Case Report

Acute Cerebellar Ataxia: A Rare Association of Hepatitis a Infection

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Abstract

Acute cerebellar ataxia (ACA) is a self-limited syndrome that is frequently post-infectious, most commonly following *Varicella* infection having an autoimmune mechanism. ACA is the commonest cause of childhood ataxia. We report a 14-year-old male who presented with acute onset wide-based gait and slurring of speech with dysdiadochokinesia, incoordination of voluntary movements, pendular knee jerk, and intentional tremors. He had worsening transaminitis and rising bilirubin during his hospital course and was subsequently found to be hepatitis A virus (HAV) immunoglobulin-M antibody positive. Thus, we report a case of ACA with HAV infection who developed jaundice after three weeks of onset of ataxia, a rarity that has not been reported so far in medical literature.

Keywords: Acute cerebellar ataxia, hepatitis A virus, jaundice

Introduction

Acute cerebellar ataxia (ACA) is a self-limited syndrome that usually occurs in children under 6 years of age and is frequently post-infectious in causation.[1] ACA is the most common cause of ataxia in children with an incidence of 1 in 100,00 to 500,000.[1,2] ACA occurs most commonly following *Varicella* infection having a post-infectious autoimmune mechanism.[3] Other infectious agents implicated include *Coxsackievirus, Echovirus, Enteroviruses, Epstein–Barr virus (EBV), Herpes simplex virus I, Measles virus, Mumps virus, Borrelia burgdorferi*, *severe acute respiratory syndrome Coronavirus 2* (SARS-CoV-2).[4] ACA manifests primarily with rapid onset of gait disturbance preceded by a prodromal illness. Other manifestations of ACA include slurred speech, nystagmus, irritability, and tremors.[2,3] Diagnosis of post- or para-infectious ACA needs the exclusion of other causes of cerebellar ataxia by appropriate history, clinical examination, biochemical tests, and neuroimaging. Hepatitis A virus (HAV) infection has been rarely associated with ACA with only two cases reported so far.[5,6] In this report, we discuss para-infectious ACA as a rare association of acute HAV infection.

Case History

A 14-year-old male without any prior comorbidities presented with a one-week history of acute onset wide-based gait and slurring of speech. He had no history of fever, convulsions, head injury, recent vaccination, or drug/toxin ingestion. He did not have any weakness or sensory signs. He had scanning speech, past pointing of fingers, dysdiadochokinesia, incoordination of voluntary movements, pendular knee jerk, and intentional tremors which worsened on fine-directed movements. He had no family history of similar complaints.

His urine toxicology screen for common substances of abuse was negative. Magnetic resonance imaging (MRI) brain showed subtle fluid-attenuated inversion recovery hyperintensity of bilateral cerebellar folias suggestive of cerebellitis [Figure 1]. Cerebrospinal fluid (CSF) analysis had normal cell count, protein, and sugar. CSF viral polymerase chain reaction (PCR) for *Herpes simplex* virus, *Epstein–Barr* virus, *Varicella zoster* virus, *Mumps* virus, and *Measles* virus was negative. On biochemical evaluation, he had elevated alanine aminotransferase (ALT) and aspartate transaminase (AST) in the range of 500–1000 IU/L (with ALT > AST) and normal alkaline phosphatase (ALP) and bilirubin at presentation [Table 1]. Para-infectious or autoimmune cerebellitis was considered. He was given intravenous methylprednisolone pulse therapy (500 mg for 5 days) at presentation (1 week after symptom onset) in view of acute cerebellitis. His hepatitis A immunoglobulin M (IgM) antibody by enzyme-linked immunosorbent assay (ELISA) was positive. Serology for other common hepatotropic viruses like *Hepatitis B, E* and *C,* EBV and *Cytomegalovirus* PCR, celiac disease serological tests (anti-tissue transglutaminase, anti-endomysial, and anti-deaminated gliadin peptide auto-antibodies) and Wilson's disease screenings tests (serum copper, ceruloplasmin, and 24-hour urine copper) were negative.

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Table 1: Laboratory investigations

	Normal range	Day 1	Day 5	Day 10	Day 15	Day 20
Hemoglobin (g/dL)	12–15	14.8	14.2	15.1	14.8	14.7
TLC (×10^3/cumm)	4.0–11.0	4.3	6.39	7.23	5.68	6.23
Platelet count (×10^3/cumm)	150–400	201	213	289	253	276
Total bilirubin (mg/dL)	0–1.4	0.8	2.2	7.7	7.0	2.3
Direct bilirubin (mg/dL)	0–0.3	0.2	1.4	6.6	5.9	2.0
Indirect bilirubin (mg/dL)	0.02–1.1	0.6	0.8	1.1	1.1	0.3
ALT (IU/L)	10–49	591	2991	2701	1807	238
AST (IU/L)	14–36	523	1329	1412	799	157
ALP (IU/L)	38–126	183	244	218	217	124
INR	0.9–1.1	1.6	2.009	1.748	1.37	1.17

g/dL: gram per deciliter; TLC: total leukocyte count;/cumm: per cubic millimeter; mg/dL: milligram per deciliter; ALT: alanine aminotransferase; AST: aspartate aminotransferase; ALP: alkaline phosphatase; IU/L: International units per liter; INR: International normalized ratio

