A case of progressive disabling sensorymotor axonal-demyelinating polyneuropathy and severe vascular encephalopathy in a patient with Polyglandular Autoimmune Syndrome Type-4 and positivity of p-ANCA and anti-GAD antibodies.

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Introduction:

Polyglandular-Autoimmune-Syndromes(PAS) are four disorders characterized by immunopathological involvement of multiple endocrine organs. In this report, we describe the case of a severe polyneuropathy in a patient with PAS type-4 and positivity of p-ANCA and anti-GAD antibodies.

Case Report

A 66-year-old woman was admitted to our department complaining weakness and sensory disorders in the limbs for about 18 months. The symptoms mainly affected her lower limbs and had gradually compromised walking ability.

The patient had a history of vitiligo, diabetes, reactive-depression, atrophic gastritis and previous stroke at 59 years. Clinical examination showed mild hypoesthesia and weakness in the upper right limb, moderate proximal and severe distal weakness in lower limbs. There were also widespreadly dysesthesiae and global sensitive deficit, in particular in lower limbs. Besides, a cognitive impairment with attentive, executive and logical-abstract deficits was found, so she performed cerebral-CT showing a severe vascular encephalopathy.

Spine-MRI excluded significant compressive causes. CSF-chimical-examination showed albumino-citological dissociation. Neurophysiological test detected a sensorymotor axonal-demyelinating polyneuropathy pattern. Blood tests showed positivity of p-ANCA antibodies and very low values of Vitamin-B12. Gastroscopy detected gastric atrophy and differentiated carcinoid. Anti-gastric parietal cell antibody test was positive. Total-Body PET and CT excluded neoplastic lesions. CSF-IEF examination, neoplastic and onconeural markers, TSH and thyroid and adrenal hormones were normal. The search for cryoglobulins and gangliosides was negative. After the detection of anti-GAD antibody positivity, a diagnosis of PAS type-4 with LADA, vitiligo, autoimmune gastric atrophy and carcinoid was done. Given the hypothesis of Cronic Progressive Inflammatory Autoimmune and metabolic polyneuropathy, the patient was treated with vitamin-B12, intravenous-immunoglobulins, steroid therapy and physical-rehabilitation with partial benefit.

Discussion and conclusion

Some reports have referred neurological manifestations in patients affected by PAS, for example cerebellar ataxia, stroke and dystonia, often in presence of anti-GAD antibodies(1). Besides, many factors potentially linked to a PAS can be involved in the pathogenesis of neurological disorders(2). Deficiency of vitamin-B12 secondary to autoimmune gastric atrophy can cause cognitive impairment, increased vascular risk and polineuropathy;autoimmune mechanisms linked to the syndrome and autoimmune diabete can be also involved in neurological damage. In addition, cases of paraneoplastic polineuropathies in patients with gastrointestinal carcinoids have been described(3). So, in case of polyneuropathy in patients with PAS, the correction of metabolic factors, a gastroscopic screeening for gastric atrophy and carcinoid and a therapy for disimmune mechanisms could be important to limit pathological progression.

Table 1. Characteristics of the autoimmune polyendocrine syndromes (APS)

APS type 1	Chronic candidiasis, hypoparathyroidism, autoimmune adrenal insufficiency (at least two of them should be present)
APS type 2	Autoimmune adrenal insufficiency (must always be present) + autoimmune thyroid disease and/or type 1 *diabetes mellitus*
APS type 3	Autoimmune thyroid disease + other autoimmune diseases (excluding autoimmune adrenal insufficiency, hypoparathyroidism, chronic candidiasis)
APS type 4	Two or more organ-specific autoimmune diseases (which do not fall into type 1, 2, or 3)

References:

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