CASE REPORT

Autoimmune polyglandular syndrome: coincidental or multiple sclerosis mimic?

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Abstract

Introduction: Multiple sclerosis (MS) is an autoimmune disorder (AD) that has been associated with other ADs, such as thyroiditis. However, association with autoimmune polyglandular syndromes (APS) has seldom been described and some reports documented central nervous system (CNS) involvement by APG.

Case Report: A 32-year-old female presented with acute, painful, unilateral vision loss. She had past medical history of follicular thyroid adenoma and lymphocytic thyroiditis, having undergone partial thyroidectomy, and diabetes mellitus type 1 (anti-GAD+), fulfilling criteria for APG type III. Her neurological examination was remarkable only for a right afferent pupillary defect. Laboratory tests showed cobalamin deficiency and positivity for anti-thyroid, anti-parietal cell and anti-intrinsic factor antibodies. Anti-gliadin and anti-tissue transglutaminase antibodies were negative. Thyroid function, cortisol and adrenocorticotropic hormone (ACTH) levels were normal. Neuraxis MRI showed periventricular, juxtacortical and infratentorial white matter lesions and two small spinal lesions, all with no gadolinium enhancement. Cerebrospinal fluid analysis, including oligoclonal bands was unremarkable. Visual evoked potentials had bilaterally increased latency values. A course of intravenous corticosteroids was started and cobalamin was supplemented. No long-term treatment was initiated. During 2-year follow-up, no other relapse has been recorded and neuraxis MRI remains stable.

Discussion: Few cases of APG have been described with inflammatory CNS involvement and/or MS. It is unclear whether there is concomitant occurrence of two ADs, or if there is a shared pathophysiology. Moreover, cobalamin deficiency is common in this condition, providing a potential cause for CNS disease. In this case, a watchful waiting approach was adopted.

Keywords: Multiple sclerosis, Autoimmune polyglandular syndrome.
Introduction

Autoimmune diseases (AD) share genetic, physiopathological and environmental characteristics [1]. This is reflected clinically in the occasional presence of more than one AD in the same patient. When a specific combination of ADs occurs, the diagnosis of an autoimmune polyglandular syndrome (APS) can be made. There are 4 types, of which types II and III are most frequent [2]. APS type III is defined as the combination of an autoimmune thyroid disease and, at least, another AD (such as type 1 diabetes mellitus, pernicious anemia, atrophic gastritis and vitiligo among others) [2]. Inflammatory involvement of the central nervous system (CNS) in these syndromes has seldom been described.

Case Report

A 32-year old, female patient presented to the emergency department with acute, mildly painful, unilateral vision loss. She complained of difficulty seeing in the center of her right eye fields and pain in the upper eyelid and supraciliary region, which was aggravated by eye movement. Upon ophthalmological and neurological examination, a right afferent pupillary defect and a right central scotoma were observed. Her visual acuity was severely compromised in her right eye (“counting fingers”), and less so in her left eye (0.60). The rest of her exam was unremarkable. When asked about her past medical history, she revealed having undergone a partial thyroidectomy 4 years prior for a follicular thyroid adenoma and having been diagnosed with primary hypothyroidism due to lymphocytic thyroiditis, currently controlled with levothyroxine. Furthermore, she had been diagnosed with type 1 diabetes mellitus [anti-glutamic acid decarboxylase antibody (anti-GAD) positive], in the previous year and was being treated with insulin. The association of these AD establishes the diagnosis of APS type III. She also reported previous episodes of paresthesia in her right arm and lower jaw, that she attributed to a C5 disk herniation, with a compatible electromyogram. She had never been pregnant and took no other medications. Her family history was elicited: her father suffered from epilepsy and her mother had an unspecified cardiopathy.

She was admitted to the Neurology ward, and an 8-day course of intravenous corticosteroids was initiated, with clinical improvement. Evoked visual potentials (EVP), cerebral and spinal magnetic resonance imaging (MRI), lumbar puncture (LP) and blood tests were performed. Her EVPs showed increased latency times bilaterally (P100: left=121ms; right=154ms). Her LP revealed slight hyperproteinorrachia, an IgG index of 0.7 (N<0.6) and negative oligoclonal bands and viral nucleic acids. Neuraxis MRI showed T2-hyperintense lesions at the C7 and T11 levels and also periventricular, juxtacortical and ponto-mesencephalic cerebral lesions (Figure 1). Her blood tests revealed vitamin B12 deficiency with positive anti-parietal cell, anti-intrinsic factor, anti-thyroglobulin and anti-thyroid peroxidase antibodies. She had normal cortisol and adrenocorticotropic hormone levels, and no other auto-antibodies were positive. Her visual acuity gradually improved and she was discharged under intramuscular cobalamin, levothyroxine and insulin (basal bolus regimen). She underwent gastric endoscopy, revealing chronic atrophic gastritis. Two years after the episode, she claims full recovery of her eyesight. No recurrence of neurological symptoms has been reported. On follow-up MRI, there was regression of the C7 hyperintensity and no evidence of new lesions.

Discussion

Involvement of the CNS in APS has been mostly described in cases of cerebellar ataxia with antibodies against GAD [3-6] or other epitopes [5]. Alternative presentations have included Vogt-Koyanagi-Harada syndrome [7], limbic encephalitis [8] and pernicious anemia with combined subacute degeneration [9]. To our knowledge, demyelinating lesions have been reported in 8 cases, three MS patients associated with APS type II [10, 11] and five (3 MS, 2 MS-like) patients with type III [11-14]. Of the latter, all for whom data is available presented with optic neuritis (n=3); 2/3 had positive oligoclonal bands in the cerebrospinal fluid (CSF) [13, 14]. MRI revealed diffuse CNS demyelination in one case [12] and periventricular lesions in two other cases [13, 14]. All cases (n=5) had concomitant diabetes mellitus and thyroiditis. Other coexisting disorders were gonadal insufficiency [13], alopecia universalis [12], coeliac disease, asthma and pernicious anemia [11]. Only one case report mentioned intervention: thyroid hormone supplementation was initiated with no other therapies [12].

Interestingly, APS type III, autoimmune type 1 diabetes and MS share genetic risk variants, including different SNPs (e.g. IL2RA) and HLA haplotypes, such as HLA-DRB1*03 [15-17]. In fact, MS patients and their relatives have an increased risk for other autoimmune diseases, compared to matched controls [18, 19]. In our patient, a definite diagnosis of MS could not be made. Although there is a likely pathogenic relation, we cannot establish with certainty whether this is concurrent clinically isolated syndrome in a patient with APS, or CNS involvement of APS, unrelated to MS pathobiology. Furthermore, cobalamin deficiency is common in APS patients, and its contribution to this case is uncertain. The role of anti-GAD antibodies could be questioned. However, the patient’s symptoms do not suggest they had a causal role in this situation. Given all the above data, a watchful-waiting approach was adopted, focusing on the management of the patient’s diabetes and thyroiditis, and maintaining cobalamin supplementation.

Abbreviations

AD: Autoimmune diseases; anti-GAD: anti-glutamic acid decarboxylase antibody; APS: Autoimmune polyglandular syndrome; CNS: Central nervous system; CSF: Cerebrospinal fluid; EVP: Evoked visual potentials; LP: Lumbar puncture; MRI: Magnetic resonance imaging

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Figure 1. Visual Representative MRI findings. (a) T2* hyperintense subcortical lesions, (b) T2* hyperintense periventricular lesions, (c) T2* hyperintense right spinal lesion at C7 level, and (d) STIR hyperintense spinal T11 lesion.

Competing interests

The authors declare no conflict of interest.

References


