

Ataxia-Telangiectasia Masquerading As Cerebral Palsy: A Case Report

Mohammad Fahad Mohiuddin¹, Leenah Mohiuddin², Rida Rizwan³, Mohammed Sarfaraz Hussain⁴, Junaid Ahmed⁵, Sofia Aamir⁶

¹MD Pediatrics, Assistant Professor, Deccan College Of Medical Sciences, Owaisi Hospital and Research Centre.

²Junior Resident (MD Pediatrics) Deccan College Of Medical Sciences.

³MBBS, Intern, Deccan College Of Medical Sciences.

⁴Junior Resident (MD Pediatrics), Deccan College of Medical Sciences .

⁵Final Year MBBS (Part II), Deccan College of Medical Sciences .

⁶MBBS, Deccan College of Medical Sciences.

Corresponding Author : Mohammad Fahad Mohiuddin

ABSTRACT

Ataxia-telangiectasia (A-T) is a rare autosomal recessive multisystem disorder caused by biallelic pathogenic variants in the *ATM* gene. It is characterized by progressive cerebellar ataxia, oculomotor abnormalities, immunodeficiency, telangiectasia, increased susceptibility to malignancy, and progressive neurological dysfunction. Because early neurological manifestations may overlap with cerebral palsy and other developmental disorders, diagnosis can be delayed. Incidence is 1 in 1,00,000 live births.

We report a 3-year-8-month-old girl born to third-degree consanguineous parents who presented with delayed motor development, recurrent falls, progressive gait instability, and right foot deformity. She had initially been evaluated for spastic hemiparesis and possible cerebral palsy. Neurological examination demonstrated generalized hypotonia, bilateral lower-limb spasticity, truncal ataxia, a spastic-ataxic gait, dysmetria, dysidiadochokinesia, slow saccadic eye movements, impaired balance, and dysarthria. Nerve conduction studies demonstrated bilateral peroneal axonal neuropathy, whereas computed tomography of the brain showed no significant structural abnormality. Serum alpha-fetoprotein (AFP) was markedly elevated at 130.4 ng/mL, and serum IgA was reduced to 36 mg/dL, while IgG and IgM were within age-appropriate ranges. Whole-exome sequencing identified a homozygous pathogenic variant in the *ATM* gene involving exons 43–45, confirming the diagnosis of A-T. Additional clinical findings included fewer than three café-au-lait macules and extrapyramidal dyskinesia.

A-T should be considered in children with developmental delay and progressive gait dysfunction, particularly when cerebellar ataxia, slow saccadic eye movements, peripheral neuropathy, or laboratory abnormalities such as elevated AFP are present particularly in a setting of parental consanguinity. Recognition of these clinical clues can prompt appropriate genetic testing and facilitate early multidisciplinary management, surveillance for complications, and genetic counselling.

INTRODUCTION

Ataxia-telangiectasia (A-T) is a rare autosomal recessive multisystem disorder caused by biallelic pathogenic variants in the ATM (ataxia-telangiectasia mutated) gene located on chromosome 11q22.3 [1]. The *ATM* gene encodes a serine/threonine protein kinase that plays a central role in the cellular response to DNA double-strand breaks and is involved in DNA repair, cell-cycle checkpoint regulation, genomic stability, and apoptosis [1,5]. Loss of ATM function results in a complex phenotype characterized predominantly by progressive neurological dysfunction, variable immunodeficiency, increased sensitivity to ionizing radiation, and an increased risk of malignancy, particularly lymphoid malignancies [1,5].

The neurological manifestations of A-T generally become apparent during early childhood. Progressive cerebellar ataxia commonly presents with delayed motor development, recurrent falls, gait instability, dysarthria, and impaired coordination. Oculomotor abnormalities, particularly slow saccadic eye movements, are important clinical clues. Peripheral neuropathy and extrapyramidal movement abnormalities may also occur [1,5].

