

## Ataxia Telangiectasia - A Case Report

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Ataxia telangiectasia (AT) a rare inherited neurodegenerative disease that causes severe disability, characterized by progressive cerebellar ataxia, oculocutaneous telangiectasia, and recurrent sinopulmonary infections. AT is caused by a defect in the ATM gene, correcting errors in duplicating DNA when cells divide, and in destroying the cells when the errors cannot be corrected. A six and half year old boy, first issue of non-consanguineous parents was admitted into department of Paediatrics, Rangpur Medical College Hospital with the complaints of repeated fall while walking and slurred speech. The patient was found mildly pale with bilateral bulbar telangiectasia, extremely low level of intellectual functioning as well as speech delay with motor and cognitive delay. There was marked hypotonia in lower limbs with diminished deep tendon reflexes. Gait was ataxic with impaired tandem gait. She was diagnosed as a case of AT. This case is reported because of its rarity and lack of awareness about the disease.

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**Key words:** Ataxia telangiectasia (AT), neurodegenerative disease, alpha-fetoprotein (AFP), carcinoembryonic antigen(CEA).

### Introduction

**A**taxia-telangiectasia (A-T) is a clinical syndrome, the name of which accurately describes its most salient features - oculocutaneous telangiectasia and progressive cerebellar ataxia.<sup>1</sup> The syndrome was not mentioned until 1941 when Louis-Bar reported a case of a 9-year-old child.<sup>2</sup> Boder et al recognized the familial incidence proposing an autosomal recessive mode of inheritance for the disease.<sup>3</sup> The ataxia-

telangiectasia mutated (ATM) kinase initiates a well characterized response to DNA damage, resulting in arrest of cell-cycle, DNA repair, or apoptosis.<sup>4-7</sup> A-T has led to much speculation about additional pathogenic mechanisms including oxidative stress.<sup>8-13</sup> How ATM is involved in oxidative stress management remains unclear as do other potential roles in cellular homeostasis in the absence of DNA damage.<sup>14</sup> The incidence of

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ataxia-telangiectasia is about 1 case in 100,000 births.<sup>15</sup> The frequency of ataxia-telangiectasia mutant alleles heterozygosity was reported to be 1.4- 2% of the general population.<sup>16</sup> Ataxia-telangiectasia occurs equally among males and females.<sup>17</sup> No characteristic features are detectable during early childhood. Ataxia is the first diagnostic hallmark, having its onset in the first years of life. Beyond the age of 5 years the progression of the ataxia becomes increasingly apparent and the child requires a wheelchair by age 10 or 11 years.<sup>18</sup> Oculocutaneous telangiectasia, the second diagnostic hallmark of ataxia-telangiectasia, usually has a later onset than the ataxia, typically at age 3-6 years.<sup>16</sup> The progression of the disease is apparent in subsequent years. The clinical diagnosis becomes most apparent after age 10 years, when clinical characteristics are fully expressed. In very young infants, the diagnosis can be elusive and easily confused with other diseases, such as mild cerebral palsy, acute infectious or episodic ataxia, and ataxia with oculomotor apraxia (AOA). Diagnosis can now be confirmed by radiosensitivity testing (colony survival assay), immunoblotting, and mutation detection. Little progress has been made in treating the progressive ataxia, and the only therapeutic options are medical management of the patient's problems such as immunodeficiency, sinopulmonary infections, neurologic dysfunction, and malignancy and rehabilitation for physical and social disabilities.<sup>19</sup> Death typically occurs early, usually from bronchopulmonary infection, less frequently from malignancy, or from a combination of both. The median age at death is reported to be approximately 20 years.<sup>20</sup>

### Case Report

A six and half year old boy, 2<sup>nd</sup> issue of his non-consanguineous parents was admitted to the department of Paediatrics, Rangpur Medical College Hospital, Rangpur on 24<sup>th</sup>

April 2014 with the complaints of repeated fall while walking for the last 2 years. He also developed problems in daily activities such as eating, carrying, gripping or holding as well as increasing difficulty with writing and colouring. Whenever he was instructed to walk, the child preferred running or walking quickly. His speech became slurred and he developed drooling of saliva. Since three and half years of age, he had been suffering from discharging right ear. One year back, he had a history of febrile seizure. His feeding history was appropriate for different ages with minimum calorie deficit. He attained his milestones of development at appropriate ages. He has a healthy eight years old elder brother and there was no familial history of such kind of illness or malignancy. Physical examination revealed mild pallor with bilateral bulbar telangiectasia. His body build and nutritional status was below average. Cranial nerves were intact with normal fundoscopic findings. There was marked hypotonia in lower limbs with diminished deep tendon reflexes. His gait was ataxic with impaired tandem gait. Sensory function was intact. Cerebellar function was abnormal, showed past-pointing, dysdiadochokinesis, nystagmus and oculomotor apraxia. Psychological assessment performed by clinical psychologists employing Independent Behaviour Assessment Scale (IBAS) and Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III) revealed speech delay and cognitive impairment with IQ score 59 (i.e. extremely low level of intellectual functioning).

