Case Reports

A case of ataxia telangiectasia

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Introduction

Ataxia telangiectasia (AT) is an autosomal recessive, complex, multisystem disorder characterized by progressive neurological impairment, cerebellar ataxia, variable immunodeficiency with susceptibility to sinopulmonary infections, impaired organ maturation, x-ray hypersensitivity, ocular and cutaneous telangiectasia and predisposition to malignancy[1]. The responsible gene (*ATM* gene) has been mapped to band 11q22-23[1].

Case report

A 4 ½ year old boy, product of a second degree consanguineous marriage, was admitted to our ward with a chest infection which was poorly responding to antibiotic therapy. The child had two episodes of similar respiratory tract infection one year back. There was also a complaint of unsteadiness of gait since early childhood and redness of both eyes for two months duration. His development was age appropriate in all four areas. There was no family history of significant illness.

On examination, the child was socially withdrawn with poor eye contact, ataxic gait and dilated vessels in both conjunctivae (Figure 1). Diffuse crepitations and rhonchi were heard over the lungs.

White cell count was $13.2x10^9$/l (N 82%). Haemoglobin was 13.5 g/dl. Erythrocyte sedimentation rate was 20 mm in the first hour. The blood picture was normal. The serum alpha fetoprotein was 144.52 ng/dl (normal <8.6).

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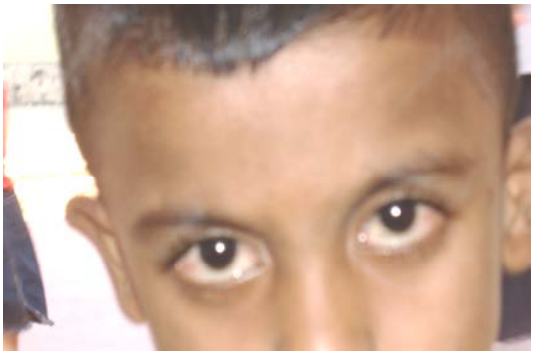

Figure 1 Dilated blood vessels in both eyes

Serum immunoglobulin was as follows: IgA 37.5 mg/dl (normal 55-152), IgG 283.2 mg/dl (normal 569-1597) and IgM 427 mg/dl (normal 22-100). T cell subsets were as follows: CD 4: 908 (500-2400), CD 8: 946 (300-1000), CD 20: 189 (200-1200), CD 56: 756 (100 -1000). Nerve conduction studies and electromyographic studies were normal. Lipid profile was as follows: Total cholesterol 129.2 mg/dl (140-239), triglyceride 49.7 mg/dl (10-200), HDL cholesterol: 40.2 mg/dl (35-85), LDL cholesterol: 80 mg/dl (75-159), VLDL cholesterol: 19 mg/dl (10-41) and LDL/HDL ratio 3.2 (2-5).

Discussion

AT is the best known DNA repair disorder[2] with a probable incidence of 1 case in 100,000 births[1]. The frequency of AT mutant allele's heterozygosis was reported to be 1.4-2% of the general population[1]. It occurs equally among males and females[1]. Three siblings with ataxia telangiectasia were reported from Sri Lanka in 1978[3].

The onset of clinical symptoms and rate of progression are variable. Ataxia has its onset in infancy, becoming apparent when the child begins to walk. Ataxia is progressive, child

requiring a wheelchair by age 10 or 11 years[1,5]. Telangiectasias have a later onset than ataxia, being first noticed after the age of 3-6 years and sometimes not until adolescence[1]. They first appear on bulbar conjunctiva and later on nose, ears, neck, anterior cubital fossae, popliteal fossae, hard palate and anterior upper chest[2]. Repeated sino-pulmonary infections are present in 48-81% of patients[1].

Patient with AT have an elevated incidence of cancers, approximately 100-fold in comparison to the general population[1]. In children, more than 85% of neoplasm cases are ALL or lymphoma[5]. 20-30% of patient suffer from mild mental retardation[6]. Characteristic facies and postural attitudes, observed in all of the children, are part of the cerebellar hypotonia[6]. Retardation of somatic growth with significant dwarfing is observed in a large proportion of the patients[1].

Choreoathetosis is seen more often in older than younger children[6]. Oculomotor signs usually precede the appearance of telangiectasia and are steadily progressive[6]. Dyssynergia and intention tremor become prominent with age. Myoclonic jerks of the trunk and the extremities occur in some patient with AT but not before age 10 years[6]. Absent or diminished deep tendon reflexes may be noticed after the age 7 or 8 years[6].

Gonadal atrophy occurs in both sexes[2]. Insulin resistant diabetes mellitus may be a feature. Growth failure with a normal level of growth hormone occurs in the late stages[3]. Cutaneous manifestations include hypo/hyper pigmentations, cafe-au-lait spots, atopic dermatitis, premature graying of hair, seborrhoeic dermatitis and keratosis pilaris[1].

Laboratory markers are important for both diagnosis and prognosis[1]. Alpha fetoprotein levels are elevated in 90% of cases[2]. Elevated levels of carcinoembryonic antigen are found in some cases[1]. There may be absent or low levels of IgA, normal or low level of IgG, and normal or elevated level of IgM[3]. A deficit in IgG2 and IgG4 subclass has been demonstrated in several patients, and IgE levels also may be absent or low. Defects of cellular immunity include a low lymphocytic count, poor response to skin test to common antigens, low T-lymphocyte proliferation in the presence of mitogens, and deficient antibody production to viral or bacterial antigens[1]. Auto antibodies may be present in some patients. There is increased chromosomal breakage after exposure of cell culture to ionizing radiation[1].

There is no specific treatment available for AT. The life span of patient with AT clearly has been prolonged by antibiotic treatment[1]. Prophylactic antibiotics or intravenous immunoglobulin therapy reduce the morbidity from sino pulmonary infections[1,2]. Recently, desferrioxamine was shown to increase genomic stability of T cells and, therefore, may present a promising tool in AT treatment[1]. Regular surveillance of heterozygotes for cancer should be part of family management[1]. Good patient and parental education should include tactful genetic counseling and explanation of the multisystem nature of the disease[1].

The neurologic features of AT are relentlessly progressive. Most of patients are wheelchair dependent by age 10-15 years, but mild forms are not rare[1]. The median age at death is reported to be approximately 20 years, usually from bronchopulmonary infection, less frequently from malignancy or from a combination of both[1].

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