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Ataxia-Telangiectasia a rare disease in two sibling

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Abstract

Ataxia-telangiectasia is a rare inherited disorder that affects the nervous system, immune system, and other body systems. Ataxia-telangiectasia occurs in 1 in 40,000 to 100,000 people worldwide. Mutations in the ATM gene cause ataxia-telangiectasia . we are going to report two sibling presented with Ataxia and Bulbar conjuctival telangiectasia.

Key Words: Ataxia telangectasia , inherited disorders , neurodegenerative disorders, alfa-feto protein

INTRODUCTION

Ataxia telangiectasia is a rare, neurodegenerative, inherited disease causing severe disability. Ataxia and telangiectasia to small dilated blood vessels, both of which are considered to be hallmarks of the disease.[1] Most children with Ataxia telangiectasia are stable for the first 4-5 years of life , but begin to manifest symptoms in early school years. People with Ataxia telangiectasia have a highly increased incidence of cancers.[2] Ataxia telangiectasia can cause features of early aging , vitiligo, warts , chronic inflammatory skin disease (granulomas) .[3] Chronic lung disease develops in more than 25% of people with Ataxia telangiectasia.[4] Most people develop telangiectasia in sclera of the eye.[5] The diagnosis of Ataxia telangiectasia is usually suspected by the Combination of neurologic features along with with telangiectasia, increased infections, and is confirmed by specific laboratory abnormalities. (elevated alpha-fetoprotein levels, increased chromosomal breakage after exposure to X-rays, absence of ATM protein in white blood cells, or mutations in each of the person's ATM genes . The case is reported for it's rarity and lack of awareness about the disease.

CASE PRESENTATION

A 10 year-old girl born of non-consanguinous marriage presented with pain abdomen, occasional vomiting and constipation. She had a history of difficulty in walking associated with fall, dysarthria, intention tremor which was progressive. She had a history of birth asphyxia with delayed milestones. She was earlier admitted for pulmonary infection and was diagnosed as a case of birth asphyxia with sequelae with Lower respiratory tract infection. She left schooling due to these problems. On general examination, the patient was conscious, cooperative, poor built. Central Nervous system examination revealed intact cranial nerves, sensory and autonomic system. Deep Tendon Reflex were diminished with extensor response on right side and incoordination of movement and ataxic gait. Telangiectasias were seen on the bulbar conjunctiva of both eyes (figure:1) .Her speech was slow, soft with delayed response. Rest of the systemic examination was within normal limits.Contrastinhanced computedtomographyofbrainshoweddiffuse volumeloss(CASE 2) Her younger sibling , A 4 year old male too had a similar history of ataxic gait with bulbar telangiectasias on both eyes.(figure :2) CentralNervous system examinations showed no apparent abnormal findings except for ataxia. Laboratory investigations revealed Hemoglobin 8gm%, Total leucocyte count 9500/cumm, platelets 4.83 lac/cumm, R.B.C count 2.6 million/cumm, reticulocyte count 0.8%. Wright stain Peripheral blood smear showed predominantly normochromic and mildly hypochromic with few microcytes. No immature cells of myeloid or erythroid series were seen. Ultrasound abdomen showed pyloric thickening of approximately 7 mm along the pyloric region and multiple enlarged mesenteric lymph nodes. Serum alfa-fetoprotein was raised (84.05 IU/ml). Serum IgE was decreased (2.58 kUA/L) and Serum IgG was within normal range (777mg/dl). Liver function tests showed no derangement .Laboratory investigation of her younger brother revealed elevated Serum alfa-fetoprotein (188.40ng/ml). Peripheral blood smear showed Red Blood cell count 5.25 million/cumm, Platelet count 3.05 lacs/cmm, Total leucocyte count 13100/cmm. No immature cells of myeloid or erythroid series were seen. Hemoglobin 9.8g/dl, MCV 62.4iu/l Reticulocytes 0.5% and No haemoparasites.On the basis of history ,examination & lab investigations a diagnosis of ataxia telangiectasia and associated Cerebral palsy in first case and ataxia telangiectasia in second case were made.

