ATAXIA TELANGIECTASIA: A CASE REPORT

Sindhurakasturi[1], Lalat Barun Patra[2], Rajesh Kumar Sethi[3], D. P. Patra[4]

HOW TO CITE THIS ARTICLE:
Sindhurakasturi, Lalat Barun Patra, Rajesh Kumar Sethi, D. P. Patra. "Ataxia Telangiectasia: A Case Report". Journal of Evidence based Medicine and Healthcare; Volume 1, Issue 9, October 31, 2014; Page: 1221-1225.

ABSTRACT: Ataxia-telengiectasia (AT) is characterized by slowly progressive cerebellar ataxia, occulomotor apraxia, choreoathetosis, telangiectasis of the skin and conjunctivae, susceptibility to sinobronchopulmonary infections, lymphoreticular neoplasia, other malignancies, and sensitivity to ionizing radiation. It was described by Syllaba and Henner in 1926, by Louis-Bar in 1941, and more definitively in 1958 by Boder and Sedgwick, who presented the first clinical and neuropathologic delineation of the disease and named it AT. [1]
KEYWORDS: Ataxia telangiectasia (AT).

INTRODUCTION: The gene for AT (ATM, AT, mutated) has been mapped to the long arm of chromosome 11 (11q23.3). It has been cloned, and it codes for a nuclear serine/threonine protein kinase ATM, which activates the cellular response to double-stranded breaks in the DNA. These proteins are involved in the cellular responses to DNA damage, cell-cycle control, and maintaining telomere length.[1]

Another basic characteristic of AT is a variety of immunologic abnormalities involving both the cellular and the humoral arms of the immune system. Low levels of serum and secretory IgA are found in 70% to 80% of patients

There is marked increase in cellular sensitivity to ionizing radiation Radio sensitivity of AT cells appears to result from an inability to recognize and respond to the presence of DNA damage by inhibition of DNA synthesis. Another feature of AT that arises from cellular sensitivity to ionizing radiation is the increased incidence of chromosomal breaks and rearrangements.

ATM protein is believed to also be involved in a complex system that prevents apoptosis after DNA damage. A defect in this system could be responsible for cell death within the nervous system as well as within the thymus and the vascular endothelium. Such a cell loss is the most striking finding on neuropathologic examination. This is most clearly seen in the cerebellar cortex where extensive loss of both Purkinje cells and internal granular cells occurs.

CASE STUDY: A 13 year old female child presented with complaints of, repeated episodes of respiratory tract infections and inability to walk without support. She was a product of consanguineous marriage with normal development of her two siblings and no history of unexplained deaths in family. She was born by normal vaginal delivery at home with antenatal and postnatal history being uneventful. She could sit without support at 8 months and walk with support at one and half year of age. Difficulty in walking gradually progressed to present state of not being able to walk without support. This was associated with difficulty in speech, tremors and swaying even during sitting position.

On examination telangiectasia was present on both bulbar conjunctivas. Skin was dry and scaly. She had signs of respiratory distress. Signs of cerebellar involvement, tittubation, truncal ataxia, swaying gait, pendular movement of eye balls and scanning type of speech were present. On examination of upper limb, tone and power was normal, deep tendon reflexes were normal, clumsiness noted in finger nose test, dysmetria, dyssynergia, disdiochokinesia were present. On examination of lower limb, tone was normal and power reduced in lower limbs, deep tendon reflexes were normal, plantar reflex showed, bilateral extensor response.

Vibration sense maintained but there was loss of position sense in small joints of toes.

No signs of meningeal irritation.

Respiratory system: Decreased breath sounds on right lower chest at the back below scapula, infra axillary and infra mammary region with crackles and ronchi on the same area, suggesting possibility of bronchiectasis.

Cardiovascular system and per abdomen findings were normal.

Investigations:

Peripheral blood smear=anemia.
Alphafeto protein=raised. More than 250 ng/ml.
Carcinoembryonic antigen=raised.
Vitamin B12 & Folic acid=normal.
Echo study=normal.
IgG & IgA=low.
MRI=Cerebellar atrophy.

