A case of adrenoleukodystrophy presenting with manic symptoms in a patient on steroids for Addison’s disease

K. S. Jyothi, Cyriac George, K. S. Shaji
Department of Psychiatry, Government Medical College, †Department of Health Services, Primary Health Centre Arthat, Thrissur, Kerala, India

ABSTRACT

Adrenoleukodystrophy (ALD) is an X-linked disorder with diverse clinical presentations. A 30-year-old male, previously diagnosed with Addison’s disease, on steroid supplementation for 18 years, presented to us with manic symptoms for 4 years. He was found to have white matter hypodensities in computed tomography head and had white matter signal changes in magnetic resonance imaging, and therefore a diagnosis of ALD was made.

Key words: Adrenoleukodystrophy, Addison’s disease, organic mood disorder, peroxisomal disorders

INTRODUCTION

Adrenoleukodystrophy (ALD) is an X-linked recessive disorder due to mutations in the ABCD1 gene in X-chromosome, characterized by impaired peroxisomal beta-oxidation of very long-chain fatty acids (VLCFA), resulting in its accumulation in plasma and all tissues, especially affecting the adrenal glands, white matter of nervous system, and Leydig cells of testes. It is the most common peroxisomal disorder, with a prevalence of about 1 in 20,000.1,2 The disease can present with diverse clinical manifestations, posing a diagnostic challenge, and sometimes atypical psychiatric symptoms may be the clinical presentation.

CASE REPORT

Our patient is a 30-year-old unmarried male, construction worker, with no prior history of any psychiatric illness. He was taking prednisolone 7.5 mg daily for the past 18 years after being diagnosed with Addison’s disease by an endocrinologist, and was functioning well till about 4 years back.

He was brought to the psychiatry department by his mother with a history of continuous manic symptoms for the past 4 years. He was having increased talk, increased self-esteem, over familiar behavior, irritability, overspending, irregularity in job, and sleep disturbance. His mother also reported that he was recklessly driving his motorbike and has fallen a few times. He was also disturbing girls and children in public places. There were no psychotic symptoms or history of substance abuse.

On further inquiry, his relatives had noticed him to be less stronger physically, compared to before, during the past 1 year. He had an accident 6 months back during work when he dropped a stone and fractured his left forearm which was surgically treated.

There was a family history of rapidly progressing paralysis and death in his brother and cousin at 9 and 12 years of age. This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

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age, respectively. The latter also had a history of receiving steroid supplementation during the illness.

The patient was not very cooperative for a detailed assessment initially. His vitals were normal. He was very jovial but became irritable at times. His talk and psychomotor activity was increased. Insight and judgment were poor. His cognitive functions were normal.

On initial investigation, his serum cholesterol and low-density lipoprotein were elevated (267 and 193). Hemogram, electrolytes, and sugar were normal. Liver, renal, and thyroid function tests were normal. Serological tests for HIV and venereal disease research laboratory were negative. Ultrasound scan of the abdomen showed minimal fatty infiltration of the liver.

Because of the atypical nature of the presentation—prolonged manic symptoms appearing many years after steroid replacement was started—we opted for a computed tomography scan of the brain. It showed white matter hypodensities involving centrum semiovale [Figure 1], parieto-occipital region, and cerebellum bilaterally [Figure 2].

Hence, we did an magnetic resonance imaging (MRI) of the brain which showed bilateral fairly symmetrical T2/FLAIR white matter hyperintensities involving deep white matter and periventricular region, sparing subcortical U-fibers, involving parieto-occipital region [Figure 3]. Similar signal changes were also noted along corticospinal tracts (in brainstem, crus of midbrain, cerebral peduncle and pons), lateral thalami, splenium of corpus callosum, middle and inferior cerebellar peduncles, and dentate nuclei of cerebellum [Figure 4]. No abnormal parenchymal enhancement was noted in the postcontrast study.

A diagnosis of ALD was made. A psychiatric diagnosis of organic mood disorder (mania) was also made. We were unable to do a VLCFA estimation as it is not available in our locality.

Meanwhile, the patient was already started on sodium valproate 600 mg daily and it was hiked to 1000 mg daily. However, the patient developed significant ataxia, so sodium valproate was reduced and stopped and he was managed on haloperidol. With 20 mg/day of haloperidol, his manic symptoms were fairly controlled. His young mania rating dropped to 14 from an initial 33 over a period of 2 weeks.

When the patient became more cooperative, a neurological assessment was made, and he was found to have cerebellar ataxia and incoordination. He had hypotonia in the upper limbs, but muscle tone was increased in the lower limbs. Deep tendon reflexes were brisk. Weakness with Grade 4 power was noted on all limbs. Ophthalmic fundus examination was normal. His cognitive functions were normal.
DISCUSSION

Addison’s disease is a fairly common condition, and the common psychiatric manifestation associated with it is depression.[3] During administration of steroids, manic symptoms may occur initially, especially with high doses.[4] Chronic use of steroids may lead to the development of depressive symptoms.[5] However, our patient had developed manic symptoms—which was continuous in nature—even though he was getting only a low dose of prednisolone for quite a long time. These atypical features prompted us for the detailed investigation and led to the diagnosis of ALD.

ALD is an X-linked peroxisomal disorder due to mutations in the ABCD1 gene in X chromosome, characterized by impaired peroxisomal beta-oxidation of VLCFAs.[6] The disease is associated with multiple phenotypes which can present along a varying age spectrum with considerable clinical diversity.[7]

The childhood-onset form of ALD is a rapidly progressing neurodegenerative disease which will result in death in almost 2 years. It may start from 3 to 8 years of age and is characterized by attention deficit, intellectual problems, behavioral problems, and neurological symptoms. An adolescent-onset form is also described, in which death occurs about 2 years following the onset of neurological symptoms. An adult-onset less severe form is also described.[2,4]

Any combination of symptoms—adrenal, gonadal, neurologic, or psychiatric—is possible in ALD and it can produce a diagnostic dilemma although the most common presentation is neurological.

An MRI of brain shows the characteristic changes—bilaterial symmetrical involvement of deep white matter in the parieto-occipital lobes, periventricular region, and the splenium of the corpus callosum—in most cases. A contrast MRI is also helpful in assessing the disease progression.[8] Diagnosis may be confirmed by demonstration of elevated plasma levels of VLCFAs.

There is no very promising treatment options for ALD so far. Dietary restriction of VLCFAs has not demonstrated any significant clinical efficacy. Dietary supplementation with “Lorenzo’s oil” may slow the disease progression if done early. Bone marrow transplantation can halt the disease progression if done sufficiently early in the course, but is of little use in advanced cases. Addison’s disease can be managed by appropriate supplementation with exogenous steroids.[1,9]

There is a clear lack of literature regarding the management of psychiatric manifestations of ALD. Lithium can precipitate mineralocorticoid deficiency in these patients.[1] We observed that valproate is associated with significant ataxia in our patient. Atypical antipsychotics may worsen the lipid profile and may cause metabolic syndrome. These issues pose challenges in the management of psychiatric symptoms.

CONCLUSION

It is of immense importance to suspect and detect ALD in patients presenting with Addison’s disease and psychiatric symptoms, rather than considering it as mere psychiatric manifestations of Addison’s disease and steroid use. This can help in the early initiation of specific treatments which may limit the disease progression and improve life expectancy of patients with ALD. Moreover, it will help in genetic counseling and early detection of susceptible individuals in the family.

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Conflicts of interest
There are no conflicts of interest.

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