We retrospectively reviewed and analyzed all available clinical, laboratory, radiologic, and brain biopsy data to determine the spectrum of features and findings associated with SREAT. A review of patients evaluated at our institution before 1996 has been published, which includes 2 of the cases in this study.⁷ A review of the EEG findings in SREAT, which included 15 patients in this study, has also been published.¹² The current article expands on the report in abstract form of 17 patients in our original data set.⁶

During this same approximately 8-year period, we treated additional patients who fulfilled the same criteria described in this article, except that no significant improvement occurred following high-dose corticosteroid treatment (ie, steroid-unresponsive encephalopathy associated with autoimmune encephalopathy). We present data on these patients and argue that they likely have a nonautoimmune or noninflammatory origin for their encephalopathy.

RESULTS

DEMOGRAPHIC AND CLINICAL FINDINGS

Twenty patients met criteria for the diagnosis of SREAT as noted herein. The symptoms and findings for the 20 patients are given in **Table 1**. All but 1 patient required hospitalization during the acute phase of illness because of the severity of their deficits. The median age at onset was 56 years (range, 27-84 years). There was a preponderance of female patients (70%). The most common associated manifestations were behavioral-cognitive abnormalities (by definition) in 20 (100%), tremor in 16 (80%), transient aphasia in 16 (80%), myoclonus in 13 (65%), gait ataxia in 13 (65%), seizures in 12 (60%), and sleep abnormalities in 11 (55%). The initial clinical diagnoses are given in **Table 2**. Misdiagnoses were common. The most frequent misdiagnoses were viral encephalitis, Creutzfeldt-Jakob disease, and degenerative dementia.

Nine patients had a history of hypothyroidism that antedated the onset of neurologic symptoms, and 2 had euthyroid goiter. Five additional patients developed hypothyroidism after the resolution of encephalopathy. Other

autoimmune disorders were present in 6 patients and included diabetes mellitus type 1 in 2 (10%), systemic lupus erythematosus in 1 (5%), and Crohn disease in 1 (5%). Two patients had symptoms of sicca syndrome (10%). Other autoimmune disorders were diagnosed subsequently in 2 patients, primary Sjögren syndrome in one (5%) and pernicious anemia in the other (5%). Subacute combined degeneration developed in the latter case before the diagnosis of pernicious anemia was made. Five patients (25%) had a family history of non-organ-specific (rheumatologic) or organ-specific autoimmune disease.

BLOOD AND SEROLOGIC ABNORMALITIES

Pertinent laboratory findings are given in **Table 3**. The serum sensitive TSH level was mildly elevated in 11 (55%). By definition, all patients had thyroid antibodies. The microsomal antibody titer was elevated in 7 of 7 tested (median, 1:6400; range, 1:400 to 1:102 400; reference range, <1:100), and the TPO antibody titer was elevated in 13 of 13 tested (median, 250 IU/mL; range, 65-4830 IU/mL; reference range, <20 IU/mL). All patients experienced a marked degree of encephalopathy, and the levels of thyroid antibodies did not correlate with the severity of neurologic deficits. Eleven patients had mild thyroid failure (serum sensitive TSH, 5.1-15.6 mIU/L). Erythrocyte sedimentation rate was mildly to moderately elevated (median, 38 mm/h; range, 30-75 mm/h) in 5 (26%) of 19 tested. The C-reactive protein level was elevated in 3 of 9 patients tested. Eleven patients (55%) had a mild elevation of serum aminotransferase levels.

CSF FINDINGS

The CSF was analyzed in all patients. No infectious origins were identified (**Table 4**). The protein level was elevated in 17 patients (85%) (range, 55-680 mg/dL [0.055-0.68 g/dL]; reference range, <45 mg/dL [<0.045 g/dL]). Neuron-specific enolase and 14-3-3 protein levels were normal in 6 patients tested. Five had mild lymphocytic pleocytosis (white blood cell count, 5-30 cells/ μ L). The CSF IgG index was normal in all of 14 tested, and the CSF IgG synthesis rate was elevated in 2.

