Case Report

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Autoimmune polyglandular syndrome type 2 and recurrent depression

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Introduction and importance: Autoimmune polyglandular syndrome type 2 (APS-2) features autoimmune Addison's disease, autoimmune thyroid disease, and/or type 1 diabetes mellitus. Addison's disease is occasionally associated with depressive symptoms, therefore patients with APS-2 might present primarily in a psychiatric clinic. Such atypical primary presentation can possibly lead to delayed and/or inadequate diagnosis and management.

Case presentation: A 57-year-old female patient was referred to our psychiatric clinic from an internal medicine hospital presenting severe depressive symptoms. Upon admission, she complained of sadness, loss of interest (anhedonia) and drive, nausea, and loss of appetite. Physical examination revealed generalized hyperpigmentation. Laboratory investigations revealed hyponatremia, hypocalcemia, macrocytic anemia along with treated hypothyroidism, and partially treated adrenal insufficiency.

Clinical discussion: A diagnosis of the APS-2 was made. Electroconvulsive therapy (ECT) was mandatory and a complete regression of the affective symptoms was achieved.

Conclusion: Organic workout in psychiatry is essential to detect diseases symptomatically or semiologically related to depression. In our case, hyperpigmentation, hypothyroidism, and adrenal insufficiency linked to depressive symptoms led to APS-2 diagnosis. ECT was challenging due to the avoidance of etomidate by the anesthesiologists, due to adrenal insufficiency. The adjustment of ECTs' energy dosage (to avoid too short and ineffective seizures) and optimization of adrenal and thyroid function was essential to reverse the severe depressive syndrome.

Keywords: Autoimmune polyglandular syndrome, Addison's disease, case report, recurrent major depressive disorder, Schmidt

Introduction

APS-2, also called Schmidt syndrome, is a rare endocrine disorder that features the presence of autoimmune adrenal insufficiency, autoimmune thyroid disease and/or type 1, and autoimmune diabetes mellitus[1] that was first described in 1926[2]. The autoimmune adrenal insufficiency [Addison's disease (AD)] is caused by the destruction of the adrenal cortex by a cell-mediated immune mechanism and is associated with HLA-DR3 and/or HLA-DR4 haplotypes; the pattern of inheritance is autosomal dominant[2,3]. The peak prevalence is among middle-aged women[4]. Treatment involves the replacement of deficient hormones[5].

HIGHLIGHTS

- In our case, hyperpigmentation, hypothyroidism, and adrenal insufficiency linked to depressive symptoms led to autoimmune polyglandular syndrome type 2 (APS-2) diagnosis.
- The adjustment of electroconvulsive therapy (ECT) energy dosage (to avoid too short and ineffective seizures) and optimization of adrenal and thyroid function was essential to reverse the severe depressive syndrome.
- ECT was challenging due to the avoidance of etomidate by the anesthesiologists, due to adrenal insufficiency.
- Organic workout in psychiatry is essential to detect diseases symptomatically related to depression.

AD is an endocrine disorder that is accompanied by deficient cortisol and aldosterone release caused by the damage of the adrenal cortex[6,7]. Possible etiologies are autoimmune, infections, neoplasia, iatrogenic, or vascular damage[7]. The clinical presentation of AD often includes fatigue, dizziness, and muscle pain[7]. Psychiatric manifestations such as depression may also be associated with it. Glucocorticoid deficiency, electrolyte, and metabolic disorders are to some extend considered possible causes of depressive symptoms accompanying the disease[8]. This case report has been reported in line with the SCARE Criteria (https://www.scareguideline.com/)[9].

Case report

A 57-year-old woman was referred to our psychiatric clinic with a recurrent major depressive episode. She initially presented with

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nausea, vertigo, and loss of appetite. Psychopathological symptoms during admission were severely depressed mood, loss of interest in daily activities, loss of drive, generalized anxiety, sleep and concentration difficulties, and loss of appetite. Furthermore, she reported fears about her professional future; these symptoms occurred for several months. At the age of 29, she suffered a first depressive episode; in the following, she received several inpatient psychiatric treatments. The patient reported occasional alcohol consumption but had no history of drug abuse. There was a positive family history of suicide in a cousin from the mother's side. Somatic history was positive for autoimmune thyroiditis, rheumatoid arthritis, adrenal insufficiency, vitamin B_{12} deficiency, nasal septum deviation, and mucosal erythema in the gastric antrum. During admission, the patient was on lorazepam 1 mg p.o. daily, L-thyroxin 125 µg p.o. daily, and hydrocortisone 37.5 mg p.o. daily. Physical examination revealed generalized hyperpigmentation. Laboratory investigations performed in the Internal Medicine Department before referral to our psychiatric clinic revealed hyponatremia. Adrenal insufficiency was suspected as the cause. Laboratory investigations performed showed hypokalemia and hypocalcemia, which was corrected with 40 mmol K^+ orally and cholecalciferol 20 000 IU p.o. daily. The patient also had macrocytic hyperchromic anemia along with low vitamin B_{12} levels, which was treated with vitamin B_{12} 1000 µg p.o. daily. Vasculitis screening showed slightly elevated antinuclear antibody titer of 1:640.