Due to its rarity and overlapping clinical features with conditions such as cerebral palsy and hereditary ataxias, AT is often underrecognized and diagnosed late (1,3,4). Progressive rather than static neurological dysfunction, particularly when accompanied by cerebellar signs, abnormal eye movements, peripheral neuropathy, or elevated AFP, should prompt consideration of an underlying neurogenetic disorder.

We present a young child initially evaluated for spastic hemiparesis and cerebral palsy who was subsequently diagnosed with A-T through clinical, biochemical, electrophysiological, and molecular evaluation.

CASE DESCRIPTION

A 3-year-8-month-old girl presented with delayed motor development, recurrent falls, progressive gait instability, and deformity of the right foot. She was born to third-degree consanguineous parents. The initial clinical concern was spastic hemiparesis, and cerebral palsy was considered because of the gait abnormality and lower-limb spasticity. According to the parents, the child had progressive swaying while walking and recurrent falls. She was unable to run for prolonged distances without falling and had difficulty climbing stairs and jumping without support. Balance was impaired during both standing and walking. A right foot deformity with intermittent equinus gait had also developed. Fine motor development was delayed, with an immature pincer grasp. Despite this, she was able to copy a circle, feed herself independently, and identify colours and body parts. Speech was understandable and consisted of short phrases.

On examination, the child had generalized hypotonia, bilateral lower-limb spasticity, truncal ataxia, spastic-ataxic gait, gait imbalance, slurred speech, impaired coordination of voluntary movements, impaired coordination of alternating movements, inward curling of toes, and slow saccadic eye movements. Deep tendon reflexes were sluggish, and peripheral neuropathy was evident on nerve conduction studies, which demonstrated bilateral peroneal axonal neuropathy. Computed tomography of the brain revealed no significant abnormality. Additional clinical findings included café-au-lait macules (<3) and extrapyramidal features in the form of dyskinesia.

Investigations revealed significant supportive findings for Ataxia-Telangiectasia. Nerve conduction studies demonstrated bilateral peroneal axonal neuropathy, while computed tomography of the brain showed no significant structural abnormality. Serum alpha-fetoprotein (AFP) was elevated at 130.4 ng/mL, and serum IgA was reduced to 36 mg/dL, with serum IgG (739 mg/dL) and IgM (107 mg/dL) within age-appropriate limits. Whole-exome sequencing identified a homozygous pathogenic variant in the ATM gene involving exons 43–45, consistent with an autosomal recessive inheritance pattern and confirming the molecular diagnosis of Ataxia-Telangiectasia. The combination of progressive truncal and gait ataxia, spastic-ataxic gait, dysmetria, dysdiadochokinesia, slow saccadic eye movements, generalized hypotonia, peripheral axonal neuropathy, extrapyramidal dyskinesia, elevated AFP, reduced IgA, and a homozygous pathogenic ATM variant supported the diagnosis. The history of third-degree parental consanguinity further supported the autosomal-recessive inheritance pattern.

