



Case Report

A rare association of dandy walker variant in a child with Ataxia Telangiectasia

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Abstract

Ataxia telangiectasia (AT) is an autosomal recessive neurodegenerative disorder caused by mutation in ATM gene. It is a complex multisystem disorder characterized by features of cerebellar degeneration, telangiectasia and immunodeficiency. Association of dandy walker syndrome with ataxia telangiectasia has been rarely reported. Here we present a case of 7 year old female child who had features of ataxia telangiectasia and on further evaluation found to have dandy walker variant.

Keywords- ataxia telangiectasia, cerebellar ataxia, ATM gene, neurological impairment

Introduction

AT is a rare complex progressive disorder which presents with combination of neurological and systemic features^{1,2}. In 1958, it was Boder et al. who recognize the clinical features, familial incidence and directed towards an autosomal recessive mode of inheritance for this disease³. The worldwide incidence was found to be 1 in 40000 to 1 in 100000 population^{4,5}. AT is caused by mutation in ATM gene which is responsible for initiating a response to DNA damage, resulting in

arrest of cell cycle, DNA repair or apoptosis. Initiation of repair of breaks in dsDNA requires ATM signaling. Dysfunction of this results in nuclear genomic instability which is the major mechanism for the pathogenesis of AT^{6,7,8,9,10}. Dandy walker syndrome is a rare congenital malformation of posterior fossa with involvement of cerebellum and 4th ventricular cystic dilatation¹¹. Association of dandy walker syndrome with AT is rarely described in literature.

We present a very rare case of AT in 7year old girl with dandy walker variant.

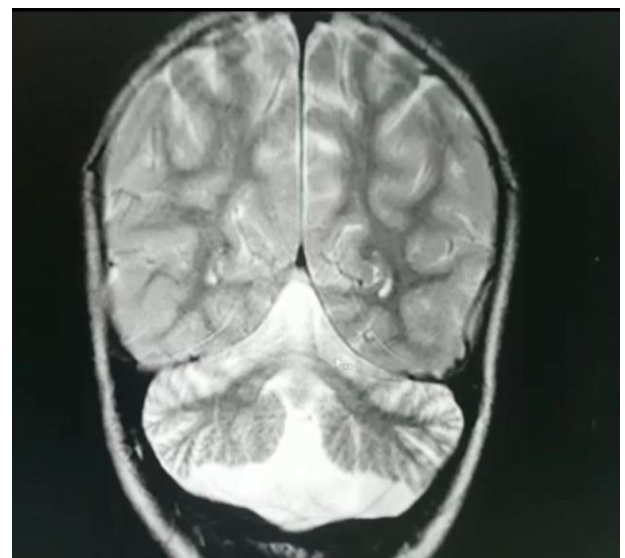
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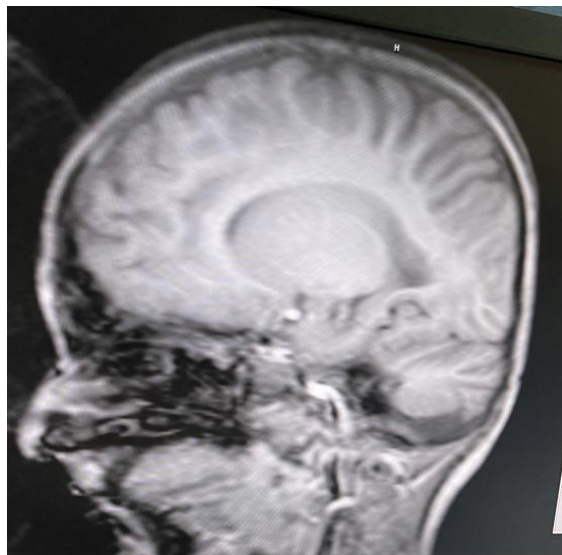
A 7 year old female child born to second degree consanguineously married couple presented with complaints of difficulty in walking, speech difficulty since 2years of age. Child was full term, normal vaginal delivery and had cried immediately after birth, weighing 2.5kg and had been discharged on day 3 of life. Parents had noticed child having an unsteady or wobbly gait when she had started to walk, associated with swaying movements of upper limbs and head, initially at the age of 2years with this unsteady gait, she was able to walk for 20steps which gradually started regressing to 4steps only at present. Previously she used to feed on her own but over the recent past she is unable to do so. Parents also had noticed that she had speech difficulty in the form of slow scanned speech with low output, initially she used to speak 2-3-word sentences at 3years of age with difficulty but over the recent past it has regressed to just one or two words. Also, significant past history of recurrent sinopulmonary infections requiring admission twice and multiple OPD and day care visits in the past were recorded. Her immediate younger sibling had died 10minutes immediately after birth due to respiratory distress. Other siblings were normal. Overall developmental age of the child was found to be approximate to 3years at present. On examination child was conscious, oriented and interacting with surroundings and cooperative, well-built but undernourished. Child had wide based ataxic gait. The head circumference was normal for age(46cm). child had malformed ears, telangiectasia in eyes, beaked nose and retrognathia. Neurological examination of the child revealed hypotonia in all four limbs, power >3/5 and sluggish deep tendon reflexes, she had slurring of speech as well as other cerebellar signs such as ataxia, swaying and inability to perform tandem walking. Ophthalmologist opinion was taken and bilateral conjunctival telangiectasia was

