Ataxia Telangiectasia: A Case Report

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Abstract
Ataxia telangiectasia (AT) is a complex multisystem disorder characterized by progressive neurological impairment, variable immunodeficiency and oculo-cutaneous telangiectasia. Ataxia telangiectasia is a member of chromosomal breakage syndromes and it is caused by a mutation in the ataxia-telangiectasia mutated (ATM) gene. We are reporting an eight year old girl of AT presented with difficulty in walking, frequent fall, trembling of the whole body, difficulty in speech. [J Shaheed Suhrawardy Med Coll, 2014;6(1):41-43]

Key Words: Ataxia telangiectasia, neurological impairment, chromosomal breakage syndromes, mutation

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Introduction
Ataxia telangiectasia (AT) is a genetically determined autosomal recessive, multisystem disorder causing neurodegeneration and immunological abnormalities resulting in increased susceptibility to infection and malignancies, endocrine deficiencies, increased sensitivity to ionizing radiation and an anomaly of DNA repair. The ataxia manifests as the child starts walking while ocular telangiectasia is usually appreciated around 4-6 years of age. Vessels over exposed bulbar conjunctiva become prominent and appear fan shaped. Neurological manifestations consist of ataxia, choreoathetosis, ocular movement abnormalities, mental retardation and dystonia. Syllaba and Henner1 first described this condition in 1929. Individuals of all races and ethnicities are affected equally. The incidence world-wide is estimated to be between 1 in 40,000 and 1 in 100,000 people2,3. Both males and females are equally affected. AT results from mutations of a single gene, ataxia-telangiectasia mutated (ATM), located on chromosome 11q22-23 encoding a large basic protein involved in cell cycle control and DNA damaging repair4,5.

Case Report
An eight years old girl came with the complaints of progressive difficulty in walking with frequent fall, trembling of the whole body, difficulty in speech for last six years. The patient was the second issue of consanguineous parents. The child was developmentally alright up to two years of age. Subsequently the parents noticed that the child had unsteadiness during walking with frequent fall which was progressively deteriorating day by day. Later the patient can't walk without support. The
speech gradually became slurred and indistinct. For the last six months the patient had generalized tonic clonic seizure. Seizure was occurred 8 times during this period.

Figure 1: telangiectasia of conjunctiva

The birth history and feeding history was uneventful. The patient had history of recurrent upper and lower respiratory tract infection. On examination, the patient was oriented and interacting with surrounding and co-operative. The patient had Choreo athetoid movement. The vital signs were normal. The patient had reddish eyes.

Figure 2: CT Scan of brain (axial view) showing widened folia of cerebellum

Neurological exam revealed cerebellar dysfunction evidenced by truncal ataxia, ataxic gait, intention tremor, past pointing, dysdiadokinesia, rebound phenomena and scanning speech. The patient had oculomotor apraxia on horizontal gaze. Other neurological examination findings were normal. Ophthalmologist confirmed that her red eyes were due to telangiectasia (Fig 1). Other systemic examination revealed no abnormality. The routine investigation reports were normal. The immunoglobulin G (IgG) and immunoglobulin G (IgM) were normal; however, immunoglobulin G (IgA) level was reduced (58.10 mg/dl). Alpha-fetoprotein level was raised (327.92 ng/ml). Neuroimaging showed atrophic change in cerebellum (Figure 2 & 3). EEG showed sharp and slow waves over left fronto-central region.

Discussion

Ataxia telangiectasia (AT) (also referred to as Louis-Bar syndrome) is a rare, neurodegenerative, inherited disease causing severe disability. Ataxia refers to poor coordination and telangiectasia to small dilated blood vessels, both of which are hallmarks of the disease.

Symptoms most often first appear in early childhood (the toddler stage) when children begin to walk. Though they usually start walking at a normal age, they wobble or sway when walking, standing still or sitting, and may appear almost as if they are drunk. In late pre-school and early school age they develop difficulty moving the eyes in a natural manner from one place to the next (oculomotor apraxia). They develop slurred or distorted speech, and swallowing problems. Some have an increased number of respiratory tract infections (ear infections, sinusitis, bronchitis, and pneumonia). Because not all children develop in the same manner or at the same rate, it may be some years before AT is properly diagnosed. Most children with AT have stable neurologic symptoms for the first 4-5 years of life, but begin to show increasing problems in early school years.