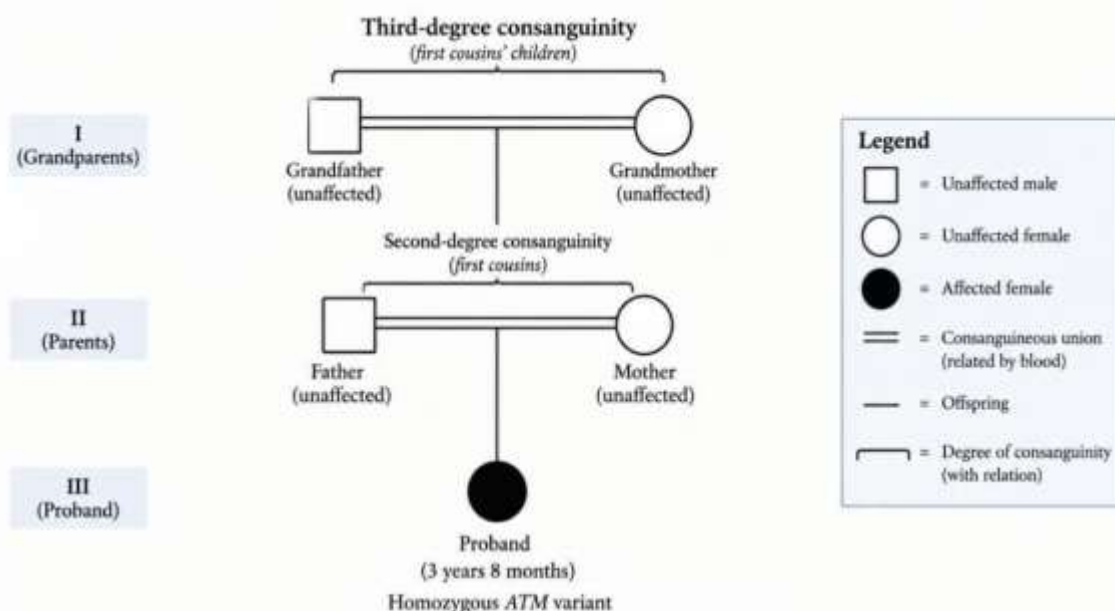


Figure 1. Three-generation pedigree demonstrating third-degree parental consanguinity (grandparents are first cousins' children and parents are first cousins). The proband is the affected female child with a homozygous pathogenic ATM variant consistent with autosomal-recessive Ataxia-Telangiectasia.

Figure 1: Sashimi plot indicating RNA sequencing read densities along skipping of exon 43 to 45 detected in ATM gene

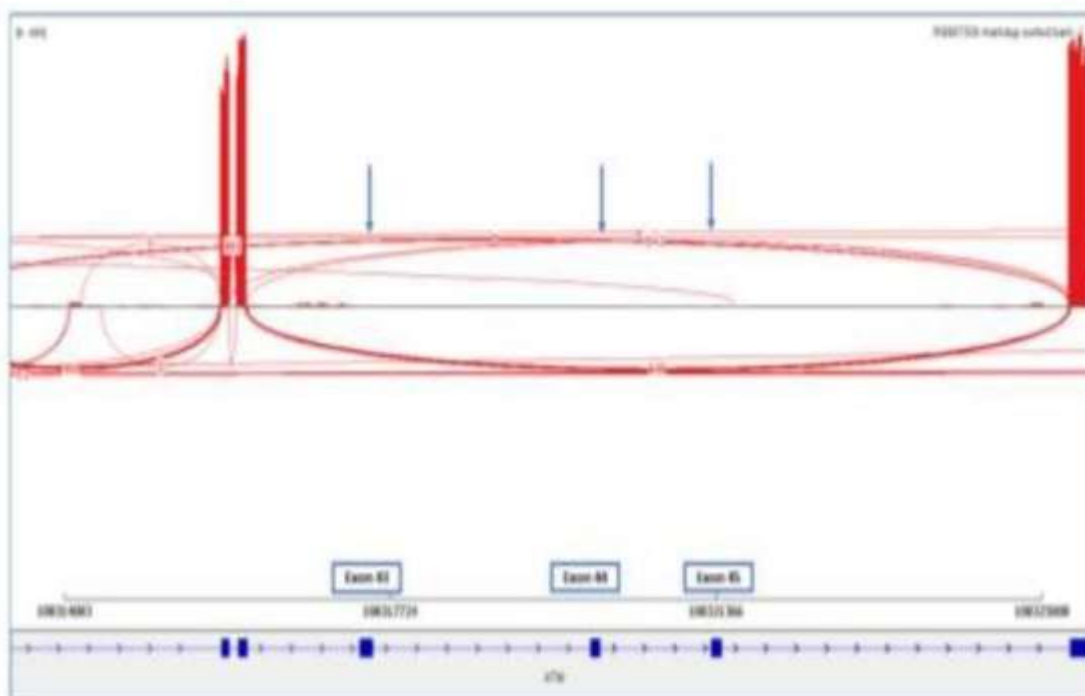


Figure 2: Comparative plot of skipping of exon 43 to 45 between case and control samples.