EEG FINDINGS

All patients underwent EEG studies, of which 19 results were abnormal. Generalized slowing was seen in 19 patients. Other findings included focal slowing, triphasic waves, epileptiform abnormalities, and photomyogenic response. One patient had a normal routine EEG result. Steroid therapy was associated with improvement or resolution of EEG abnormalities in all 17 patients who had EEG follow-up.¹²

MRI FINDINGS

Cranial MRI was performed in 19 patients (1 patient had a permanent pacemaker). Fourteen patients (74%) had normal imaging results or nonspecific white matter abnormalities consistent with age. Four patients had a diffuse increased signal on T2-weighted and fluid-attenuated inversion recovery (FLAIR) images in the cerebral white matter, and 1 MRI showed extensive dural enhancement. Following cortico-

Table 3. Serologic and Other Laboratory Abnormalities in 20 Patients With Steroid-Responsive Encephalopathy Associated With Autoimmune Thyroiditis

Serologic or Laboratory Test	No. of Patients*
Thyroperoxidase antibody positive	13/13
Thyroid microsomal antibody positive	7/7
Thyroglobulin antibody positive	6/10
Antinuclear antibody positive	6/20
Extractable nuclear antigen antibody positive	1/20
Rheumatoid factor positive	1/17
Gliadin antibody positive	1/11
Erythrocyte sedimentation rate elevated	5/19
C-reactive protein level elevated	3/9
Liver aminotransferase levels (AST/ALT) elevated	11/20

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase.

*Denominator represents total number of patients tested.

Table 4. Cerebrospinal Fluid Abnormalities in 20 Patients With Steroid-Responsive Encephalopathy Associated With Autoimmune Thyroiditis

Parameter	No. of Patients*
Protein level elevated	17/20
Leukocyte count elevated ($>4/\mu$ L)	5/20
IgG synthesis rate elevated	2/14
IgG index elevated	0/14
Oligoclonal bands increased (>2)	1/12

*Denominator represents total number of patients tested.

steroid therapy, the MRI findings normalized in the 4 cases with white matter signal changes (as exemplified in the study by Bohnen et al¹³); meningeal enhancement has persisted for throughout 5 years in the other patient.

CEREBRAL ANGIOGRAPHY

Cerebral angiography was performed in 5 patients to look for evidence of vasculitis. Findings were normal in each case except for 1, which showed a nonspecific slow transit time in the distribution of the anterior cerebral artery.

MENINGEAL OR BRAIN BIOPSY

Meningeal or brain biopsy was performed in 2 cases. Histologic findings were entirely normal in the 1 patient with striking meningeal thickening and dural enhancement on MRI. In another patient with diffuse white matter signal changes on imaging, histologic findings included patchy myelin pallor, scant perivascular chronic inflammation, mild gliosis, and microglial activation.

THERAPY

By definition, marked clinical improvement was seen in all patients following high-dose corticosteroid therapy, in which 15 returned to their normal neurologic baseline status and 5 had mild residual symptoms, which included tremor in 1, gait impairment in 1, mild forgetfulness in 1, mild forget-

Table 5. Data From 12 Patients With Subacute Encephalopathy Associated With Autoimmune Thyroiditis Who Experienced No Significant Clinical Improvement Following High-Dose Corticosteroid Treatment

