

Case Report

Classic ataxia-telangiectasia in a Sudanese boy: Case report and review of the literature

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ABSTRACT

Ataxia-telangiectasia (A-T) is a rare hereditary neurodegenerative disorder. Ataxia and telangiectasias are the hallmarks of the disease. A spectrum of manifestations may be seen in one family. There is no gold standard diagnostic test and diagnosis relies on clinical evaluation, exclusion of similar conditions, and supportive laboratory tests. More than 99% of individuals with classic A-T have mutations in ATM, the only gene known to be associated with ataxia-telangiectasia.

We report a 28-months-old Sudanese boy who was presented with unsteady gait, frequent falls and telangiectasias of the eyes. He also has had frequent episodes of respiratory tract infections.

Key words: Ataxia-telangiectasia;
Immuno-deficiency; Child; Sudan.

INTRODUCTION

Ataxia-telangiectasia (A-T) is a rare hereditary neurodegenerative disorder. Ataxia and telangiectasias are the hallmarks of the disease. Classic A-T is characterized by progressive cerebellar ataxia starting between one and four years of age, and is also associated with immunodeficiency, frequent infections, oculomotor apraxia and choreoathetosis (which develop later), and an increased risk for malignancy. The prevalence of A-T in the US is 1:40,000-1:100,000 live births, but it varies with the degree of consanguinity in a country. A spectrum of manifestations may be seen in one family. There is no gold standard diagnostic test and the diagnosis relies on clinical evaluation, exclusion of similar conditions, and supportive laboratory tests. More than 99% of individuals with classic A-T have mutations in ATM, the only gene known to be associated with ataxia-telangiectasia. Nevertheless, molecular genetic testing is available in advanced diagnostic laboratories against cost. We report a 28-months-old Sudanese boy who manifested classic A-T.

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CASE REPORT

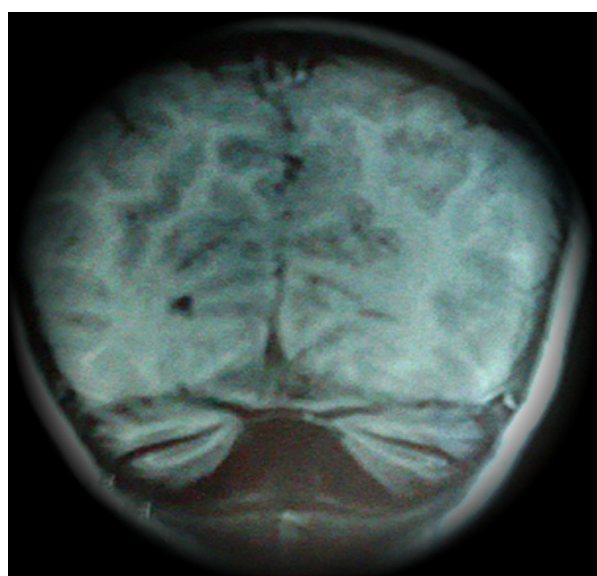
A 28-months-old Sudanese boy presented with delayed walking (20 month), unsteady gait and frequent falls, and delayed slurred speech. He had recurrent respiratory and ear infections associated with psychomotor delay but his somatic growth was normal. On examination, he showed florid bulbar conjunctiva telangiectasia (Figure1). Movement patterns demonstrated ataxia but no extra pyramidal

movements or ocular apraxia. Magnetic resonance image (MRI) showed cerebellar atrophy (Figure 2). Investigations revealed low lymphocyte count and IgA. Alpha-fetoprotein (AFP) testing was not available. The child was treated symptomatically and supportively with antibiotics for recurrent infections and multivitamins. Speech therapy was advised and intravenous immunoglobulin therapy was suggested, but could not be afforded by the family.

Figure 1. Bulbar conjunctiva telangiectasia.



Figure 2. Coronal MRI image showing cerebellar atrophy.



DISCUSSION

Ataxia-telangiectasia (A-T) or Louis-Bar syndrome is a rare neurodegenerative inherited disorder that affects many parts of the body and leads to severe disability [1]. The disease is inherited in an autosomal recessive fashion and is due to mutations in the ATM gene located on chromosome 11q22-23 [2]. ATM gene is important in DNA repair. The prevalence is estimated to be between 1 out of 40,000 and 1 out of 100,000 persons worldwide [3].