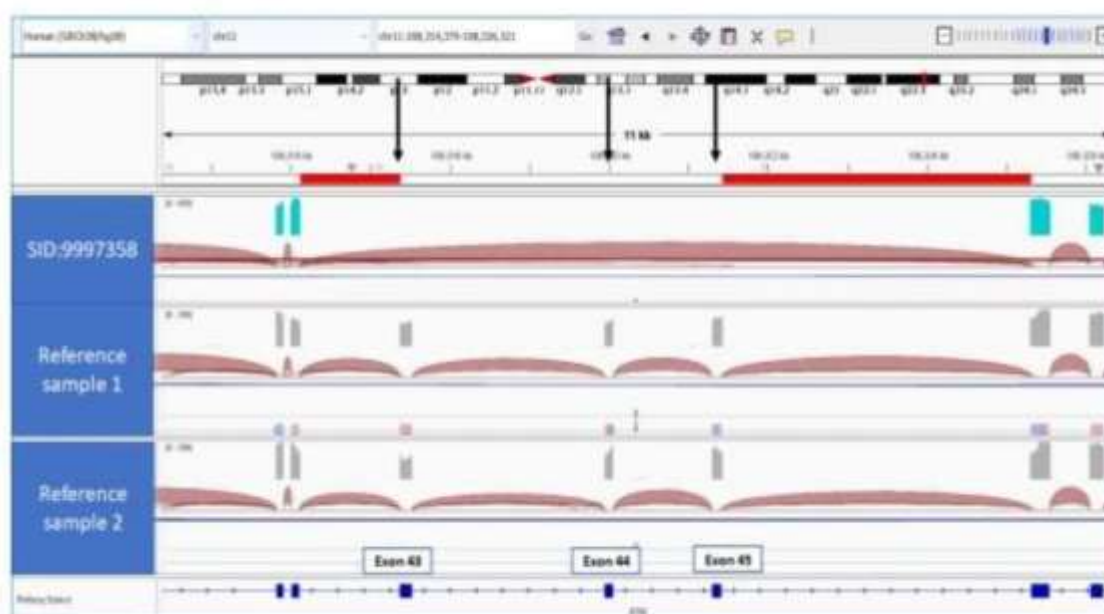


Figure 3: Representative figure on the out of frame consequence in the sample



RESULTS

PATHOGENIC VARIANT WAS DETECTED

Gene* (Transcript)	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification ⁵
ATM (+) (ENST00000675843.1) NM_000051.4	chr11:108316114_108325309del r.6198+1_6573-1del p.(Gln2066delinsIleSerHisThrTer) Exon 43 to 45	Homozygous	Ataxia-telangiectasia (OMIM#208900)	Autosomal Recessive	Pathogenic

TABLE 1: Investigations

PARAMETERS	AT PRESENTATION	REFERENCE / NORMAL RANGE (AGE APPROPRIATE)
Complete Blood Count	Within normal limits	Hemoglobin: 11.5–15.5 g/dL Total leukocyte count (TLC): 4,000–11,000 /mm ³ Platelets: 1.5–4.5 lakh /mm ³ (Reference ranges vary with age)

