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Case Report OMICS International

Atypical Presentation of Previously Described Classical Ataxia Telangiectasia Pathogenic Mutation

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Abstract

Ataxia Telangiectasia (A-T) is a rare genetic disorder characterized by Cerebellar ataxia, telangiectasia, immunodeficiency and susceptibility for malignancies. The clinical presentation and severity varies in affected patients, which could point out an aspect of gene heterogeneity of this disease that is yet to be identified. This case highlights a rare presentation of a patient diagnosed with A-T, with absence of recurrent and/or severe sinopulmonary disease. A multidisciplinary approach, genetic counselling and preventive care for early cancer detection should be ensured.

Keywords: Ataxia telangiectasia; Immunodeficiency; Malignancy; Sinopulmonary disease; Cerebellar atrophy

Introduction

Ataxia Telangiectasia is an autosomal recessive syndrome presenting with cerebellar ataxia, telangiectasia, immune defects, and a predisposition to malignancy [1]. Immune defects commonly presents with a history of recurrent sinopulmonary disease [2]. We report a case of a 5 year old male with A-T, with absence of recurrent and/or severe sinopulmonary disease.

Case Presentation

A 5 year old boy recently emigrated from Honduras was referred to the neurology clinic due to unsteady gait, multiple café au lait spots and developmental delays. The mother reported that the child had a clumsy gait and frequent falls since he started ambulation. His developmental milestones were delayed: He spoke after the age of two and walked after eighteen months of age.

He was born full term by cesarean section with no complications and no history of consanguinity. The family history was remarkable for a paternal five y/o cousin with Malignant Kidney Tumor. The child never presented recurrent sinopulmonary disease.

Physical examination showed BMI: 15=30% Height: 104 cm=4% Weight: 16 kg=5% and stable vital signs. He presented with ocular telangiectasia, without cutaneous involvement. Horizontal nystagmus on maximal gaze to side appreciated. Chest, Cardiovascular and abdominal examinations were normal. Skin examination presented with multiple café au lait spots (7, distributed on upper extremities, left thigh, abdomen and back), no cutaneous telangiectasia. CNS examination showed an alert, oriented child with dysarthria, monotonous speech, unsteady gait (not wide-based), upon marching the trunk tilted to either right or left side, mild chorea and dystonic hyperkinesia. The rest of the CNS examination including fundus was normal.

The patient failed his vision screening. Complete hemogram and peripheral smear were normal. The alfa-fetoprotein was elevated (366.1 ng/ml) and the IgA, IgE and CEA levels were within normal range.

Chromosome rearrangement testing was consistent with chromosomal instability syndrome. The brain MRI was performed showing a diffuse cerebellar atrophy (Figure 1). *ATM* gene sequencing revealed compound heterozygosity c.7913G>A/c.8714dupC. On subsequent follow-up, we noted that the patient was improving on language skills as well as fine and gross motor development with reduced frequency of falls, however ataxia is progressively worsening. X-ray exposure has been avoided as much as possible in order to prevent malignancy.

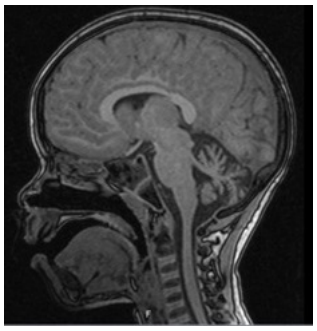

Figure 1: Brain MRI showing diffuse cerebellar atrophy.

Discussion

Ataxia Telangiectasia (A-T) is a rare, multisystem, neurodegenerative genetic disease. The pattern of inheritance is autosomal recessive, caused by mutations in the ataxia telangiectasia mutated (*ATM*) gene. A-T is characterized by cerebellar ataxia, oculocutaneous telangiectasia, immunodeficiency, radiation sensitivity and increased risk of malignancy [1,2].

It affects all races and ethnicities equally except for consanguineous populations. The incidence is 1 in 20,000 to 100,000 [3,4]. A-T is classified into a severe and mild form described as "classic" and "variant" respectively.

Clinical presentation varies in these patients, making it difficult to distinguish clinically from other chronic ataxic syndromes and, therefore the diagnosis may be delayed. Ataxia, oculomotor problems and extrapyramidal symptoms (chorea, dystonia, etc.) are the common neurological features in A-T. Ocular Telangiectasia has a peak presentation at 5-8 years [5]. Telangiectasia may be absent in patients with A-T. Two out of 3 patients with A-T have defects in the cell mediated and humoral immunity. Serum levels of IgG or IgA are diminished or absent in 80% and 60% of patients [2]. The defect is quite variable but often manifests as recurrent sinopulmonary infections [6,7]. The clinical presentation of immunodeficiency in ataxia-telangiectasia can change during life, therefore close lifetime follow up is ensured. Endocrine abnormalities include poor growth, delayed pubertal development and Insulin-resistant diabetes. Mild to moderate cognitive impairment is commonly seen in these patients and may deteriorate overtime. Patients have a malignancy lifetime risk between 10% and 38%, mainly of lymphoid origin [8-10].

Elevated alpha feto-protein (AFP), although not specific, is commonly seen in patients with A-T [11]. White blood cell count and Immunoglobulin levels are helpful to evaluate for the presence of an immunodeficiency. The diagnosis of A-T is confirmed by genetic testing. Magnetic resonance imaging (MRI) is the preferred diagnostic imaging. Diffuse atrophy of the cerebellum can be present in patients with A-T [12]. There is no cure for A-T, nevertheless, a multidisciplinary approach will ensure symptomatic management and supportive care [13,14]. The life expectancy is approximately 25 years with the most common causes of mortality being chronic lung disease and cancer [15,16]. Children not considered to be immunodeficient should be immunized with pneumococcal and influenza vaccines.

Conclusion

Ataxia Telangiectasia is a rare disorder with catastrophic outcomes. This case describes an uncommon presentation of a patient with a confirmed A-T and absent history of recurrent sinopulmonary disease. Genetic and clinical heterogeneity is evident in these patients, therefore care should be tailored to the needs of each patient in order to improve the quality of life and long term prevention and monitoring for malignancies. Genetic counseling and prenatal diagnosis for future pregnancies are beneficial for the family.

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