The first indications of A-T usually occur in early childhood. Clinically progressive ataxia and telangiectasias appear first, and prominent

telangiectasias usually occurs by the age of 5 years. Telangiectasias are occasionally present at birth while in some cases may not develop until the teenage years. They are mainly on the bulbar conjunctiva, external ears, nares, and later may involve other body surfaces.

Initially some children seem to improve, but eventually it becomes obvious that balance control is abnormal. The child may have delayed walking than usual or manifests reluctance to let go of supporting people or objects. Some children continue to walk unsteadily for longer than usual and fall frequently.

Thymic hypoplasia may be present [4]. Increased infections due to immune system disorder appear in about 70% of the cases. The child may present with recurrent chest, sinus and ear infections, and there is an increased risk of malignancy.

Oculomotor apraxia (inability to follow an object across visual fields), slurred speech, choreoathetosis, hypotonia and areflexia, and psychomotor and growth retardation are features of the disease. Endocrinopathies are common, and extreme sensitivity to ionizing radiation is also part of the clinical picture. Ataxia-telangiectasia can have somewhat incomplete penetrance; some patients have a mild form of the disease that starts later and has less severe symptoms. Towards the end of the first decade most patients begin to use a wheelchair.

Ataxia-telangiectasia appears in three forms;

- (a) Pure A-T where patients present with all/most of the diagnostic symptoms,
- (b) Attenuated A-T or type II where a patient lacks some of the typical findings but shows radio-sensitivity and
- (c) Carrier A-T where individuals with a single ATM mutation may have an increased risk of cancer.

Diagnosis is usually achieved clinically by examination and identification of both ataxia and oculo-telangiectasia or skin telangiectasia. Laboratory tests often show elevated serum AFP level, low lymphocyte count and other immunological abnormalities. MRI and computed tomography (CT) scans may show cerebellar atrophy. MRI is the preferred method, as any exposure to ionizing radiation should be avoided. Cytogenetic and molecular testing will confirm the diagnosis.

Possible differential diagnoses include ataxia oculomotor apraxia type 1 and type 2, and ataxia-telangiectasia-like disorder (ATLD) [9-11]. Two

Sudanese siblings (living in Saudi Arabia) and one isolated case (from the Northern State of Sudan) were among the 90 established ataxia oculomotor apraxia type 2 cases reported by Anheim et al [9]. This collaborative study [9] included cases from 15 countries worldwide.

Patients with ATLD are very similar to A-T patients in showing a progressive cerebellar ataxia, hypersensitivity to ionizing radiation and genomic instability [6]. However, ATLD can be distinguished from A-T by the absence of telangiectasias, normal immunoglobulin and AFP levels, later onset of the condition and a slower progression of the disease [10]. ATLD is due to MRE11 gene mutation which is located on chromosome 11q21 [1]. Recently, a new missense mutation, a G-to-C change at nucleotide 630 of the MRE11 gene, was described in 10 ATLD Saudi Arabian patients from three unrelated families [11]. A heterozygous carriers' frequency of 0.5% was recorded in the Saudi population, with similar high consanguinity rate to Sudan, for this mutation [12, 13].

Treatment is symptomatic and supportive. Physical and occupational therapy may help maintain mobility. Speech therapy may also be needed. Regular use of intravenous immunoglobulins may help to improve immune function and reduce the frequency of infections. Aggressive antibiotic therapy is required for bacterial infection, avoidance of radiological exposure and screening for cancer is an imperative part of the follow up.

At the beginning of the second decade, most patients with A-T lose their mobility and start to use a wheelchair. They develop limb ataxia and abnormal movements; those include small fidgeting jerks of the hands and feet, athetosis, dystonia, myoclonic jerks and tremors.

Dysarthria may develop in the first decade, becoming

worse for 5 to 10 years and then remain static. Patients generally can be understood, although conversation may be a slow process. Eye movements become restricted to vertical and horizontal saccadic apraxia. Reading and following moving objects becomes difficult. [7]

Severe mental retardation is not common in A-T. However, many children seem to have slower thinking speed and need special schooling. A-T patients are often

very thin. This may be due to a poor appetite, or the inherent characteristics of the disorder. Patients tend to have delayed puberty. This seems more common in those who are thin or are prone to infections. People with A-T have an increased incidence (around 1% risk per year) of tumors, particularly lymphomas and leukemia, but due to sufferers' hyper-sensitivity to ionising radiation, radiotherapy and chemotherapy are rarely used.[8]

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