Figure 3: MRI of brain (sagittal view) showing gross cerebellar atrophy

AT is caused by a defect in the ATM gene. In simple terms, the protein produced by the ATM gene recognizes that there is a break in DNA, recruits other proteins to fix the break, and stops the cell from making new DNA until the repair is complete. Prominent blood vessels (telangiectasia) over the white (sclera) of the eyes usually occur by the age of 5-8 years, but sometimes later or not at all. The absence of telangiectasia does not exclude the diagnosis of A-T.

About two-thirds of people with A-T have abnormalities of the immune system. The most common abnormalities are low levels of one or more classes of immunoglobulins.
Ataxia Telangiectasia (A-T) is characterized by low numbers of lymphocytes (especially T-lymphocytes) in the blood, immunodeficiency with low levels of immunoglobulins (especially IgA, IgG subclasses, and IgE), and combined humoral and cellular immunodeficiency. A-T follows a progressive course. It must be stressed that the course of the disease can be quite variable and it is difficult to predict the course in any given individual. Even within families, where the specific genetic defect is the same, there can be great variability in the type and severity of different neurologic problems and immunodeficiency.

### References

1. Syllaba L, Henner K: Contribution a l'indépendence de l'athetose double idiopathique et congenitale. Rev Neurol 1926; 1: 541-562
2. Cabana MD, Crawford TO, Winkelstein JA, Christensen JR, Lederman HM: Consequences of the delayed diagnosis of ataxia telangiectasia. Pediatrics 1998; 102:98-100
3. Chun HH, Gatti RA: Ataxia-telangiectasia, an evolving phenotype. DNA Repair (Amst) 2004, 3(8-9):1187-96
4. Lange E, Borresen AL, Chen X, Chessa L, Chipplunkar S, Concannon P, Dandekar S, Gerken S, Lange K, Liang T, et al: Localization of an ataxiatelangiectasia gene to an approximately 500-kb interval on chromosome 11q23.1: linkage analysis of 176 families by an international consortium. Am J Hum Genet 1995, 57(1):112-9
5. Gatti RA, Berkel I, Boder E, Braedt G, Charmley P, Concannon P, Ersoy F, Foroud T, Jaspers NG, Lange K, et al: Localization of an ataxiatelangiectasia gene to chromosome 11q22-23. Nature 1988
6. Boder E. Ataxia-telangiectasia: an overview. Kroc Foundation series 1985;19: 1-63
7. Cabana, MD; Crawford, TO, Winkelstein, JA, Christensen, JR, Lederman, HM. Consequences of the delayed diagnosis of ataxia-telangiectasia. Pediatrics 1998;102 (1 Pt 1): 98-100
8. Nowak-Wegrzyn A, Crawford TO, Winkelstein JA, Carson KA, Lederman HM. Immunodeficiency and infections in ataxia-telangiectasia. The Journal of pediatrics 2004;144 (4): 505-11
9. Reiman A, Srinivasan V, Barone G, Last JL, Wootton LL, Davies EG, et al. Lymphoid tumours and breast cancer in ataxia telangiectasia; substantial protective effect of residual ATM kinase activity against childhood tumours. British journal of cancer 2011;105 (4): 586-91
10. Thompson D, Duedal S, Kirner J, McGuflóg L, Last J, Reiman A, et al. Cancer risks and mortality in heterozygous ATM mutation carriers. Journal of the National Cancer Institute 2005;97 (11): 813-22
11. Paller, AS; Massey, RB, Curtis, MA, Pelachyk, JM, Dombrowski, HC, Leickly, FE, Swift, M. Cutaneous granulomatous lesions in patients with ataxia-telangiectasia. The Journal Of Pediatrics 1991;119 (6): 917-22
12. McGrath-Morrow SA, Gower, WA, Rothblum-Oviiat C, Brody AS, Langston C, Fan LL, et al. Evaluation and management of pulmonary disease in ataxia-telangiectasia. Pediatric Pulmonology 2010;45 (9): 847-59
13. Lefton-Greif MA, Crawford TO, Winkelstein JA, Loughlin GM, Koerner CB, Zahurak M, et al. Oropharyngeal dysphagia and aspiration in patients with ataxia-telangiectasia. The Journal of pediatrics 2000;136 (2): 225-31
14. Sun X, Becker-Catania SG, Chun HH, Hwang MJ, Huo Y, Wang Z, et al. Early diagnosis of ataxia-telangiectasia using radiosensitivity testing. The Journal of pediatrics 2002;140 (6): 724-31
15. Chun HH, Sun X, Nahas SA, Teraoka S, Lai CH, Concannon P, et al. Improved diagnostic testing for ataxia-telangiectasia by immunoblotting of nuclear lysates for ATM protein expression. Molecular Genetics Metabolism 2003;80 (4): 437-43