Ataxia telangiectasia case report from tertiary-care hospital of North Karnataka

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Abstract
Ataxia-telangiectasia (AT) is a primary immunodeficiency disease with multisystem disorder characterized by progressive neurologic impairment, variable immunodeficiency, impaired organ maturation, oculo-cutaneous telangiectasia, and a predisposition to malignancy. It is a variable immunodeficiency involving both cellular and humoral responses and a predisposition to cancer. In 1995, a large gene was identified on chromosome 11q22-q23, known as AT Mutant(ATM) gene and the lack of its gene product, the ATM protein, is responsible for the clinical features of AT. Here we present a case of ataxia telangiectasia in a 16 year old female who presented with progressive ataxia.

Keywords: Ataxia telangiectasia, humoral immunity, immunodeficiency.

Introduction

Ataxia telangiectasia at is an autosomal recessive, multisystem disorder characterized by progressive neurological impairment, cerebellar ataxia, ocular and cutaneous telangiectasia, variable immunodeficiency with susceptibility to sinopulmonary infections, impaired organ maturation, x-ray hypersensitivity and a predisposition to malignancy[1]. We report a case of ataxia telangiectasia with progressive ataxia.It was first described in the medical literature in the mid-1920s, but was not named as a specific disorder until 1957 by Dr. Elena Boder. The incidence is about 1 in 40,000-3,00,000 live births. Males and females are equally affected and there is no racial or geographical preferences[2].

Case report

A 16 years female presented to us with difficulty in walking and talking. Poor performance started when she was 5years old and increased in last 5 years. No history of recurrent infections. No history of similar complaints in the family. On examination vitals were stable, with clubbing and bilateral bulbar and mucosal telangiectasia seen. Central nervous system examination-mental functions were normal, speech was scanning type, cranial nerves were normal. Incoordination seen in both upper and lower limbs with ataxic gait. Reflexes were diminished. Fundus, skull, spine and peripheral nerves were within normal limits.

Investigations: complete haemogram, peripheral smear, urine routine, liver function tests were normal. Flow cytometry showed reduced total lymphocyte count, marked reduction in CD4 cell count and reduced B-cells with equal CD4 and CD8 ratio. Immunoglobulin:-IgA- 0.19g/L, IgM- 37.5g/L, IgG-12.7g/L, Alpha feto protein- 159microgram/L. MRI showed cerebellar atrophy.

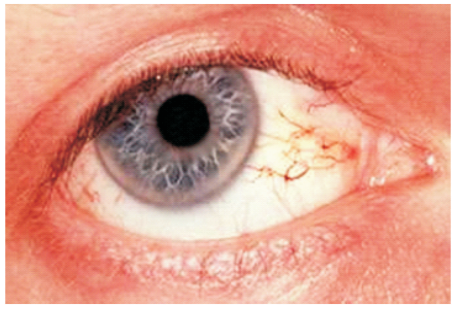

Figure 1. Bulbar telangiectasia

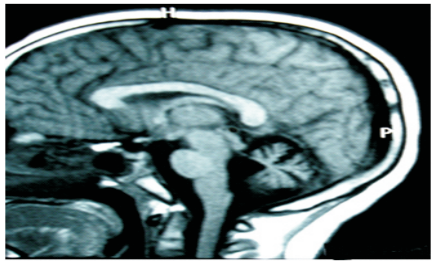

Figure 2. Cerebellar atrophy

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Discussion

Ataxia Telangiectasia is an inherited primary immune-deficient disorder involving many issues in the body. Multiple symptoms may include neurological abnormalities, dilated blood vessels (telangiectasia), variable immunodeficiency humoral and cellular immunity. There is increased risk for certain kinds of cancer[3].

It is an autosomal recessive trait with the mutation in ataxia-telangiectasia mutated (ATM) gene long arm of chromosome11 at 11q-22-23; 1 in 40000to 1 lakh population.1% of US population may be carriers of AT. The affected person presents with the following symptoms like delayed walking, ataxic gait, and telangiectasia, severe recurrent respiratory infections, with delayed mental development, movement disorder and nystagmus. The patient will have mask like face with reduced tendon reflexes and multiple skin changes like pigment changes, eczematous and atrophic lesions are seen. Growth failure and absence of pubertal development are characteristic of the disease. There is hypo plastic tonsils, lymph nodes and spleen.

Laboratory tests reveal most commonly humoral immunological defects in the form of diminished or absent serum IgA and IgG2 and impaired antibody responses to vaccines[5]. Serum IgG level is generally normal even when some IgG subclasses are reduced. Patients with IgG2 or IgG4 appear to be at higher risk for infection[6]. Increased IgM levels and gammapathy may occur in AT[7].There is also reduced B and T cell series, increased alpha fetoprotein, tendency of chromosomes to break on exposure to radiation.

The ataxia-telangiectasia mutated (ATM) kinase initiates a well characterized response to DNA damage, resulting in arrest of cell-cycle, DNA repair, orapoptosis[8]. Mutations in the ATM gene, though tolerated, result in the fatal childhood disorder ataxia-telangiectasia (AT). ATM signaling is required to sense and initiate repair of DNA double-strand breaks. Therefore, nuclear genomic instability resulting from loss of this function is regarded as a major mechanism underlying the pathology of A-T[9]. Pulmonary infections in AT are usually caused by viruses during the first two years of life, and by common bacterial pathogens in later childhood, such as Hemophilus influenzae, Streptococcus pneumoniae, Pseudomonas aeruginosa and Staphylococcus aureus. These common infections are often correlated with the severity of humoral defect, and hence are the rationale for using gamma-globulin[6].

The lifetime prevalence of cancer in A-T patients is 10–30% [11] whichis the second most common cause of death[10]. Of these cancers, 40% are non-Hodgkin's lymphomas, 25% are leukemia's, 25% are assorted solid tumors and 10% are Hodgkin's lymphomas[11]. There are reports of co-inheritance of hemoglobin E trait and differences in the type of humoral immune deficiencies, laboratory findings, and their susceptibility to develop different types of malignancies[12]. Complication includes pulmonary infection, lymphoma, diabetes mellitus and progressive kypho-scoliosis.

There is no specific treatment available for the condition. Thymic transplants, thymic hormones and bone marrow transplant are some modalities tried to reduce the morbidity of the patient.some promise exists in the use of antioxidantsand the development of methodology designed to target specific prototypes of mutations in the ATM gene in situ[13]. Cloning and sequencing of gene (ATM) for gene therapy, drugs to correct function of altered proteins, direct replacement of functional protein can be tried. Patients with ataxia telangiectasia are wheelchair bound by teens, fatal by 20s. Management includes genetic counseling, examination of all the family members, identification of A-T homozygote and providing appropriate care, regular surveillance of the heterozygote for malignancy[14].

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