

CASE REPORT**ATAXIA TELANGIECTASIA IN AN ETHIOPIAN CHILD**Ayalew Moges, MD^{1*}, Abebe Mekonnen, MD¹, Belachew Firde, MD²**ABSTRACT**

Ataxia telangiectasia is a rare, progressive, multisystem, autosomal recessive disorder that has a large number of complex and diverse manifestations, which vary with age. It is characterized by progressive cerebellar ataxia, oculocutaneous telangiectasia, and recurrent respiratory and sinus infections. Diagnosis of Ataxia telangiectasia is often made on clinical evaluation, exclusion of similar conditions, and supportive laboratory tests. The management of Ataxia telangiectasia is multidisciplinary, requiring neurologist, physiotherapist and nutrition program. Treatment is symptomatic and supportive including counseling of parents or caretakers. We report a 10 year old Ethiopian girl who presented with progressively increasing gait difficulties, scoliosis, ocular manifestations and bilateral chronic suppurative otitis media.

Key words: Ataxia telangiectasia; Immunodeficiency; Cerebellar atrophy; Ethiopia

INTRODUCTION

Ataxia Telangiectasia (AT) or Louis Bar syndrome is a rare (1:40,000-1:300,000 live births per year (1, 2), multisystem, autosomal recessive disease characterized by neurological impairment (progressive cerebellar ataxia, axonal peripheral neuropathy, oculomotor apraxia, and movement disorders such as dystonia, choreoathetosis, myoclonus, tremor, Parkinsonism), telangiectasias, recurrent sinopulmonary infections, susceptibility to cancer, increased alpha-fetoprotein, decreased IgA levels and radio hypersensitivity (3).

AT is caused by biallelic mutations in ATM gene, which plays a pivotal role in the control of cell cycle and in the response to DNA double strand break damage and Chromatin changes. Elevated AFP occurs due to immature liver. Males and females are equally affected. No racial or regional preferences are found. It usually begins around the age of 5 years old (4). The mean age of diagnosis is around 3 years of age (5) but it may occur to the age of 10 years (6).

Diagnosis is usually achieved clinically by examination and identification of ataxia in early childhood and ocular or skin telangiectasia usually after the age of 3-4 years. Neuroimaging, genetic tests and other laboratory tests are also important. The management of AT is multidisciplinary, requiring pediatrician, infectious disease specialist, child neurologist, hematologist, physiotherapist, occupational therapist, speech therapist, social worker etc.

The course of AT can be variable. Many patients are confined to a wheelchair in their teens. So far, to the knowledge of the authors, there is no case report on AT in Ethiopian children. We report the case of a 10 years old Ethiopian girl with classic manifestations of AT.

CASE SUMMARY

A 10 year old Ethiopian child, born of a non-consanguineous marriage, is the eldest in a family of two. Her younger brother is healthy. There is no history of similar illness in her family up to three generations (Figure 1). She was in good health until the age of 2 years, when she had bilateral chronic suppurative otitis media, which was treated with oral antibiotics and eardrops with poor response. Since the age of six years, she started to have progressively increasing difficulty in walking, keeping balance, coordinating hand movements and slurring of speech. She has also red eyes and frequent attack of respiratory tract infections.

Clinical examination revealed cerebellar ataxia, scoliosis, dysarthria and oculocutaneous telangiectasias on bulbar conjunctivae, nose and ear lobes (Figure 2). Oscopic examination revealed sub totally perforated tympanic membrane on both sides.

¹ Pediatrician and Pediatric Neurologist, Department of Pediatrics and Child Health, School of Medicine,

College of Health Sciences, Addis Ababa University, Ethiopia. ² Neuroradiologist, Department of Radiology, School of Medicine, College of Health Sciences, Addis Ababa University, Ethiopia. ³ Pediatrician, Betsegah Mothers' & Children's Medical Center, Addis Ababa, Ethiopia.

*Corresponding Author E-mail: ayalewmg@yahoo.com

Magnetic resonance images (MRI) showed diffuse cerebellar atrophy (Figure 3) and opacified middle ear and mastoid air cells. Alpha-fetoprotein (AFP) was elevated but serum IgA level was not determined.

She was given antibiotics for recurrent infections and multivitamins. Parents were counseled.

