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Ataxia telangiectasia: Serological Presentation

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Abstract

Ataxia telangiectasia is a rare autosomal recessive multisystem disorder,having an incidence of 1:40,000 to 1:100,000 with an equal ratio in males and females, characterized by cerebellar ataxia, variable immunodeficiency, oculocutaneous telangiectasia, increased x ray hypersensitivity and susceptibility to malignancies. The causative gene has been localized to chromosome 11q22-23. Here a case of an 8 year old boy is described who presented with progressively increasing gait difficulties, immunological and ocular manifestations, bilateral CSOM, and abdominal tuberculosis. The case an almost classical presentation of ataxia telangiectasia, highlights the diagnostic work up and the serological findings for early detection and genetic counseling of the parents.

Key Words: ataxia telangiectasia, alpha-fetoprotein, immunodeficiency

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Introduction

Ataxia telangitectasia (ATM) is a rare hereditary neurodegenerative disease usually found in early childhood [1] . It is characterized by a progressive cerebellar in coordination, with the patient being wheel chair bound by 10-11yrs of age [1]. Oculocutaneous involvement in the form of telangiectasia may manifest itself by 3-6 yrs of age. The patient usually suffers from repeated sinopulmonary infections attributed to variable reduction in levels of serum and secretory IgA and IgE and are one of the major cause of mortality in such children. The causative ATM gene has been localized to band 11q22-23. ATM has sequence homology to a family of proteins that are related to the phosphatidylinositol-3-OH-kinases (PI (3) K) [1], and have a role in DNA repair, which is presumed to be responsible for increased susceptibility to malignancies. Serum levels of oncofetoproteins like AFP and CEA are found to be increased.

The cause of elevated AFP has been attributed to immature liver, due to a defective interaction between ectodermal

Here we present a case of a child who complained of progressive motor dysfunction, immunological dysfunction and ocular manifestations of telangiectasias, and was on medication for frequent cough and cold. We estimated his as well as his mothers' serum AFP and CEA levels using enzyme linked immunosorbent asssay, serum IgE and IgA levels as well as other relevant serological investigations.

The results showed elevated AFP levels with no rise in CEA levels. Patient's serum also showed slight elevation in liver function tests, not a well documented findings in patients of ataxia telangiectasia.

Case presentation

An 8 year old boy presented with progressively increasing difficulty in walking, and coordinating hand movements since two years and also complained of reddening of eyes. He was being treated for frequent cough and cold. The boy had a past history of bilateral chronic suppurative otitis media and taking antitubercular treatment for Koch abdomen. There was no history of delay or abnormality in developmental milestones.

There was no significant history of a similar disease in any sibling or any other family member. On examination sclera of both the eyes revealed dilated blood vessels (Fig. 1).

Neuromotor examination showed incoordination of movement more marked in lower limbs. Deep tendon reflexes were normal.

No abnormality seen on CT scan.

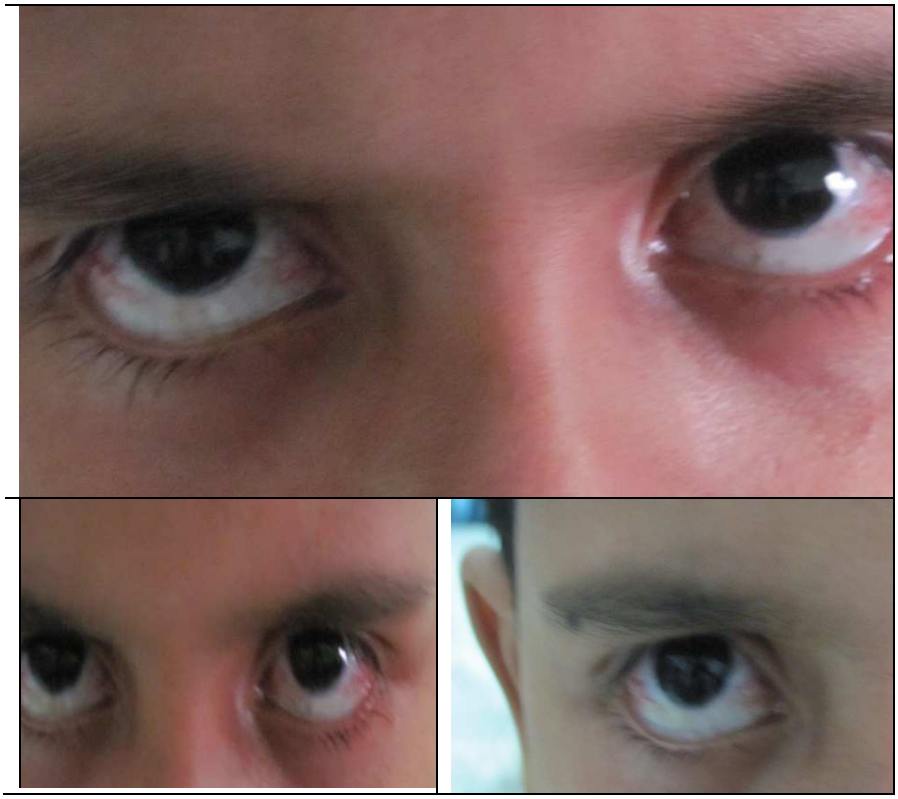

Figure 1: *Shows conjunctival telengiectasias (network of dilated blood vessels) present in bilateral eyes, a characteristic finding in Ataxia Telengiectasia*