Patient No./Sex/ Age, y	Antibody*	Treatment	Outcome
1/M/67	TM, 1:400	Methylprednisolone, 1 g intravenously for 3 d, then prednisone, 60 mg orally with gradual taper	No improvement, progressive encephalopathy with death 1 y later; autopsy showed CJD
2/F/72	TPO, 170	Methylprednisolone, 1 g intravenously for 5 d	No improvement, progressive encephalopathy with death 8 mo later; autopsy showed CJD
3/M/75	TM, 1:102 400	Methylprednisolone, 1 g intravenously for 5 d	No improvement, progressive encephalopathy with death 1 y later; autopsy showed nLBD
4/F/53	TM, 1:25 600	Methylprednisolone, 1 g intravenously for 5 d	No improvement, progressive encephalopathy with death 2 y later; autopsy showed NIBD
5/F/56	TPO, 723	Methylprednisolone, 1 g intravenously for 3 d	No improvement during 3 d of therapy, transferred to local hospice care with death 5 d later; no autopsy performed
6/M/72	TM, 1:400; TG+	Methylprednisolone, 1 g intravenously for 5 d	No improvement, progressive encephalopathy with death 5 y later; no autopsy performed
7/F/85	TPO, 184	Methylprednisolone, 1 g intravenously for 5 d	No improvement, progressive encephalopathy during following 4 y
8/F/28	TPO, 25; TG+	Methylprednisolone, 1 g intravenously for 5 d	No improvement, fluctuating encephalopathy during the following 1 y
9/F/66	TPO, 1150	Methylprednisolone, 1 g intravenously for 5 d	No improvement, static encephalopathy during the following 2 y
10/M/71	TG+	Prednisone, 60 mg for 30 d, with taper	No improvement, progressive encephalopathy during the following 2 y
11/F/73	TPO, 1031	Methylprednisolone, 1 g intravenously for 5 d	No improvement during subsequent 3 mo, lost to follow-up
12/F/78	TPO, 114	Methylprednisolone, 1 g intravenously for 5 d	No improvement; progressive encephalopathy during the following 1 y

Abbreviations: CJD, Creutzfeldt-Jakob disease; NIBD, neurofilament inclusion body disease; nLBD, neocortical-predominant Lewy body disease; TG+, thyroglobulin antibody positive; TM, thyroid microsomal antibody titer; TPO, thyroperoxidase antibody level.

*The reference ranges in Mayo Medical Laboratories (Rochester, Minn, and Scottsdale, Ariz) at the time the samples were analyzed were as follows: TM, less than 1:100; TPO, less than 20 IU/mL; and TG, negative.

fulness and tremor in 1, and mild forgetfulness and gait impairment in 1. Intravenous methylprednisolone, 1 g/d for 5 days, was used in 17 patients followed by a course of oral steroids in 6 patients. Oral prednisone, 60-100 mg/d for 10 to 30 days, was used in 3 patients. Eight patients (40%) were able to discontinue the use of steroids after initial treatment and had no relapses. Three required treatment of relapses with additional short courses of intravenous methylprednisolone, and 9 patients required continuous treatment with oral steroids or with other immunomodulatory therapy to maintain remission. These other therapies included azathioprine (n=3), methotrexate (n=2), cyclophosphamide (n=1), and intravenous immunoglobulin (n=1). Thyroid hormone therapy was initiated in patients with laboratory evidence of hypothyroidism, but neurologic improvement did not correlate with thyroid hormone therapy.

STERIOD NONRESPONDERS

Data on 12 patients with a subacute encephalopathy associated with autoimmune thyroiditis who failed to improve with high-dose corticosteroids are given in **Table 5**. All of these patients fulfilled criteria 1 through 6 as stated in the "Methods" section. The 2 patients with autopsy-proven Creutzfeldt-Jakob disease (cases 1 and 2) and case 5 had an increased signal in the cerebral cortical ribbon on FLAIR-positive and FLAIR-negative diffusion-weighted images and increased neuron-specific enolase

