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Ataxia Telangiectasia A case report

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Abstract : Ataxia telangiectasia(AT) is a rare autosomal recessive complex multisystem disorder characterised by progressive cerebellar ataxia, variable immunodeficiency with susceptibility to sino pulmonary infections, impaired organ maturation, ocular and cutaneous telangectasia and predisposition to malignancy. We report a case of 14 year old boy presented with cardinal clinical features of AT together with muscle atrophy and sensory axonal demyelination on nerve conduction study.

Keyword : Ataxia telangiectasia(AT), immunodeficiency

14 year old boy second born child of second degree consanguineous parents presented to our OPD with complaints of cough with expectoration for 2 weeks and one episode of hemoptysis. The patient was apparently normal till 5 years of age when his parents first noticed unsteadiness in his gait. At the age of 7 years patient developed difficulty in speech and congestion of the conjunctiva. He developed involuntary movements involving all 4 limbs at the age of 10 years that was absent during sleep. The patient has frequent respiratory infections since birth. His birth history is uneventful and developmental milestones were normal till 5 yearsof age. The patient has one elder brother of 18 years old who has no similar complaints. On examination the patient was anemic with congestions in both eyeballs that is radiating from the both corners to limbus (FIG 1). Patient had left ear CSOM (safe type). Patient was conscious and cooperative. Cranial nerves were intact. There was hypotonia and muscle wasting of all 4 limbs (FIG 2), diminished deep tendon jerks and flexor planter reflexes. Gait was wide based and ataxic. Touch, pain and temperature sensations were diminished. Vibration and position sense were preserved. Romberg sign was negative. Cerebellar dysfunction in the form of dysarthria, intention tremor, past pointing and dysdiadochokinesia, ataxic gait were apparent. Choreic movements of limbs were also seen.
On investigation Complete blood count, blood sugar (fasting & postprandial), Lipid profile, LFT, Serum electrolytes, HIV serology, USG abdomen and ECG were within normal limits. Chest xray showed features of right upper and middle zone patchy infiltrates. Sputum AFB were negative. Pus C/S from ear discharge showed pneumococcus. MRI brain showed features of Cerebellar atrophy (FIG 3) and mucosal thickening suggestive of pansinusitis (FIG 4) . Nerve conduction study showed mixed axonal and demyelination neuropathy of both upper limbs sensory nerves and B/L peroneal nerves(FIG 5). Serum a-feto protein was 605ng/l

. Serum immunoglobulins levels were measured which showed low total serum IgA (0.23g/L), low IgE (0.8 IU/L) and high IgG (20.90 g/L). There was no specific treatment was provided for AT. Patient was treated with antibiotics for ear and chest infections. Physiotherapy was advised.

Fig 1 : showing ocular telangiectasia

Fig 2 : showing wasting of limb muscles.

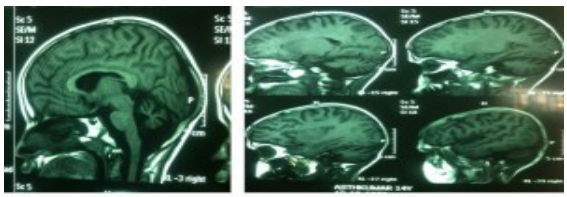

Fig 3: MRI Brain showing cerebellar atrophy

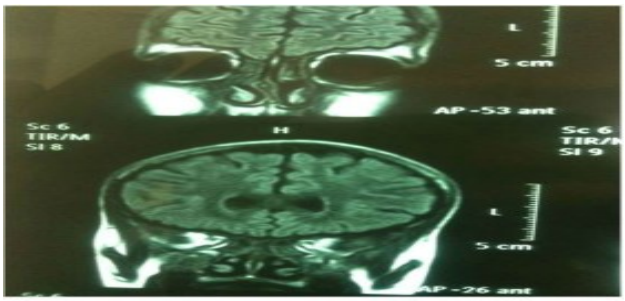

Fig 4 : MRI Brain showing mucosal thickening suggestive of pansinusitis

Fig 5: Nerve conduction study showing mixed axonal and demyelinating neuropathy of upper limb sensory nerves and B/L peroneal nerves

Discussion :

Ataxia-telangiectasia (AT) is an inherited autosomal recessive multi-system disease characterized by progressive neurological dysfunction, especially in the cerebellum, oculo-cutaneous telangiectasia, immunodeficiency, recurrent sino-pulmonary infections and a high incidence of neoplasm (1). The clinical hallmark of AT, and present in all cases, is the progressive cerebellar ataxia which is mainly a truncal ataxia becoming manifest at about 2-5 years of age (2). The phenotype is also characterized by oculomotor apraxia, a tendency to drool and slow, slurred speech. Often this is mistaken for cerebral palsy or mental retardation but most AT individuals seem to have a normal IQ (3). Motor dysfunction is variable, often a combination of ataxia, dystonia and chorea. A peripheral axonal neuropathy is common and is manifested by decreased deep tendon reflexes (4,5) The second cardinal feature, the oculocutaneous telangiectasia, develops later than the ataxia sometimes appearing as late as 10 years of age (1). On the conjunctiva, the telangiectasia give the eyes a “bloodshot” appearance, distributing symmetrically on the conjunctiva as fine, bright, red streaks. Ataxia-telangiectasia patients are prone to recurrent sinopulmonary infections as a result of a variety of cellular and humoral immunodeficiencies. The most common humoral immunological defects are diminished or absent serum IgA and IgG2, and impaired antibody responses to vaccines . 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 (6,7). The most tragic manifestation of AT, however, is the cancer predisposition associated with it. The lifetime frequency of cancer in AT patients approaches 38%, with 1 in 20 developing more than one malignancy. AT can be distinguished from other autosomal recessive ataxias such as Friedrich’s Ataxia (FA) by an earlier age of onset of cerebellar symptoms and the presence of dystonia and chorea later on in the teens. Unlike AT, FA patients have pyramidal weakness of the legs, extensor plantar responses and symptoms related to posterior column involvement(8). The diagnosis of Ataxia Telangiectasia (A-T) is usually based on characteristic clinical findings and supported by laboratory tests. One of the most helpful laboratory tests used to assist in the diagnosis of A-T is the measurement of alpha-fetoprotein levels in the blood(9). Other diagnostic tests include:

1. Detection of the protein (ATM) made by the A-T gene using a
western blot
2. Measurement of cellular damage (cell death orchromosomal
breakage) after exposure of cells to x-rays in the laboratory
3. Sequencing (reading the spelling) of the A-T gene (ATM)

There is no effective therapy for slowing the progression of the ataxia. Since the greatest mortality is caused by sino-pulmonary infections, prompt treatment with antibiotics. The single most important supportive therapy for AT patients is aggressive physical therapy. Given the cancer predisposition, early detection of any underlying malignancy is paramount. Desferrioxamine has been shown to increase genomic stability of ataxia-telangiectasia cells and, therefore, may present a promising tool in ataxia-telangiectasia treatment(10).Concerning the role of increased oxidative stress in ataxia-telangiectasia pathophysiology, several clinical trials based on antioxidants in ataxia-telangiectasia patients have been constructed and are currently underway.

Early diagnosis of AT 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 (11). Hence proper counselling is the most important aspect in management.

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