Table 1. *Details of laboratory investigation. showed*

	Patient	Mother	Normal
Sr. Alpha-fetoprotein	140.6	0.73	<8.5ng/ml
Sr. CEA	5.16	4.3	<5ng/ml
Sr. IgA	1.610	3.040	0.52-4.68IU/ml
Sr. IgE	4.0	259.5	<1.5-378iu/ml
Sr. Alkaline Phosphate	358	55	15-112Iu/L
SGPT	124	48	9-40U/L
SGOT	85	38	9-40IU/L
Sr Bilirubin(total)	0.7	0.5	0.5-1.2mg/dl
Sr. Albumin	4.1	2.0	3.5-5.0g/dl
Sr Protein	6.6	7.1	6.0-8.0g/dl
Sr. Urea	20.66	0.5	15-42mg/dl
Sr. Creatinine	0.59	0.85	0.5-1.2mg/dl
Sr. LDH	299.2	291.9	240-480IU/L
Vitamin B12	644.0pg/ml	ND*	211-911pg/ml
Creatinine Phosphokinase	32.3	ND*	25-200

Discussion

Tlthough ataxia telangiectasia has a poor prognosis, with no cure and high mortality being usually due to sinopulmmonary infections, early diagnosis has implications not only for the patient but also for the parents and siblings. Since it is an autosomal recessive disorder, there are 25% chances of further offsprings being affected .Furthermore there are increased chances of breast cancer in female

carriers, hence mothers should be cautioned for regular screening [3].

Serum AFP and CEA are expected to be raised in patients of ATM. The synthesis of alpha fetal protein of hepatic origin by patients with ataxia telangiectasia suggests that liver is not fully developed in these patients. These findings support the hypothesis that a primary abnormality of patients with ataxia-telangiectasia is a defect in tissue differentiation. This abnormality may be due to a defective interaction between the ectodermal and mesodermal germ lines, an interaction that seems to be required for the differentiation of gut-associated organs such as the thymus and liver [2,4]. Increased levels of serum AFP can be an important tool for early diagnosis and screening of patients of childhood ataxia [5]. Moreover there is also evidence of progressive increase in levels of alpha-fetoprotein with age in patients of ataxia telangiectasia [6]. In our case we found only elevated AFP level, with no significant rise in CEA level. A study carried out in China showed a similar finding of selective rise in AFP levels in Ataxia telangiectasia patients [7] .Liver function tests of the child also showed increased serum alkaline phosphatase, SGPT and SGOT, which might signify mild derangement in liver function associated with liver dysfunction, though there is no definite evidence consistent with such findings in all or majority of patients of ataxia telangiectasia.

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The most frequent deficiencies of humoral immunity are diminished or absent serum and salivary IgA, diminished or absent serum IgE and impaired antibody responses to a variety of bacterial and viral antigens. Deficiencies of cellular immunity are commonly found by both in vivo and in vitro analyses. Histological confirmation of these immune deficiencies is readily observed in the lymphoid tissue .Respiratory infections, leading to respiratory failure are one of the leading causes of morbidity and mortality in patients of ataxia telangiectasia[8] There has been an emphasis on early assessment of pulmonary status and use of intravenous immunoglobulins in reducing acute infections and improve lung function in variable immune deficiency , an example being a case report of an adolescent boy developing bronchiectasis due to delayed diagnosis [8] .Our patient showed evidence of immunodeficiency, with frequent sinopulmonary infections (frequent cough and cold, CSOM) and abdominal tuberculosis, which might indicate impaired cell mediated immunity. Though the patient showed immunological manifestations, IgA and IgE levels were within normal limits, but with both levels being near the lower limit of normal.

As in our case serum AFP has a major significance as a diagnostic marker for the early diagnosis of any patient presenting with progressive childhood ataxia [5] and can be used as a first line investigation. Our case suggests a possibility of deranged liver function tests in occasional patients, probably due to immature organ development, though further study on this aspect is needed. No elevation in serum CEA in our case along with previous evidence [7], may need further assessment of the sensitivity of serum CEA as a marker for ataxia telangiectasia. Normal serum levels in mother were consistent with theory of a normal phenotype in heterozygotes. A high index of suspicion, early diagnosis, prevention and treatment of sinopulmonary infections, use of modalities targeting to halt progressive neurodegenerative changes, use of antioxidants[9], reducing the risk or treatment of tumors; correcting immunodeficiency; alleviating bronchial complications[8], regular screening for malignancies, avoidance of radiomimetic drugs and radiation therapy [10], along with genetic counseling can reduce morbidity to a great extent. Moreover genetic counseling of the parents, explaining the chances of further siblings being affected, as well as cautioning them for high risk of malignancies particularly mothers for breast cancer, and need for regular screening is needed as well.

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Abbreviations: CSOM (Chronic suppurative otitis media).

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