

ATAXIA TELANGIECTASIA — A Case Report

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SUMMARY

A 17 year old male with ataxia telangiectasia [Louis-Bar Syndrome] is presented here with a review of the literature with regards to the mode of inheritance, clinical manifestations, diagnosis and treatment of this disorder.

INTRODUCTION

Ataxia telangiectasia (often abbreviated A-T) is a heredo-familial syndrome of progressive cerebellar ataxia beginning in infancy, progressive oculocutaneous telangiectasia, susceptibility to sino-pulmonary infection, including bronchiectasis and lymphoreticular neoplasia.

Its multiple facets include characteristic facies, apraxia of eye movements, simulating ophthalmoplegia; choreoathetosis; progeric hair and skin changes; growth retardation; endocrine abnormalities, including ovarian agenesis and hypoplasia or absence of the thymic gland with an abnormal immune mechanism. Mental retardation may occur.

The first report of a family with ataxia telangiectasia is attributed to Syllaba and Henner (1926). The next report was published by Louis-Bar (1941), who regarded the disease as one of the Phakomatoses. The disorder was further elaborated and delineated as a distinct clinico-pathological entity by Biemond (1957) and Boder and Sedgwick (1957); these latter authors suggested the name Ataxia-telangiectasia and Centerwall and Meller (1958) proposed the eponym Louis-Bar Syndrome.

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CASE REPORT

The patient is a 17 year old Indian male who was first seen at the University Hospital in May 1973 at the age of 10 years. He presented then with a history of not being able to walk by himself for a period of one year. Apparently this difficulty in walking had been progressively worsening over the one year period. Initially he had an unsteady gait and tended to fall to the right side more than the left. Six months later he also spilled food all over while eating and gave a history of occasional enuresis. No convulsions were noted. No significant respiratory complications were noted at that time.



Fig. 1. Expressionless facies and inability to stand without support.

He defaulted treatment but was subsequently referred here again in August this year from the Cheshire Home with a history of recurrent respiratory infections over the last three years.

He had not gained weight or height in proportion to his age over the last few years, despite having a fairly good appetite. No history of bleeding tendencies was noted.

The developmental history is significant. He was born at full term and had a normal delivery. However, his developmental milestones were all delayed. He sat up at 12 months and started walking and talking at 24 months. He had attended school up to standard 3 before his first admission in 1973. He had always been the last in the class examination.

The family history available is also of significance. He is the product of a consanguineous marriage and he has a younger sister with Titubation (staggering or reeling gait). However, she has not been fully investigated as yet.

Physical examination revealed the presence of marked growth retardation. His nutritional status was poor and he was pale. The skin was dry and rough with a few areas of hyper- and hypo-pigmentation over the back. No telangiectases were noted over the face, neck, ears or extremities.

Prominent bulbar conjunctiva telangiectases were seen over both eyes (Fig. 2). The fundi were normal. A high arched palate was present but no mucosal telangiectasia were noted. The nostrils revealed ulcerations and encrustations. No significant lymphadenopathy were detected. The cardiovascular system was normal, pulse = 82/min. and the blood pressure was 100/70 mmHg. The respiratory system revealed abnormalities. The patient was slightly orthopnoeic at rest and had a noisy nasal respiration. The chest cage was deformed with a prominent sternum. Occasional crepitations and rhonchi were heard over both lung fields. The abdomen was normal with no enlargement of the liver or spleen. The genitalia were normal. No testicular atrophy was seen and

pubic and axillary hair growth were normal.



Fig. 2. Illustrates the bulbar conjunctival telangiectasia in both eyes.

Abnormalities of the central nervous system were prominent. The patient was mentally subnormal and had a dull facial expression. He had slow dysarthritic speech and was unable to stand or walk. Truncal ataxia was evident. Athetosis of the fingers were noted. The cranial nerves were intact. Prominent cerebellar signs were present with past pointing, intentional tremors and dysidokokinesia. Nystagmus was present but not sustained. Hypotonia of the upper and lower limbs was detected and the motor power was Grade 4. Deep tendon reflexes were present but uniformly diminished. Plantar reflexes were down-going. Another prominent feature was the Apraxia of voluntary gaze. Scoliosis of the thoracic spine was also present.