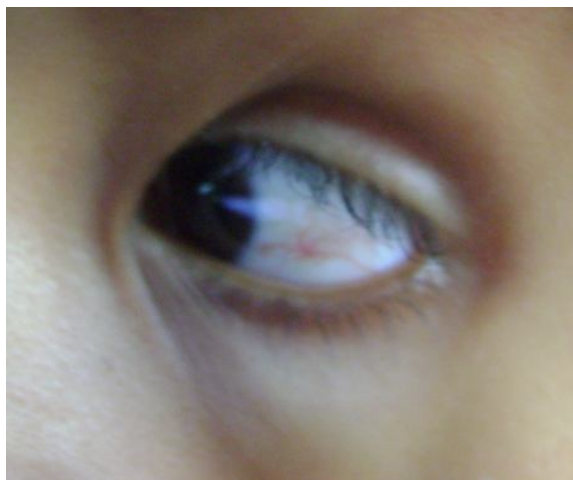


Fig.-1: Telangiectasia of conjunctivae

Investigations revealed Hb-10.10 g/dl; ESR-52 mm in 1<sup>st</sup> hour; TLC-12000/cumm; DLC-Neutrophil - 47%, Lymphocyte - 26%, Eosinophil - 27%; S. Creatinine 0.8 mg/dL; RBS-95 mg/dL; S. CPK -183 U/L (Normal value 25-130 U/L); Urine R/M/E - Pus cell 0-2/HPF; MT- 5 mm after 72 hours; Serum  $\alpha$ -Fetoprotein - 215 ng/L (Normal value: 8-20 ng/ml); Serum CEA- 2.04 ng/L (Normal value: <3 ng/ml); MRI of brain showed mild cerebellar atrophy with mildly dilated 4<sup>th</sup> ventricle.

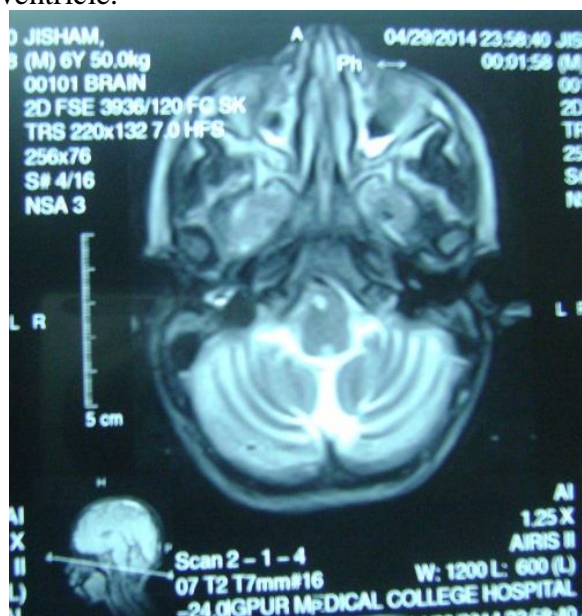


Fig.-2a: MRI of brain



Fig.-2b: MRI of brain

Fig.-2a & 2b both showed mild cerebellar atrophy with mildly dilated 4<sup>th</sup> ventricle.

After counseling, symptomatic treatments were ensured. Physical and speech therapy were also advised.

**Discussion**

In our index case, there was progressive cerebellar ataxia, bulbar telangiectasias, raised serum alpha-fetoprotein and characteristic MRI findings. These clinch us to reach the diagnosis of Ataxia telangiectasia. In general, Ataxia-telangiectasia (AT) is a multisystem disorder characterized by progressive neurologic impairment, cerebellar ataxia, progressive immunodeficiency, ocular and cutaneous telangiectasia, increased risk of lymphoreticular malignancy and hypersensitivity to ionizing radiation. Telangiectasia can also appear on sun exposed areas of skin such as face and ears, occasionally arise in liver and lungs.<sup>21</sup> Both humoral & cellular immunity are impaired in patients with AT. The most common immunologic abnormality is the absence or

decreased level of serum & salivary level of I<sub>g</sub>A. This deficiency has been found in 50 to 80 percent of this patients.<sup>22</sup> Patients with AT have an increased susceptibility to sinopulmonary infection, x-ray hypersensitivity, and predisposition to malignancy.<sup>23</sup> Chromosomal abnormalities in specific cell population are characteristic finding in AT patients. The specific defect has been shown as an increased tendency for spontaneous breakage & rearrangement of chromosome 2,6,7,8,14,22 & X.<sup>24,25</sup> Clinical characteristics include progressive ataxia (100%), telangiectasia of skin or conjunctivae (83.8%) and of ears (70.2%), eye movement disorder (apraxia of horizontal and vertical saccadic eye movements)(80.6%), choreoathetosis (87.1%), dysarthria in almost all cases. The index case had progressive ataxia, telangiectasia over bulbar conjunctiva and dysarthria.

Mental retardation occurs in nearly 10% of patients, showed in a study.<sup>26</sup> It is not a common feature of the disease, but an arrested cognitive development for new skills appears in some patients as they grow. Our case had extremely low level of IQ.

Serum  $\alpha$ -fetoprotein level, a useful screening test is usually elevated in AT which is evident in our case. CEA(Carcinoembryonic antigen), a serum carcinofetal protein present in fetal circulation like AFP is considered to be the product of immature cells that are later repressed as differentiation of the tissue progresses. Sugimoto<sup>24</sup> et al found that mean level of plasma CEA in AT patients were significantly higher than in patients with isolated I<sub>g</sub>A deficiency, chronic neurologic disease, chronic intestinal disease.

Our index case has mild Cerebellar atrophy with mildly dilated 4<sup>th</sup> ventricle on MRI suggesting further the possibility of ataxia Telangiectasia.<sup>27</sup>

### Conclusion

Ataxia Telangiectasia (AT) follows 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 similar, there can be great variability in the type and severity of different neurologic problems and immunodeficiency. Many patients are confined to a wheelchair in their teens. Some patients are able to attend college and live independently and some have lived into the fifth decades of life.

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