Figure 1: Family Tree

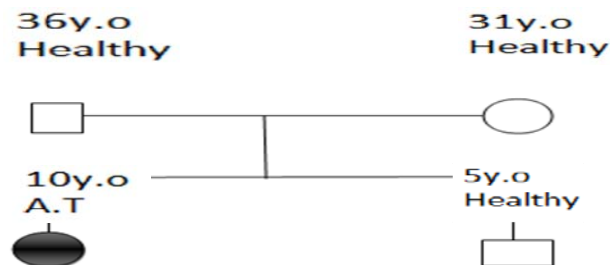


Figure 2: Conjunctival telangiectasias present in both eyes

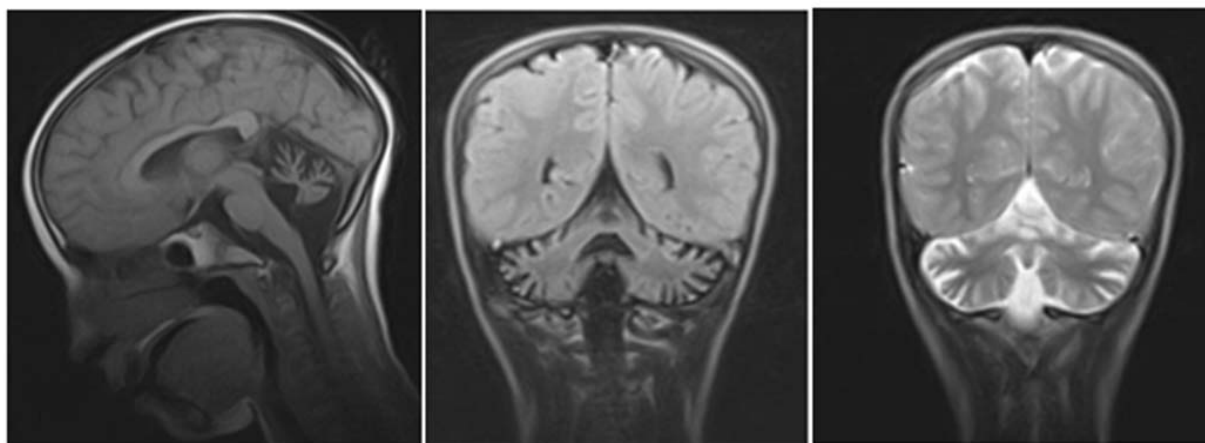


Figure 3a

Figure 3b

Figure 3c

Figure 3 : Sag SE T1 (a), Cor FLAIR (b) and Cor FSE T2 showed diffuse cerebellar atrophy involving vermis and both cerebellar hemispheres.

Figure 3: MRI brain showing cerebellar atrophy

DISCUSSION

Ataxia-telangiectasia (AT) or Louis Bar syndrome is a rare neurodegenerative inherited disorder that affects many parts of the body and leads to severe disability (7). The disease is inherited in an autosomal recessive fashion and is due to mutations in the ATM gene located on chromosome 11q22-23 (8). ATM gene is important in DNA repair. The prevalence is estimated to be between 1 out of 40,000 and 1 out of 300,000 persons worldwide (1, 2).

Ataxia telangiectasia has multisystem manifestations including progressive neurological manifestations, like tremor, chorea, athetosis, dystonia, ataxia, dysarthria, oculomotor apraxia and dysphagia which worsen through childhood into adult life (9). Oculocutaneous telangiectasias usually appear at about 3 or 4 years of age (9). Telangiectasias are occasionally found in the bladder or other internal organs.

Patients will also have recurrent infections usually affecting the chest, ears and sinuses that can lead to chronic lung disease and chronic otitis media with hearing impairment (9). A wide range of immunological abnormalities, including deficiencies of immunoglobulin (particularly classes A and E), poor responsiveness to pneumococcal polysaccharide vaccine, reduced lymphocyte numbers particularly affecting T and B cells and thymic hypoplasia, slurred speech, drooling, and dysphagia leading to low body weight are common.

Less common clinical manifestations include vomiting and choking, particularly in the morning, non-infective granulomatous skin disease, deformities of the feet and lower limbs, scoliosis, incontinence of bladder and bowel, diabetes mellitus, which tends to develop during adolescence or adulthood in about 25% of patients (9).

AT occurs in three forms. The first form is pure AT where patients present with all/most of the diagnostic symptoms. The second form is attenuated AT or type II where a patient lacks some of the typical findings but shows radio-sensitivity. The last form is carrier AT where individuals with a single ATM mutation may have an increased risk of cancer.

Immunodeficiency affects over half of all patients with AT and when present can contribute significantly to morbidity and mortality, which is the case of our patient, who presented with respiratory infections and chronic suppurative otitis media since childhood, highly suggestive of immunodeficiency.