MRI of the brain showed multiple bifrontal gliosis with no space-occupying lesions present. A cerebrospinal fluid (CSF) analysis was unremarkable except for identical oligoclonal bands in both, the serum and the CSF. A gastroscopy was performed and showed antral mucosal erythema. A diagnosis of APS-2 with adrenal insufficiency (AD), thyroid insufficiency, hypogonadism (gonadal insufficiency), and pernicious anemia was confirmed by the Endocrinology Department. A gynecological workup ruled out a malignoma; echocardiography and mammography were unremarkable; a Papanicolaou test (PAP test) revealed stage IIp. There were no relevant drug history, family history of any relevant genetic information, or other psychosocial history.

Oral antidepressant combination treatment with sertraline 100 mg daily and bupropion 300 mg p.o. daily improved the patient's symptoms. Further antidepressant combinations (sertraline 50 mg p.o. daily and amitriptyline 200 mg p.o. daily, a monotherapy with tranylcypromine, and a further monotherapy with vortioxetine did not lead to any significant improvement. We performed 20 right unilateral ECT sessions (Thymatrin IVTM) and started augmentation with lithium 450 mg p.o. daily along with the existing antidepressive treatment (amitriptyline 100 mg and mirtazapine 15 mg p.o. daily). Hydrocortisone (up to 75 mg/d), fludrocortisone (0.05 mg/d), L-thyroxin (up to 150 µg/d), dehydroepiandrosterone (25 mg orally per day), and vitamin D were supplemented. During the ECT sessions, the standard anesthetic etomidate was avoided due to its suppressive effect on adrenal cortisol production[10]. The anesthetic alternatives (see below) resulted in very short seizure duration, which initially made the treatment considerably more difficult. She additionally received a total of 23 cognitive behavioral therapy sessions. The treatment caused a significant improvement of depressive symptoms, and the patient was discharged in almost complete remission [Clinical Global Impression, Improvement item (CGI-I = 2)].

Discussion

In the present case, depressive symptoms were associated with a rare APS-2. From the literature, it is well known that patients with autoimmune AD might also primarily present with depressive symptoms[8,11,12]. Unfortunately, the psychiatric symptoms associated with AD have not attracted much attention in recent research until now[8]. The etiology of psychiatric symptoms in patients with autoimmune AD is not fully understood[8]. Possible etiological mechanisms are related to the deficiency of glucocorticoids, electrolyte disturbance, metabolic disorders, and electrophysiological changes[8]. In addition, altered thyroid is known to be associated with depressive symptoms[13].

Typical features of APS-2 such as thyroid and adrenal insufficiency[1] were present in our case. Type 1 autoimmune diabetes mellitus is occasionally present in this syndrome[1], but it was absent in our case. Minodora *et al.* presented a 65-year-old female with comorbid depression in Schmidt syndrome, who had a 13-year history of recurrent depressive disorder treated with tricyclic antidepressants, selective serotonin reuptake inhibitors, neuroleptics, and benzodiazepines[14]. To the best of our knowledge, this is the second reported case of recurrent depressive syndrome in association with APS-2, and the first treated with ECT.

Regarding the ECT management of patients with autoimmune AD, etomidate, a rapid-acting sedative-hypnotic that is frequently used in the induction of short-term anesthesia[15], is known to cause adrenal suppression due to inhibition of 11 beta-hydroxylation, especially in patients with autoimmune AD[10]. Etomidate is known to provide the most prolonged seizure duration in comparison to other alternatives, for example, ketamine or propofol[16]. This factor might affect the efficiency of the ECT treatment sessions. Thus, psychiatrists need to consider the possibility of shorter seizure duration and probably less effective ECT due to avoidance of usage of etomidate by anesthesiologists.

Adequate adjustment of energy dosage by psychiatrists might help to maintain a satisfactory seizure duration and hence effective ECT management. Moreover, the detection of organ-specific autoantibodies could help in the detection of patients that are at risk of developing APS-2[17]. This is crucial, as starting treatment of hypothyroidism in patients with autoimmune thyroiditis and undiagnosed adrenal insufficiency might provoke an acute adrenal crisis[5]. This could occur due to enhanced hepatic metabolism of corticosteroids, which could be induced by thyroxine[17]. Hence, physician's knowledge of rare clinical pictures of endocrinal autoimmune syndromes might help in accurate diagnosis and treatment in early clinical stages.

Conclusion

Our case supports the concept that recurrent depressive syndrome can be provoked by adrenal insufficiency, and that endocrinal disorders might increase the risk of recurrent depressive syndrome. Patients with depressive symptoms and hyperpigmentation should receive broad endocrinal investigations to detect potential adrenal insufficiency. Psychiatrists should be aware that for ECT, anesthetic alternatives to etomidate are probably associated with shorter seizure duration and should thus adjust the energy dosage accordingly. Adequate communication and coordination between psychiatrists, endocrinologists, and anesthesiologists before conducting ECT in patients with AD is necessary to improve the efficiency of ECT and the patient's safety.

Ethical approval

Not applicable.

Informed consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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None.

Authors' contribution

M.E.: prepared the manuscript. E.N.: helped in the implementation and to draft the manuscript. M.G.: developed and corrected the manuscript and was involved in the clinical management of the patient. C.S.L.: supervised the manuscript and participated in its design and coordination. All authors read and approved the final manuscript.

Conflicts of interest disclosure

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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