or 14-3-3 protein levels; thus, these patients were suspected to have Creutzfeldt-Jakob disease ante mortem. However, because of our experience with another patient with an increased signal in the cortical ribbon on FLAIR images who responded to corticosteroids (B.B., unpublished data, 1997) and the report of increased 14-3-3 protein levels in other patients diagnosed as having Hashimoto encephalopathy who responded to steroids,¹⁴ we treated these 3 patients with steroids in the unlikely but possible event that an autoimmune or inflammatory mechanism was the cause of their illness. The patient with autopsy-proven Lewy body disease had a history of dream enactment behavior that was highly suggestive of rapid eye movement (REM) sleep behavior disorder and thus of underlying Lewy body disease,¹⁵ but the markedly elevated thyroid microsomal antibody titer led the physicians involved in his care to diagnose him as having probable Hashimoto encephalopathy and to treat him with steroids. The patient with neurofilament inclusion body disease had clinical and radiologic features typical of frontotemporal dementia,¹⁶ but the markedly elevated thyroid microsomal antibody titer led to her treatment with corticosteroids also; this patient is case US1 in the study by Josephs et al.¹⁷ Most of the remaining patients have experienced progression in their encephalopathy, suggesting an underlying neurodegenerative disorder.

This large series of patients provides an additional characterization of SREAT and should aid in improving recognition of patients in whom to consider instituting therapy. The clinical findings are varied but consistent with those reported previously.¹¹ Cognitive impairment and behavioral changes are the defining characteristics of any encephalopathy. Other features that characterize SREAT include fluctuating symptoms, tremor, myoclonus, transient aphasia, sleep abnormalities, seizures, and gait difficulties. Headache, neuropsychiatric features, and lateralized motor or sensory deficits were present in a few cases. Given the nonspecific nature of the neurologic and laboratory findings, and the age at onset spanning several decades, it is not surprising that alternative initial diagnoses were considered in all of our patients. Notably, disorders such as Creutzfeldt-Jakob disease, Alzheimer disease, and dementia with Lewy bodies were suspected in many cases, underscoring the need to consider autoimmune encephalopathy even in those with features that suggest irreversible prion and degenerative disorders.

The levels of thyroid antibodies were variable. All patients were encephalopathic, but antibody levels did not correspond to the severity of the clinical deficits. The presence of thyroid antibodies in serum, not the level, was the clinically relevant issue, indicating that SREAT should be considered in patients with encephalopathy even if thyroid antibody levels are only mildly elevated. Furthermore, SREAT should be considered in patients with encephalopathy regardless of whether they are euthyroid or mildly hypothyroid.

As has long been recognized for patients with autoimmune thyroid disease, multiple other autoimmune disorders commonly coexist.^{4,5,18-21} One third of our patients had evidence of multiple autoimmune disorders. The finding of elevated serum levels of liver aminotransferases in 60% of our cases was not anticipated. Whether the elevated liver enzyme levels represent a forme fruste of autoimmune hepatitis or some other process is not clear, but this finding warrants further investigation.

The finding of elevated CSF protein levels in most of our patients is consistent with prior reports.^{8,11,22} However, it is important to recognize that normal CSF protein levels, absence of lymphocytic pleocytosis, normal IgG synthesis rate, and absence of oligoclonal bands do not exclude the diagnosis of SREAT.

The MRI abnormalities found in some of our patients were consistent with an active encephalopathic process, including diffuse white matter signal abnormalities and meningeal enhancement. In several patients these abnormalities resolved following steroid therapy, a phenomenon that has been reported previously.¹³ Most patients with the diagnosis of SREAT had normal neuroimaging results, including normal cerebral angiography findings. These imaging characteristics are different from the striking mesial temporal lobe abnormalities encountered in subacute inflammatory autoimmune or paraneoplastic limbic encephalitis.^{1,2}

Although the data in this study may improve the recognition of potential patients with SREAT, the underlying pathogenesis remains unclear. The putative role of thyroid auto-

immunity in the pathogenesis of Hashimoto encephalopathy is complicated by the fact that serum TPO levels are elevated in approximately 10% of healthy adults, and the prevalence of individuals with elevated TPO levels increases with increasing age.²³ Thyroid autoantibodies are also commonly found in patients with other autoimmune neurologic disorders, including paraneoplastic and nonparaneoplastic limbic encephalitis.² It therefore seems unlikely that thyroid antibodies are the direct cause of the encephalopathy. We consider TPO antibody 1 of several related thyroid and gastric autoantibody markers of neurologic autoimmunity.

