

A Rare Homozygous Pathologic ATM Gene Variant with Severe Immune Deficient Phenotype of Ataxia Telangiectasia in an Emirati Sib-Ship

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Abstract

Ataxia telangiectasia (AT) is a rare neurodegenerative autosomal recessive disorder with multisystem manifestations. A defect in the gene present on chromosome 11q22-23. is responsible for this disorder [1] AT often causes physicians to an incorrect or missed diagnosis due to its diverse clinical picture, which includes progressive cerebellar ataxia, abnormal eye movements, telangiectasia and immune deficiency [1]. Management of these cases requires multidisciplinary approach.

Keywords: Ataxia telangiectasia (AT); ATM Gene

Introduction and Case Report

In December 2015, a 23 month old Emirati boy presented to the emergency department of Mafraq Hospital with a 10 day history of fever, cough and occasional shortness of breath, along with poor feeding, lethargy and vomiting during the last week. For his illness, he was seen two days prior in a private clinic and a chest radiograph was done suggestive of necrotizing pneumonia, and otitis media with a dental abscess. He was asked to go to the nearest hospital for immediate treatment for his illness.

On arrival to Mafraq Hospital, the patient was found to be febrile and sick looking, although responsive, alert and hemodynamically stable. On detailed examination, the positive findings included failure to thrive, poor dental hygiene, a perforated and draining right tympanic membrane. He had right middle zone decreased air entry in the lungs with bilateral crepitation, a finding correlating to pneumonic infiltrate and cavitation on chest radiograph (Figure 1). Skin manifestation included punctate cicatricial hypopigmented macules scattered on the limbs and a small haemangioma on the scalp; there was no telangiectasia or abnormal vascular rash. Neurological examination showed wide based ataxic gait with hypotonia and hyporeflexia.



Figure 1: Large right mid zone consolidation and cavitation.

According to the parents, there was some degree of delayed walking and unsteady gait in the patient. His family history was significant for a brother who had ataxic gait as well, died due to chest infections at the age of 5 years and no diagnosis was reached that time. Blood investigations were remarkable for microcytic hypochromic anemia, mild leukocytosis and CRP of 229 mg/L. Based on the clinical picture, radiographic and laboratory findings, he was admitted as aggressive pneumonia and otitis media and was started empirically on ceftriaxone and vancomycin.

Paediatric neurology team were consulted on the patient regarding his ataxia and developmental delay, and on their recommendation, immunoglobulin levels and alpha fetoprotein (AFP) level was requested in suspicion of ataxia telangiectasia.

Immunology workup revealed critically low IG, IgG (< 0.3 g/L), IgA (< 0.04 g/L) and a strikingly high level of AFP at 19 IU/ml. Based on complete clinical picture, a clinical diagnosis of ataxia telangiectasia was made and genetic testing sent for confirmation. Patient's family were counselled on avoidance of unnecessary radiation.

The patient continued to improve, and on the fifth day of admission he was given intravenous immunoglobulin (IVIG) infusion. He was discharged in a stable condition with plan for monthly IVIG infusions to improve his immune status. An MRI was done post discharge showing a small incidental left occipital venous angioma (Figure 2).

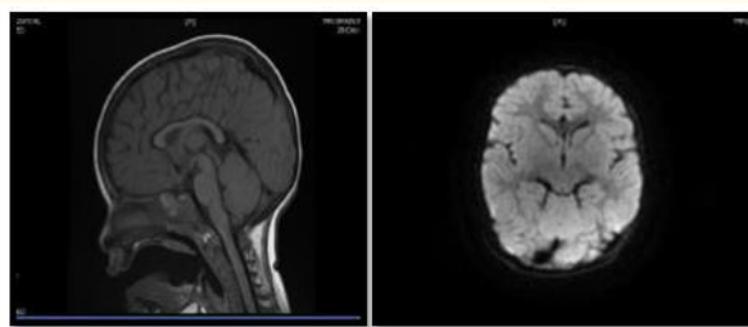


Figure 2: Altered small signal intensity of left occipital lobe seen as high signal in T2 and flair. Venous angioma.

Genetic testing confirmed the diagnosis of ataxia telangiectasia by identifying a rare homozygous likely pathogenic variant in c.2921+3A>T in intron 19 of ATM gene (Figure 3) only one homozygous patient has been described for this variant so far. The family was called and counselled about the disease. We assume the deceased sibling had the same mutation and parental testing is planned.

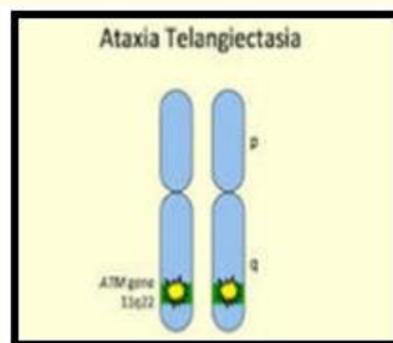


Figure 3: Chromosomal locus of the ATM gene.

Conclusion

The diagnosis of ataxia-telangiectasia should be considered in children presenting with gait disorder and severe infections suggestive of immunological defects even in the absence of telangiectasia [2]. With this case report we aim to shed light on this rare diagnosis and guide physicians towards recognizing the signs and symptoms of this uncommon entity [3-8].

Acknowledgments

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