Investigations done revealed the following: Haemoglobin concentration = 8.3 g%; total white count 12,600/ul (N 68%, E 13%, L 17%, M 3%). Peripheral blood film revealed hypochromia, microcytosis, and anisocytosis and a few target cells. Stool examination revealed the presence of ascaris, trichuris and ankylostoma. Chest x-ray showed interstitial pneumonitis and a partial collapse of the left upper lobe. Skull x-ray showed a small pituitary fossa and hypertrophy of the left inferior turbinate. Mantoux test was negative. Electrocardiography and Electroencephalography were normal. Immunoglobulin study revealed IgA 53 mg%, IgG >1974 mg% and IgM >

430 mg%. Facilities for IgE were not available. Alpha foetoprotein was 82 ug/ml using radio-immunoassay (Normal is 10-25 ug/ml). Urine aminoacid chromatography revealed increased excretion of alanine and glycine. Nerve and muscle biopsy done in 1973 were normal. They were not repeated at this admission.

DISCUSSION

Our patient is a fairly typical case of ataxia-telangiectasia presenting with most of the features of this disorder.

Ataxia telangiectasia has a high incidence of familial occurrence and genetic studies have indicated an autosomal recessive inheritance (McKusick and Cross, 1966 and Ferak *et al.* 1968). Evidence is strong that it is a heredodegenerative neurological and multisystemic disorder, which equally affects males and females and shows no racial or geographic predilection.

Children with ataxia telangiectasia display characteristic somatic features. They have a dull, sad, hypotonic facial expression and conspicuous growth retardation.

Progressive cerebellar ataxia is the most common presenting feature which appears in infancy or early childhood and progresses steadily to adolescence. The ataxia involves primarily the head and trunk at first and later the extremities. Choreoathetosis also occurs. In general, choreoathetosis may become more prominent in older children, in contrast to the usual, more purely cerebellar picture in younger children (Sedgwick and Boder, 1972).

Oculomotor signs are almost uniformly present. The deficit is described as an apraxia of voluntary gaze. When conjugate gaze is attempted in any direction, the movements seem slowly initiated, and may often be preceded by blinking or turning of the head. However, the movements can be completed if the patient is given sufficient time. The abnormalities of conjugate gaze are observed only on voluntary movements; they are not observed on involuntary movements, as when

the head is passively turned. Patients who survive beyond adolescence usually develop dysarthritic speech. They also show involvement the spinal cord and peripheral nerve with impairment of vibratory sense, distal weakness, fasciculation and atrophy.

Telangiectasia is another cardinal feature of this disorder. It has a later onset than the ataxia and is usually noticed between 3 to 6 years of age. However, it has been reported that it may be noticed as early as one year and even at birth. Telangiectasia of the bulbar conjunctiva are characteristic and initially they appear as 'blood-shot' eyes and simulate conjunctivitis. Later, they show the characteristic streaky pattern. Telangiectasia are also found in the buccal mucosa, the face in a butterfly distribution, the external ears, the extremities over the cubital and popliteal areas and dorsal aspects of the hands and feet. The telangiectases are mostly venous and they seldom cause haemorrhages.

Recurrent sinopulmonary infection is a prominent feature in ataxia telangiectasia, ranging from acute rhinitis with infection of the ears and sinuses to recurrent pneumonia and chronic bronchitis, which may progress to bronchiectasis and pulmonary fibrosis severe enough to cause clubbing of the fingers and toes and, ultimately, respiratory insufficiency and death. Most of the chronic infections are due to common bacterial pathogens rather than to viruses, fungi or tubercle bacilli (Peterson and Good, 1968). However, they do not respond well to the usual antibiotic therapy.