CT Brain	No significant abnormality detected	No structural brain abnormality
Nerve Conduction Studies (NCS)	Bilateral peroneal axonal neuropathy	Normal nerve conduction studies; no evidence of axonal neuropathy
Serum Alpha-Fetoprotein (AFP)	130.4 ng/mL (Elevated)	Age-dependent: At birth: 10,000–100,000 ng/mL 1–12 months: <100 ng/mL >1 year: <10 ng/mL (Persistent elevation beyond infancy is abnormal)
Serum IgG	739 mg/dL (Normal)	Age-dependent: 0–6 months: 300–1,200 mg/dL 6–12 months: 400–1,300 mg/dL 1–5 years: 500–1,400 mg/dL >5 years: 600–1,500 mg/dL
Serum IgA	36 mg/dL (Decreased)	Age-dependent: 1–5 years: 20–100 mg/dL >5 years: 70–400 mg/dL
Serum IgM	107 mg/dL (Normal)	Age-dependent: 1–5 years: 40–200 mg/dL >5 years: 40–230 mg/dL
Whole Exome Sequencing (WES)	Homozygous pathogenic ATM gene variant detected	No pathogenic ATM variant detected
Genetic Variant	ATM (+), Exons 43–45, Homozygous	No pathogenic/likely pathogenic ATM variant
Inheritance Pattern	Autosomal Recessive (AR)	No disease-causing biallelic ATM variant
Clinical Genetic Interpretation	Consistent with AtaxiaTelangiectasia, likely pathogenic	No pathogenic ATM-related disease
Neuroimaging	No structural brain abnormality identified	Normal brain structure for age
Clinical Examination Findings	Truncal ataxia, spasticataxic gait, slow saccadic eye movements, dysmetria, dysidiadochokinesia, generalized hypotonia	Normal coordination, gait, ocular movements, and muscle tone for age
Dermatological Findings	Café-au-lait macules (<3)	No abnormal pigmentation or telangiectasia

Family History	Third-degree parental consanguinity	No significant consanguinity/family history of similar illness
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Based on the clinical, immunological, electrophysiological, and genetic findings, a final diagnosis of Ataxia-Telangiectasia was established. The child was subsequently managed with physiotherapy, occupational therapy, supportive treatment, and genetic counselling, with recommendations for long-term neurological follow-up and surveillance for disease-related complications.

TREATMENT AND FOLLOW-UP

Following confirmation of A-T, the child was managed with a multidisciplinary supportive approach. Physiotherapy and occupational therapy were initiated to address gait instability, truncal ataxia, impaired balance, lower-limb spasticity, motor dysfunction, and difficulties with fine motor activities and activities of daily living [1,6].

Symptomatic treatment was provided for the extrapyramidal movement disorder.

Amantadine was administered for dyskinesia and associated motor manifestations [9]. Idebenone was prescribed as an adjunctive mitochondrial-supportive therapy [8]. The child also received MitoQ7 syrup as a mitochondrial-supportive supplement and NanoDeksel syrup for vitamin D supplementation.

Long-term follow-up was planned because A-T is a progressive multisystem disorder requiring ongoing neurological, immunological, respiratory, nutritional, and malignancy surveillance [1,6]. Genetic counselling was provided to the family, with discussion of the autosomal recessive inheritance pattern and implications for future pregnancies.

DISCUSSION

A-T is a clinically heterogeneous inherited disorder resulting from loss of function of the ATM protein, which is essential for the cellular response to DNA damage and maintenance of genomic stability [1,5]. The resulting phenotype involves multiple organ systems, with progressive neurological dysfunction being one of the most recognizable features during childhood.

The present case illustrates an important diagnostic challenge: the early neurological manifestations of A-T may resemble cerebral palsy. The child initially presented with gait abnormality, lower-limb spasticity, recurrent falls, and foot deformity, leading to consideration of spastic hemiparesis and cerebral palsy. However, the subsequent recognition of truncal ataxia, dysmetria, dysidiadochokinesia, slow saccadic eye movements, and peripheral neuropathy suggested a progressive neurological disorder.

An important distinction is the **clinical course**. Cerebral palsy is a non-progressive disorder resulting from an injury or abnormal development of the developing brain, although functional manifestations may change over time. In contrast, A-T is a progressive neurodegenerative condition. Therefore, deterioration or emergence of new neurological signs in a child previously labelled as having cerebral palsy should prompt reassessment of the diagnosis. The presence of slow saccadic eye movements was particularly informative in this case. Abnormal saccades are a recognized neurological manifestation of A-T and, when associated with progressive ataxia, should increase suspicion of the disorder [1]. Peripheral neuropathy further broadened the neurological phenotype and provided an additional clue toward an inherited neurodegenerative disorder.

Neuroimaging in this child was unremarkable. A normal CT scan does not exclude A-T, particularly in the early stages of disease. Consequently, a normal structural brain study should not deter further investigation when the clinical phenotype suggests a progressive inherited ataxia.