This deficit is often mixed, progressively worsening in cellular immunity (CD4 and CD8) but also in humoral immunity mainly immunoglobulin A and in addition, subclasses of Immunoglobulin G (5). The IgM levels are normal or sometimes high. This immune deficiency is responsible for respiratory disorders that are common and may precede the onset of neurological signs. It is often repeated bronchial infections, sinusitis, diffuse lung diseases, bronchiectasis, and rarely interstitial lung disease. Patients with AT also have increased sensitivity to ionizing radiation, most notably γ and X. Thus, radiologic examination should be limited to the maximum in these patients (10). A high chance of development of cancer has been reported in homozygous patients (100 times greater than in the normal population) (11).

This predisposition is partly due to the increased radio sensitivity but especially acquired chromosomal abnormalities. For homozygous individuals, it is essentially lymphoma (50%), lymphoid leukemia (30%), and carcinomas (20% especially in adults (12,13). Among females heterozygous for the gene mutation, breast cancers are more often seen than in the general population (5).

Diagnosis is usually achieved clinically by identification of both ataxia and ocular 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 of AT.

When a clinical diagnosis of AT has been made or there is a reasonable clinical suspicion of AT, genetic confirmation should be obtained by identifying the ATM mutations present. The management of AT is multidisciplinary, requiring neurologist, physiotherapist and nutrition program (5). Treatment is symptomatic and supportive. Physical and occupational therapy may help maintain mobility. Speech therapy may also be needed. Regular use of intravenous immunoglobulin 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. Counseling of parents/caretakers on disease course and prognosis is crucial.

ACKNOWLEDGEMENT

We would like to express our sincere gratitude and appreciation to the residents and nurses in the Pediatrics Neurology Clinic and the parents of this child.

Competing Interest:

The authors declare that this manuscript was approved by all authors in its current form and that no competing interest exists.

REFERENCES

1. Chun HH, Gatti RA. Ataxia-Telangiectasia, an Evolving Phenotype. *DNA Repair*. 2004;3 (8-9): 1187-1196.
2. Taylor AM, Byrd PJ. Molecular Pathology of Ataxia-Telangiectasia. *Journal of Clinical Pathology*. 2005; 58:1009-1015.
3. Ball LG, Xiao W. Molecular basis of ataxia telangiectasia and related diseases. *Acta Pharmacol Sin*. 2005; 26: 897-907.
4. Tranchant C, Anheim M. Ataxies cérébelleuses autosomiques récessives. *Presse Med*. 2009; 38: 1852-1859.
5. Bott L, Thumerelle C, Cuvellier C, Deschildre A, Vallée L, Sardet A. Ataxie-télangiectasie: de la Clinique à la physiopathologie. *Archives de pédiatrie*. 2006; 13:293-298.
6. Perlman S, Becker CS, Gatti RA. Ataxia-Telangiectasia: Diagnosis and Treatment. *Seminars in Pediatric Neurology*. 2003; 10: 173-182.
7. Haydar El Hadi Babikir. Classic ataxia-telangiectasia in a Sudanese boy: Case report and review of the literature. *Sudan J Paediatr*. 2011; 11(1): 60–63.
8. Savitsky K, Bar-Shira A, Gilad S, Rotman G, Ziv Y, Vanagaite L, et al. A single Ataxia-Telangiectasia gene with A product similar to PI-3 kinase. *Science*. 1995; 268: 1749–53.
9. Ataxia telangiectasia in children - Guidance on diagnosis and clinical care. The A-T Specialist Centre Nottingham City Hospital Campus, Nottingham University Hospitals NHS Trust, the University of Birmingham, The Ataxia Telangiectasia Society, 2014.
10. Kühne, M., Riballo, E., Rief, N., Rothkamm, K., Jeggo, P.A. and Löbrich, M. A Double-Strand Break Repair Defect in ATM-Deficiency Cells Contributes to Radio sensitivity. *Cancer Research*. 2004; 64(2):500-8.
11. Thompson, D., Daedal, S., Kirner, J., McGuffog, L., Last, J., Reiman, A., et al. Cancer Risks and Mortality in Heterozygous ATM Carriers. *Journal of the National Cancer Institute*. 2005; 97: 813-822.
12. De Laet, C., Casimir, G., DuchPteau, J., Vamos, E., Devaick, C., Sariban, E. and Feaster, A. Lymphome T Leucémisé comme première manifestation d'une ataxie télangiectasie. *Archives de pédiatrie*. 1996; 3: 681-684.
13. Cavaciuti, E., Lauge, A., Janin, N., Ossian, K., Hall, J., Stoppa-Lyonnet, D. and Andrieu, N. Cancer Risk According to Type and Location of ATM Mutation in Ataxia-Telangiectasia Families. *Genes, Chromosomes Cancer*. 2005; 42: 1-9.