DISCUSSION: Ataxia is presenting symptom in this syndrome, being evident when the child begins to walk at the end of the first year of life, manifesting as ataxic gait and abnormal swaying movement of the trunk while walking.[2] Our patient started walking late at 20 months of age. She started to have truncal ataxia which gradually worsened with age. Magnetic resonance imaging (MRI) demonstrated a mild cerebellar atrophy.

A selective atrophy involving lateral portions (middle cortex) of the hemispheres was favored by Tavani et al. who also suggested that the neurological deterioration is correlated to the degree of atrophy.[3]

Telangiectasia is a second major clinical manifestation of the disease. It usually has a later onset than ataxia, occurring between two and eight years of age usually on ocular sclera. [2] In our patient telangictasia involved the bulbar area and extended to the corneal border. Other ophthalmologic examination was unremarkable.

By reviewing the literatures, the cutaneous changes seen in patients with Ataxia Telangiectasia include cutaneous telangiectasias, mottled hyperpigmentation and hypopigmentation, a poikilodermatous appearance.[4] Other pigmentary changes include Café au Lait spots, multiple ephelides and vitiligo. Hypertrichosis, alopecia areata, multiple verrucae, atopic dermatitis, keratosis pilaris and acanthosis nigricans have also been described in patients with AT. Scalp hairs coarse and brittle with diffuse graying were seen in our patient.[5]

There was no cutaneous telangiectasia in our patient, Alfa-fetoprotein (AFP) level was high which is a confirmatory test that support our diagnosis of AT. AFP is a human fetal serum protein is found at levels of <10 ng/ml in children more than one year of age.[6] Elevated serum alpha fetoprotein (AFP) is seen in more than 95% of patients with AT.[8] AFP testing has been recommended by some researchers in all toddlers and children with undiagnosed progressive ataxia.[6][7]

In AT there is a highly variable primary immunodeficiency, involving both cellular and humoral immunity.[8] Although early publications correlated AT with the selective deficiency of IgA, the immunity disorders that these patients can show are very diverse and do not always correlate with the clinical expression of the immunodeficiency.[7][9] Our patient had low levels of IgA and Ig G; she had recurrent respiratory tract infections. The most frequently isolated infection was streptococcal pneumonia as in other studies.[9]

Patients with ataxia-telangiectasia have an elevated incidence of cancers, approximately 100-fold in comparison to the general population. In children, more than 85% of neoplasm cases are acute lymphocytic leukemia or lymphoma. In adults with ataxia-telangiectasia, solid tumors are more frequent.[10]

POINTS OF INTEREST: There is unusual plantar extensor in this case so following differential diagnosis was considered:

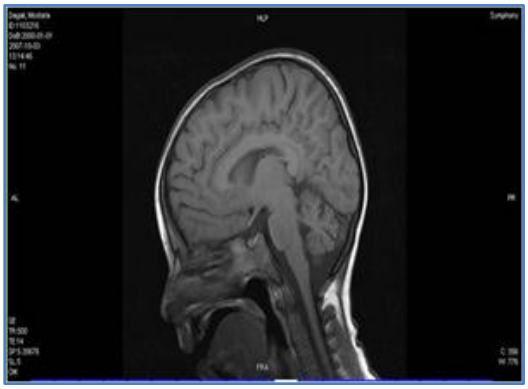
Fredrick's ataxia.

Sub-acute combined disease of spinal cord.

Ataxia telangiectasia.

There are no skeletal abnormalities or cardiac changes in our patient and along with early age of onset of ataxia the diagnosis of Fredrick's Ataxia has been ruled out. Vitamin B 12 values being normal sub-acute combined disease of spinal cord is also ruled out and we consider Ataxia Telangiectasia as the diagnosis.