Immunodeficiency is a cardinal feature of this disorder and it is an important factor in causing recurrent sinopulmonary infections. The defect in the immunological system is a dysgammaglobulinaemia, characterised by selective deficiency of IgA in the serum, saliva, tears, nasal and respiratory mucosa and IgE deficiency in the serum. IgG, IgM and IgD are usually normal. The thymic gland is hypoplastic or absent.

Cell mediated immunity has been reported to be abnormal in 60% of patients with ataxia telangiectasia (Sedgwick and Boder, 1972). Various types of lymphoreticular malignancies have

been described with ataxia telangiectasia and these include malignant lymphoma, lymphatic leukaemia, lymphosarcoma, reticulum cell sarcoma, reticuloendotheliosis and Hodgkin's disease. Occasionally, dysgerminoma, frontal glioma and medulloblastoma have been associated with this syndrome.

Endocrine disorders may occur. Characteristic manifestations are Hypogonadism with sexual infantilism and delayed development of primary and secondary sexual characteristics. They have a decreased urinary excretion of 17 ketosteroids and increased urinary excretion of FSH. An unusual form of diabetes mellitus has been described in some patients. It has a late adolescent onset and is characterised by hyperglycaemia without glucosuria and ketosis, hyperinsulinism and peripheral resistance to the action of insulin (Barlow *et al.* 1965).

Progeric changes of the skin and hair are also important features of this condition. The wasting of the face, graying hair and stooping posture give the older children an appearance of premature aging. Pigmentary changes are frequent, with areas of hyper- and hypo-pigmentation of the skin. Skeletal abnormalities are not a frequent feature but kypophoscoliosis, when it appears, develops late and only in non-ambulatory patients.

Chromosomal abnormalities are yet another feature of this disorder. It has been estimated to occur in 80% of the patients. The abnormalities are similar to those seen in patients with Fanconi's anaemia and Bloom syndrome, both of which are pre-leukemic states (Miller, 1966).

Early in the illness, the intelligence of these children is usually unaltered but by the age of 9 or 10 some intellectual decline appears and this is related to the speech defect and increasing physical limitations, with consequent social and cultural deprivation.

The possibility of a causal relationship between the vascular changes, neurological symptoms and immunological defects has been entertained.

Cerebral vascular changes do not seem sufficient to account for the progressive cerebellar degeneration. It has been postulated that the thymus and lymphatic tissue may have some protective role in the metabolism of nervous tissue and its impairment may account for both the vascular and cerebral alterations.

Diagnosis of the syndrome when full blown presents no difficulty clinically and some of the following investigations may further support the diagnosis. Immunological studies may reveal the disease even before the appearance of telangiectasia. The IgA and IgE are characteristically low in the serum and secretions. The chest x-ray may show a mediastinal lymphoma in addition to the lung pathology. The skull x-ray may reveal the absence of adenoids and tonsillar tissue. Blood studies reveal lymphopenia and occasionally eosinophilia. Endocrinological investigations should be aimed at carbohydrate metabolism and gonadal functions. Electrodiagnosis in the later stages of the disease may indicate peripheral nerve damage and neurogenic muscular atrophy.

Prognosis

The course of the disease is slowly progressive. A high percentage of patients are confined to the wheel-chair by the time they reach adolescence. Chronic sinopulmonary infections leading to bronchiectasis develop in 85% of the cases (Boder and Sedgwick). Incidence of lymphoreticular malignancy is as high as 10% in patients with Ataxia-telangiectasia (Gatti and Good, 1971). Patients commonly succumb to these complications but survivals up to 40 years have been reported.

Treatment

There is no specific treatment for this disease. Chronic sinopulmonary infections should be treated with the appropriate antibiotics and in the presence of bronchiectasis, postural drainage and breathing exercises should be carried out regularly. Although serum IgA is deficient in most of these patients parenteral administration of gammaglobulin is not necessary since this

contains very low. IgA levels. Fresh plasma infusions have been used to replenish serum IgA levels when necessary. Thymic and splenic-cell transplants have been tried with little success. Physical therapy, social and psychological support are an integral part of the treatment. It is also important that family members be screened for malignancies and diabetes mellitus. Genetic counselling is also imperative.

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