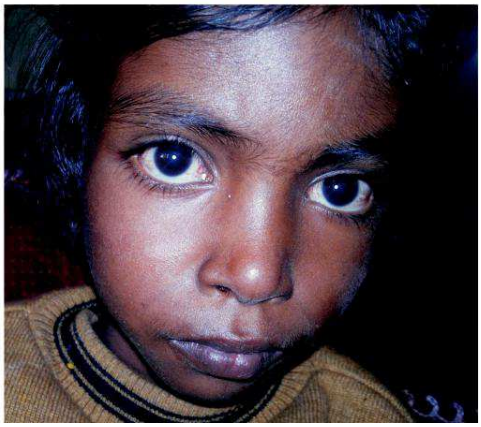

Figure 1 A 10 yr old female child with Bulber Telanglectesias on both eyes.

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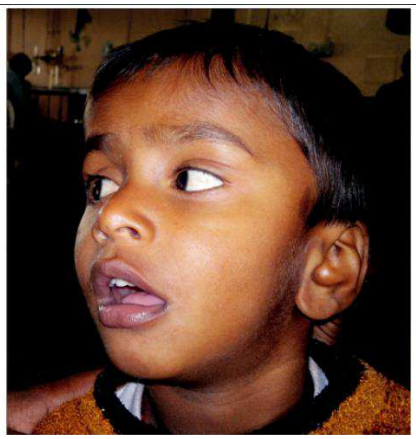

Figure 2 sibling with bilateral bulbar conjuctival telangiectasia

DISCUSSION

In our case, there is a history of progressive ataxia, bulbar telangiectasias ,respiratory tract infections, raised serum alfa- feto protein in both sibling and decreased serum IgE in the case 1. These are the clinches us to reach the diagnosis of Ataxia telangiectasia. Ataxia telangiectasia also referred to as Louis–Bar syndrome, affects many parts of the body : It impairs certain areas of the brain including the cerebellum, causing difficulty with movement and coordination. It weakens the immune system causing a predisposition to infection. It prevents repair of broken DNA, increasing the risk of cancer . 1 Ataxia telangiectasia is caused by a defect in the ATM gene which is responsible for managing the cell's response to multiple forms of stress including double-strand breaks in DNA.[6] The first indications of Ataxia telangiectasia usually occur during the toddler years. Children start walking at a normal age, but may not improve much from their initial wobbly gait. Children with Ataxia telangiectasia often appear better when running or walking quickly in comparison to when they are walking slowly or standing in one place. Around the beginning of their second decade children with typical forms of Ataxia telangiectasia start using a wheelchair for long distances. During school years children may have increasing difficulty with reading, writing, coloring, and using utensils to eat, speech and also developed extra movements such as chorea , athetosis, dystonia, myoclonic jerks, tremors .7,8 telangiectasia 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 it. Telangiectasia can also appear on sun-exposed areas of skin such as face and ears, occasionally arise in the liver and lungs.[9] A-T have abnormalities of the immune system. The most common abnormalities are low levels of one or more classes of immunoglobulins.10 Women who are A-T carriers have approximately a two-fold increased risk for the development of breast cancer compared to the general population .11 Chronic lung disease develops in more than 25% of people with A-T. Three major types of lung disease can develop: [1] recurrent and chronic sinopulmonary infections, [2] lung disease caused by ineffective cough, swallowing dysfunction, and impaired airway clearance, and [3]restrictive interstitial lung disease .12 The diagnosis of A-T is usually suspected by the combination of neurologic clinical features with telangiectasia and sometimes increased infections , and confirmed by specific abnormalities (elevated alpha-fetoprotein levels, increased chromosomal breakage or cell death of white blood cells after exposure to X-rays, absence of ATM protein in white blood cells, or mutations in each of the person's ATM genes . Increased sensitivity of cells to x-ray exposure. Cerebellar atrophy on MRI scan.13,14, 15 There are several other disorders with similar symptoms or laboratory features that physicians may consider when diagnosing A-T. 16 The three most common disorders that are sometimes confused with A-T are: Cerebral palsy , Friedreich ataxia, Cogan oculomotor apraxia, as in our first case rise in alpha feto protein helpful in diagnosing Ataxia telangiectasia apart from CP. The life expectancy of people with A-T is highly variable. The average is approximately 25 years , but continues to improve with advances in care. The two most common causes of death are chronic lung disease and cancer . There is no treatment known to slow or stop the progression of the neurologic problems. Treatment of A-T is symptomatic and supportive. Physical, occupational and speech therapies and exercise may help maintain function but will not slow the course of neurodegeneration. Therapeutic exercises. Should not be used to the point of fatigue and should not interfere with activities of daily life. Certain anti-Parkinson and anti-epileptic drugs may be useful.

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