There are currently no licensed therapies for A-T. Treatment is directed against specific Symptoms. Erydex (Dexamethasone sodium phosphate) a dexamethasone analogue is under phase II clinical trial. It is thought that by providing patients with a lower but constant plasma concentration of dexamethasone, beneficial anti-inflammatory effects will be observed with a concomitant reduction in adverse effects associated with long term glucocorticoid therapy. If successful there will be improvement in neurological functions.[11]



CONCLUSION: Ataxia telangiectasia is mainly a clinical diagnosis and should be suspected in the presence of ataxia of early onset in infants and toddlers, ocular/ occulo-cutaneous telangiectasia and abnormal cellular or humoral immunity in early childhood. Unnecessary, costly investigations should be avoided. No definite treatment is available. Management includes, genetic counseling, examination of all the family members, identification of AT homozygote and providing appropriate care, regular surveillance of the heterozygote for malignancy.

REFERENCES:

1. Menkes, John H.; Sarnat, Harvey B.; Maria, Bernard L.: Child Neurology, 7th ed; Philadelphia: Lippincott Williams & Wilkins, 2006.
2. Boder E. Ataxia-telangiectasia: an overview. Kroc Found Ser 1985; 19:1–63.
3. Tavani F, Zimmerman RA, Berry GT, Sullivan K, Gatti R, Bingham P. Ataxia telangiectasia: the pattern of cerebellar atrophy on MRI. Neuroradiology 2003; 45: 315–9.
4. Boder E. Ataxia-telangiectasia: an overview. In: RA Gatti and M Swift, Editors, Ataxia-telangiectasia: genetics, neuropathology, and immunology of a degenerative disease of childhood, Alan R. Liss, New York 1985:1.
5. Kwiatkowski DJ, Short MP. Tuberous sclerosis, Arch Dermatol 1994; 130: 348–4.
6. Cabana MD, Crawford TO, Winkelstein JA, et al. Consequences of delayed diagnosis of ataxia telangiectasia. Pediatrics 1998; 102: 98–100.
7. Taylor AMR, Rosney CM, Campbell JB. Unusual sensitivity of ataxia-telangiectasia cells to bleomycin. Cancer Res 1979; 39: 1046–50.
8. Regueiro JR, Porras O, Lavin M, Gatti RA. Ataxia-telengiectasia: a primary immunodeficiency revisited. Immunol Allerg Clin North Am 2000; 20: 177–6.
9. Ayache R, Najjar MF, Obeid H, Pousse H, Gueddiche MN. Ataxia telangiectasia: Clinical and biological study in 17 cases. Ann Biol Clin 1994; 52: 117–20.
10. Su Y, Swift M. Mortality rates among carriers of ataxia-telangiectasia mutant alleles. Ann Intern Med 2000 Nov 21; 133 (10): 770–8.
11. ClinicalTrials.gov. Intra-erythrocyte dexamethasone sodium phosphate in ataxia telangiectasia patients (IEDAT01). Available from URL: http://clinicaltrials.gov/ct2/show/NCT01255358?term=erydel&rank=1 Accessed 23 January 2012.

CASE REPORT

AUTHORS:

1. Sindhurakasturi
2. Lalat Barun Patra
3. Rajesh Kumar Sethi
4. D. P. Patra

PARTICULARS OF CONTRIBUTORS:

1. Junior Resident, Department of Paediatrics, Konaseema Institute of Medical Sciences & Research Foundation.
2. Assistant Professor, Department of Paediatrics, Konaseema Institute of Medical Sciences & Research Foundation.
3. Senior Resident, Department of Paediatrics, Konaseema Institute of Medical Sciences & Research Foundation.
4. Professor and HOD, Department of Paediatrics, Konaseema Institute of Medical Sciences & Research Foundation.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Lalat Barun Patra,
Assistant Professor,
Department of Pediatrics,
KIMS & RF, Amalapuram,
E-mail: drlalatbarun@gmail.com

Date of Submission: 08/10/2014.
Date of Peer Review: 09/10/2014.
Date of Acceptance: 20/10/2014.
Date of Publishing: 28/10/2014.