

Case Report

Adolescent-onset X-linked Adrenoleukodystrophy Presenting as Treatment-resistant Bipolar Disorder

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ABSTRACT

A small proportion of bipolar disorder of adolescent onset can be secondary to underlying neurological disorder (secondary mania). We report a case of treatment-resistant mania secondary to cerebral form of adrenoleukodystrophy of adolescent onset. This case demonstrates the need for clinicians to be alert to the possibility of rare neurological diseases that can present with psychiatric manifestations.

Key words: Adolescent onset adrenoleukodystrophy, bipolar disorder, manic episode

INTRODUCTION

On retrospective interviews, 30% of adult bipolar patients report onset of bipolarity before 13 years, and 40% report onset between 13 and 18 years of age.^[1] A proportion of these early onset bipolar disorders is secondary to underlying medical disorders, such as epilepsy, endocrine disorders, neuro-infection, head trauma, metabolic disorders,^[2] and vascular insults.^[3] Frontal lobe syndrome especially orbitofrontal lesion or right anterior prefrontal lesion can present with mania-like symptoms,^[4] which could be secondary to frontal lobe tumor or other causes.

X-linked adrenoleukodystrophy (ALD) is a peroxisomal metabolic disorder, which can present with cerebral involvement having childhood, adolescent or adult onset

forms characterized by inflammatory demyelinating leukoencephalopathy, only Addison's disease, or a peripheral form of adult onset (adrenomyeloneuropathy) with or without cerebral involvement. It expresses more in male sex. Females are generally asymptomatic carriers, though sometimes they may present with milder forms of the disease.^[5]

This case report highlights an uncommon psychiatric presentation of X-linked ALD.


CASE REPORT

A 15-year-old boy presented to our outpatient department (OPD) with 9 months history of

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How to cite this article: Ray A, Girimaji SC, Bharath RD. Adolescent-onset X-linked adrenoleukodystrophy presenting as treatment-resistant bipolar disorder. Indian J Psychol Med 2017;39:685-7.

Access this article online	
Website: www.ijpm.info	Quick Response Code 
DOI: 10.4103/IJPSYM.IJPSYM_36_17	

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insidious onset, continuous course of overfamiliarity, over-talkativeness, disinhibited behavior, wandering away from home, increased appetite, and decreased academic performance. Sleep was preserved while on medication. He had a family history of bipolar illness in paternal uncle, and normal birth and developmental milestones with average school performance till the eighth standard. The boy was sociable premorbidly with no complaint of hyperactivity. Before presenting to us, he was treated by many psychiatrists with combinations of valproate 500 mg with olanzapine 20 mg and valproate 500 mg with risperidone 4 mg, with no improvement. The addition of lithium 600 mg with both the regimens did not provide any significant improvement. Then he was tried on clozapine 200 mg along with clonidine 400 mcg with no improvement either. On this regime, he visited our OPD. Initially, it was decided to give an adequate trial of thymoleptics and increase valproate to 20 mg/kg/day dose with risperidone 6 mg dose with tapering down the existing regime of clonidine and clozapine. Initially, there was an improvement of psychomotor agitation and other manic symptoms, but soon he started to have a headache with vomiting and started to look excessively drowsy. Serum ammonia was found to be high with 151 mg/dl. Serum lactate, lipid profile, liver function test, renal function test, thyroid function test, serum electrolytes, complete hemogram, tandem mass spectrometry, urine for abnormal metabolite were all within normal limits. Valproate-induced metabolic derangement was thought of, and lithium 600 mg cross-titrated with valproate. With this, his psychomotor agitation reappeared, and he continued to have an episodic headache. On one occasion, when a headache culminated in altered sensorium, magnetic resonance imaging (MRI) was done. MRI revealed extensive signal changes involving cerebral white matter which were well-defined and symmetrical T2/FLAIR hyperintensity involving bilateral frontal and the genu of corpus callosum giving a “batwing” appearance. Anterior thalamic nuclei, ventral midbrain, and right hippocampus also showed signal changes. There was the characteristic peripheral advancing edge enhancement with contrast [Figure 1]. These findings were features suggestive of X-linked ALD. However, there were no clinical features that could suggest ALD-like any visual or motor symptoms and adrenal deficiency symptoms a clinical diagnosis of frontal lobe tumor was strongly entertained by neurology consultant, and headache, that was thought to be secondary to increase in intracranial tension, treated with mannitol infusion in the ward and changed over to syrup glycerol orally on discharge. The child was followed up after 4 months with repeat MRI which showed no extension of the lesion, there was