Serum AFP provided an important biochemical clue. Persistent elevation of AFP after infancy is characteristic of A-T and can support the diagnosis in an appropriate clinical context [1,2]. In this patient, AFP was 130.4 ng/mL at 3 years of age, substantially above the expected level after infancy. Immunological abnormalities are also variable in A-T. The reduced IgA level in this child, with relatively preserved IgG and IgM, illustrates the variable nature of the immunodeficiency associated with the disorder [1,7].

The absence of prominent telangiectasia at presentation does not exclude A-T.

Telangiectasias may develop later, and their absence in a young child can contribute to diagnostic delay. Similarly, the presence of fewer than three café-au-lait macules was not considered diagnostic but represented an additional cutaneous finding.

The extrapyramidal dyskinesia observed in this patient is also noteworthy. Although cerebellar ataxia is the dominant neurological manifestation of classic A-T, extrapyramidal movement abnormalities have been described and may contribute to the clinical heterogeneity of the disorder.

The history of parental consanguinity was an important clue to autosomal recessive inheritance. WES subsequently identified a homozygous pathogenic *ATM* variant involving exons 43–45, providing molecular confirmation of the diagnosis. Molecular testing is particularly valuable in atypical or early presentations in which the classical phenotype is incomplete [1].

Management of A-T remains predominantly supportive and multidisciplinary. Physical and occupational therapies are important for maintaining mobility, coordination, and functional independence [1,6]. Speech and nutritional support may become necessary as neurological dysfunction progresses. Because of the variable immunodeficiency and increased risk of malignancy, longitudinal immunological and clinical surveillance is essential [1,6].

The use of antioxidant or mitochondrial-supportive therapies such as idebenone in A-T has a theoretical biological rationale related to oxidative stress and mitochondrial dysfunction, but these approaches should be regarded as adjunctive rather than established disease-modifying treatments. Similarly, symptomatic treatment of movement abnormalities should be individualized according to the patient's clinical manifestations.

An important practical lesson from this case is that **progressive motor impairment should not automatically be attributed to cerebral palsy**. In a child with developmental delay and gait dysfunction, the presence of progressive ataxia, truncal instability, dysmetria, slow saccades, peripheral neuropathy, unexplained movement abnormalities, elevated AFP, immunological abnormalities, or a relevant family history should prompt consideration of an inherited neurogenetic disorder. Early recognition can shorten the diagnostic pathway and allow appropriate counselling and surveillance.

CONCLUSION

Ataxia-telangiectasia should be considered in children presenting with developmental delay and progressive gait abnormalities, particularly when the neurological phenotype includes truncal ataxia, dysmetria, dysdiadochokinesia, slow saccadic eye movements, peripheral neuropathy, or extrapyramidal manifestations. The presence of elevated serum AFP and immunological abnormalities can provide important supportive evidence, even when classical telangiectasia is not yet apparent.

In children initially considered to have cerebral palsy, a **progressive rather than static course** and the emergence of additional neurological signs should prompt diagnostic reassessment. In the present case, the combination of clinical findings, elevated AFP, reduced IgA, peripheral axonal neuropathy, parental consanguinity, and a homozygous pathogenic *ATM* variant established the diagnosis of A-T.

Early molecular diagnosis facilitates appropriate multidisciplinary management, surveillance for immunological and malignant complications, and genetic counselling for the affected family.

HIGHLIGHTS

Ataxia-telangiectasia can initially present with features that resemble cerebral palsy.

- A progressive course, truncal ataxia, slow saccadic eye movements, and peripheral neuropathy are important diagnostic clues.
- Elevated serum AFP and immunological abnormalities can support the diagnosis.
- Absence of prominent telangiectasia in a young child does not exclude A-T.
- Homozygous pathogenic variants in *ATM* provide molecular confirmation.
- Early diagnosis enables multidisciplinary supportive care, long-term surveillance, and genetic counselling.

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