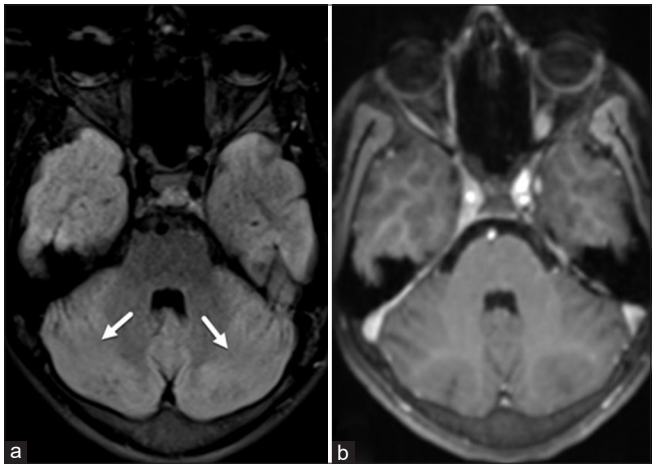

Figure 1: Subtle FLAIR hyperintensity of bilateral cerebellar folias suggestive of cerebellitis (pointed by arrows in image) (a). T2 FLAIR; (b). T1 post contrast MRI Brain

CSF antibodies against N-methyl-D-aspartate (NMDA) receptor, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) 1, contactin associated protein 2 (CASPR), voltage-gated potassium channel (VGKC), leucine-rich glioma-inactivated protein 1 (LGI-1), and gamma-amino-butyric acid (GABA) B receptor were negative. Over one week of hospital stay, he had symptomatic improvement in the form of improved speech and decreased swaying while walking. Steroids were stopped after the initial five days. His AST and ALT which were in the range of 500–1,000 IU/L rose to 2,000–3,000 IU/L over the next one week of hospital stay with an increase in bilirubin to 7 mg/dl. There were no features of acute liver failure and he was managed conservatively, and subsequently his liver enzymes started falling back to normal followed by a falling trend of serum bilirubin. On follow-up after one and three months he was completely asymptomatic and doing well.

Discussion

Cerebellar ataxia has a myriad of causes which can be broadly divided into congenital, acquired, and idiopathic etiologies. Among the acquired causes, ACA is the most common and mostly affects previously well children under the age of 6, while it can also impact adolescents and older children.[1] ACA is an inflammatory syndrome which occurs due to direct infection or post-infectious autoimmune mechanism.[7] The list of pathogens that have been implicated in post-infectious ACA include viruses like *Varicella, Enterovirus, EBV, Herpes simplex, Influenza*, *Measles* and *Mumps,* and a few bacterial infections like *Legionella, Mycoplasma*, and *Salmonella*.[4]

Differential diagnoses of ACA include infectious, toxic, immune-mediated (Miller Fisher syndrome, celiac disease, paraneoplastic cerebellar degeneration, multiple sclerosis), structural and vascular disorders, metabolic and genetic causes like biotinidase deficiency, Maple syrup urine disease, Hartnup disease, mitochondrial disorders like Leigh syndrome.[8] Recurrent episodes of liver failure, delayed early motor milestones, optic atrophy, and peripheral neuropathy may occur in autosomal recessive spinocerebellar ataxia-21(SCAR21).[9]

Diagnostic approach to ACA begins with detailed history and clinical examination.[10] Neuro-imaging with MRI is critical followed by CSF analysis if meningitis/encephalitis is suspected.[11] It is recommended to do a urine toxicology screen for alcohol, benzodiazepines, and heavy metals.[12] Once structural causes and toxins are ruled out an extensive evaluation is done for any associated infectious causes. Clinical examination and investigations will provide clues regarding the probable associated infection. In our case, the patient had elevated liver enzymes indicating the involvement of hepatotropic pathogens. HAV infection has been rarely associated with neurological complications like encephalitis, transverse myelitis, Guillain-Barre syndrome, and chronic inflammatory demyelinating polyneuropathy by various pathogenic mechanisms.[13-15] There are only two reported cases so far of HAV-associated ACA.[5,6]

Tuthill *et al*.[5] reported a case of ACA in a 5-year-old child who presented with unsteady gait and slurring of speech with positive anti-HAV IgM antibody titers who was conservatively managed with improvement in ataxia within 48 hours without therapeutic intervention. Kaninde *et al*.[6]

reported a similar case of ACA with a similar outcome in a 3-year-old child presenting with fever, jaundice, and unsteady gait who was on nitrofurantoin prophylaxis due to a history of recurrent urinary tract infections. Diagnostic evaluation showed positive HAV serology and MRI features suggestive of acute cerebellitis and a possible link between autoimmune triggering factors like nitrofurantoin and HAV infection in ACA was suspected. Our case presented with ACA and then went on and developed jaundice after three weeks of onset of ACA, a rarity that has not been reported so far in medical literature.

Supportive care is the primary form of treatment for ACA. Few case studies recommend administering glucocorticoids or intravenous immune globulin in patients who are resistant to treatment. After the initial presentation, symptoms often disappear without any implications in two to three weeks.[16]

What is known

ACA is the commonest cause of childhood ataxia, which usually has a post-infectious autoimmune etiology and presents with rapid onset of gait disturbance preceded by a prodromal illness. The commonly implicated pathogens include viruses like *Varicella, Enterovirus, Epstein–Barr, Herpes simplex, Influenza*, *Measles*, and *Mumps* and a few bacterial infections like *Legionella, Mycoplasma,* and *Salmonella.*

What is new

Hepatitis A virus (HAV) infection has been rarely associated with ACA with only 2 cases reported in medical literature so far. Our case report thus highlights the importance of including HAV in the diagnostic evaluation of ACA.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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