diagnosed. Other systemic examination was normal. All routine investigations were within normal limits. Serum AFP levels were significantly high (109ng/ml). serum IgG and IgA levels were low. MRI brain was suggestive of hypoplastic inferior cerebellar vermis, enlarged posterior fossa and communication of CSF spaces with the fourth ventricle- a variant of dandy walker syndrome. Conservative line of management was advised by paediatric neurologist. Physiotherapy and speech therapy have also been advised.



Picture showing bilateral conjunctival telangiectasias





MRI images showing bilateral inferior vermis hypoplasia, enlarged posterior fossa and communication of CSF spaces with the fourth ventricle, a variant of dandy walker syndrome

Discussion

Ataxia refers to poor coordination and telangiectasia to small dilated blood vessels¹². Patients with AT have increased susceptibility to sinopulmonary infections and predisposition to malignancy¹³. The classical presentation of AT includes truncal ataxia with unstable gait more prominent during standing or sitting position. By the end of first decade most of the children might be wheel chair dependent. Oculomotor apraxia and dysarthria can occur gradually. Scholastic performance might be altered also due to additional visual handicap¹⁴. In majority of cases of AT, telangiectasias are very common, usually present by 6 years of age, typically involving conjunctiva and the areas of face and ears which are exposed to sun¹⁵. Sometimes they are also found in brain and urinary bladder¹⁶. In our case, the child was noticed to have unsteady, wobbly gait when she started to walk from the age of 2 years. She also had telangiectasias in the eyes. In about 75% of cases of AT, an immunoglobulin deficiency occurs. Usually IgG and IgA levels are low when compared to IgM and this is responsible for frequent upper respiratory tract and sinus infections along with chronic inflammatory and autoimmune disorders. In majority of cases of AT,

there is raised alpha-feto protein (AFP) levels^{17,18}. Even in our case, the levels of AFP were significantly high and the levels of IgG, IgA and IgM were mildly lower which attributed to recurrent sinopulmonary infection. MRI done in our case was suggestive of cerebellar hypoplasia which is characteristic radiological finding of AT but also there was hypoplastic inferior cerebellar vermis, enlarged posterior fossa along with communication of CSF spaces with the 4th ventricle which was suggestive of a variant of Dandy walker syndrome (DWS). The incidence of DWS is 1 in 25000 to 35000 live deliveries which is a rare condition occurring in embryonic phase during the development of cerebellum affecting the posterior fossa¹⁹. The common clinical features of DWS are macrocephaly, signs of raised intracranial pressure, delayed development of motor milestones, altered intellectual and cognitive functions noticed as early as in the first year of life along with less common neurological signs like nystagmus, truncal ataxia, cranial nerve palsy and inarticulation of speech^{20,21,22,23}. In our case, child had truncal ataxia with delayed motor milestones but had normal head size without any signs of raised intracranial pressure and also had presented very late at the age of 7 years.

Conclusion

AT is usually associated with various clinical signs such as cutaneous telangiectasias, cerebellar atrophy, ataxia and altered immunity leading to frequent infections of sinuses and respiratory tract with increased chances of malignancies but its association with DWS has been rarely described in literature. Certain clinical features like decreased cognition, ataxia, delayed developmental milestones, cerebellar atrophy, hypoplasia of cerebellar vermis have been found in both the conditions which can be misleading. Early radiological diagnostic evaluation in cases of AT is essential to rule out Dandy walker association as the later condition in some cases may not present with classical clinical findings.

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