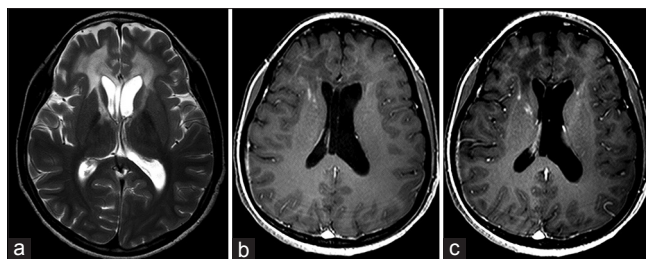


Figure 1: Magnetic resonance imaging brain in axial sections reveals symmetric T2 hyperintense signal changes (a) involving the bilateral lobar and periventricular white matter with extension into the genu of corpus callosum and the anterior limb of internal capsule bilaterally. The relative lack of mass effect despite the size of the lesion points against neoplastic lesions and the characteristic advancing margin enhancement on postcontrast T1 images (b and c) is a diagnostic feature of adrenoleukodystrophy

neither mass effect on MRI nor papilledema on clinical examination. Cerebrospinal fluid (CSF) study was also unremarkable. Symptomatically child only partially improved and neuropsychological assessments revealed deficits in focused attention and verbal working memory which suggested frontal lobe involvement. There were also deficits in visuo-perceptual ability, visuo-conceptual ability, visuoconstructive ability, which suggested temporoparietal involvement. A trial of oral steroid was given along with mood stabilizers and antipsychotics. Child partially improved with reduction of a headache, vomiting, aggression with better sleep and appetite; however, overfamiliarity, restlessness, sexualized behavior toward opposite sex persisted. Very long chain fatty acid was found to be elevated, C26:0 were 0.73 ($>$ controls [0.23 ± 0.09]), and C26/C22 were 0.11 ($>>$ normal value of 0.01 ± 0.004), at this point, a final diagnosis of X-linked ALD was made. Family was counseled about the nature and prognosis of illness and continued on the same treatment. Interestingly, 5 months later, the child was maintaining stable course without further deterioration.

DISCUSSION

According to available case reports and reviews, X-linked ALD can rarely present with behavioral symptoms in children and young adults in forms of psychosis^[6] or attention deficit and hyperactivity disorder^[7] or social withdrawal, irritability, obsessional behavior, rigidity.^[8] However, only one case report of an adult presenting with episodic bipolarity could be found.^[9] No such reports were found in child and adolescent population. We have also seen another child with hyperactivity and bipolarity associated with leukodystrophy, however subtyping of leukodystrophy could not be done in that child (in press).

In this case, the treatment resistance of the mood symptoms along with valproate-induced headache and vomiting, with hyperammonemia indicated toward the possibility of metabolic causation like urea cycle disorder or respiratory chain disorders.^[10,11] However, all the related biochemical investigations such as tandem mass spectrometry were normal. Hence, those possibilities were not tenable. In view of a headache even on the reduction of valproate and ammonia and accompanying vomiting and unconsciousness directed toward the possibility of increased intracranial pressure and possible cerebral pathology. Although the radiological features were suggestive of ALD, rarity of such presentation coupled with the absence of other symptoms of adrenal insufficiency, and more common clinical possibility of frontal lobe syndrome drifted initial treatment focus toward space-occupying lesion of the brain.^[12,13] However, no other supportive investigations like an increase in cell count in CSF analysis, increase in size of the putative mass lesion on radiological follow-up or papilledema could be found. Hence, taking the risk of stereotactic biopsy for further confirmation of diagnosis was not felt justified by the neurosurgery team. Hence, the other possibility according to the radiological suggestion of ALD was explored and found to be positive.

This case illustrates the importance of being alert to the possibility of psychiatric presentation of rare neurological diseases such as ALD as to reach an early diagnosis and ensuring that patient gets the benefit of best possible management of the underlying neurological disorder.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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