Several other etiologies have been proposed, including hypothyroidism itself, humoral factors, antigen-antibody complexes, overt vasculitis, intrathecal thyroid antibodies, and global cerebral hypoperfusion.^{11,24-27} It is certainly possible that more than 1 etiologic mechanism could lead to an autoimmune or inflammatory encephalopathy that responds to corticosteroids. Systematic studies of patients with encephalopathy, which could include a battery of serum and CSF autoimmune markers or other radiologic studies, may offer insights into the pathogenetic mechanisms.

The nomenclature in the autoimmune encephalopathies remains confusing. Encephalopathy, steroid responsiveness, and evidence of autoimmunity in the serum and CSF are common to most forms of autoimmune meningoencephalopathy, including Sjögren syndrome,²⁸ systemic lupus erythematosus,²⁹ and cerebellitis associated with glutamic acid decarboxylase autoantibody.²³ The term *nonvasculitic autoimmune inflammatory meningoencephalitis* has been suggested to facilitate the recognition and treatment of the autoimmune encephalopathies with similar clinical features.³⁰ In our view, the term *Hashimoto encephalopathy* implies that the encephalopathy is caused by Hashimoto thyroiditis, but as noted in this article, no conclusive evidence of this exists. We therefore view *nonvasculitic autoimmune inflammatory meningoencephalitis* as the most appropriate term for encompassing all subtypes of steroid-responsive encephalopathies of nonvasculitic origin and favor the terms *steroid-responsive encephalopathy associated with autoimmune thyroiditis*⁶ or *steroid-responsive encephalopathy associated with Hashimoto thyroiditis*³¹ for the subtype of nonvasculitic autoimmune inflammatory meningoencephalitis described in this report. Debate over the nomenclature will likely continue until the precise autoimmune or inflammatory processes are identified and proved to be pathogenic.

Some may argue with our use of the term *steroid-responsive* in describing this entity, in which the response to a treatment defines the entity of interest. Although we recognize the inherent circularity of defining a syndrome based on response to treatment (as could also be argued regarding the utility of levodopa responsiveness in diagnosing Parkinson disease), we conceded to the considerable practical utility of emphasizing steroid responsiveness that we hope will improve the diagnosis and therapy of encephalopathic patients. We hypothesize that patients with an encephalopathy associated with thyroid antibodies who do not markedly improve with corticosteroids represent those with a nonautoimmune or noninflammatory disorder, and our 4 patients who underwent autopsy and who did not respond to high-dose corticosteroids support this contention. We suspect that most of the other nonresponders in Table 5, and most others who do not respond

to corticosteroids, have an underlying neurodegenerative or prion disorder. The issue for physicians who evaluate patients with a subacute encephalopathy associated with autoimmune thyroiditis is whether corticosteroid therapy is justified. Given the fact that the alternative diagnoses, such as Creutzfeldt-Jakob disease or a neurodegenerative disorder, can be incurable, a corticosteroid trial may be warranted in appropriate patients. Perhaps certain features or findings may predict which patients will and will not respond to corticosteroids, and this important issue is certainly worthy of further study.

We acknowledge several limitations of this study. Because of the retrospective nature of this clinical series, not all patients underwent the same tests and evaluations. Our data should not be viewed as inclusive of all patients with SREAT at our institution during an 8-year period. In addition, the data should not be viewed as showing the entire spectrum of neurologic and laboratory findings associated with SREAT. In this period of study, numerous patients seen at our institution with a steroid-responsive encephalopathy were not tested for thyroid autoimmunity and therefore would not have been identified for inclusion in our analysis. However, we hope that our findings improve the recognition of patients who may have an autoimmune or inflammatory mechanism underlying their encephalopathy, as well as stimulate further research into SREAT and other forms of nonvasculitic autoimmune inflammatory meningoencephalitis.

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