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# A Rare Case of Ataxia Telangiectasia with Pulmonary Tuberculosis

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## Abstract

*Ataxia Telangiectasia (A-T, Louis Bar syndrome) is a rare autosomal recessive multisystem disorder caused by a mutation in the ATM gene located at 11q22-q23, involved in DNA repair and cell-cycle regulation. The diagnosis of A-T is based on the typical clinical picture-ataxia and telangiectasias. However the definitive diagnosis is by identification of the mutated ATM gene with supportive evidence of raised alpha-feto-protein (AFP) and reduced IgA fraction. Recurrent sinopulmonary infections are common affecting 90% of patients and usually results in chronic bronchitis, bronchiectasis or both. Here we report a rare association of pulmonary tuberculosis with A-T. This 11 year old female had typical clinical features of ataxia and telangiectasia with elevated AFP (254ng/ml) and reduced IgA (<10mg/dl). Sputum for AFB was positive with radiological findings suggestive of pulmonary tuberculosis. Because of the rarity of A-T in India, we report this case to help pediatricians make an early diagnosis. Keywords-Ataxia telangiectasia, DNA repair, sinopulmonary infections, pulmonary tuberculosis, ATM gene*

## INTRODUCTION

The initial clinical description of the disease Ataxia Telangiectasia (A-T) was reported by Syllaba and Henner in 1926[1], who called it *congenital double athetosis- aconjunctival vascular plexus syndrome*. The first case described in

literature was a 9 year old Belgian male child with progressive cerebellar ataxia and bilateral oculocutaneous telangiectasia reported in 1941 by Madame Louis Bar; classifying the case as a previously unrecognised *phakomatosis*. Three additional independent reports subsequently

appeared in the literature[Bimond,1957;Boder and Sedgwick,1957,1958]. Initially known as the Louis Bar syndrome, the term ataxia telangiectasia was introduced in 1958 by Boder et al, who recorded the clinical features and identified the familial incidence proposing an autosomal recessive mode of inheritance for the disease. Hence the disease is sometimes referred to as Boder-Sedgwick syndrome.

The disease is characterised by progressive cerebellar ataxia, choreoathetosis, immunodeficiency and proclivity to sinopulmonary infections and lymphoreticular malignancies.

Although sinopulmonary infections are a part of the disease, it usually is confined to either bronchitis or bronchiectasis. The occurrence of sputum positive pulmonary tuberculosis is a rare association and hence reported. The report highlights the refractory nature of the disease, the difficulties in medical management and the problems posed by late diagnosis which can compromise patient care.

## CASE REPORT

An eleven year old female, the 6<sup>th</sup> order child of a consanguineous marriage; belonging to lower socio-economic status presented in the outpatient department with complaints of fever, night sweats and cough of 15 days duration. The child had 15-20 past episodes of recurrent respiratory infections with 4 hospitalisations. The mother also noticed in the child congestion in both eyes since 2 years of age which was first confined to the corners but later progressed medially.



Fig 1- Ocular telangiectasia in both eyes

Developmentally the child was normal upto 2 years of age following which she was unable

to walk and 8 years later became completely bedridden with frequent falls on deliberate attempts to stand. Presently, the child can sit without support and her vocabulary is confined to a few words mainly bi-syllables

Her 5 siblings were disease free and she was born at home; the birth weight was recorded to be 3kg. She was not given any vaccines since birth except OPV due to lack of knowledge and inaccessibility. There was no contact history of tuberculosis

On examination, the child was grossly emaciated and febrile with moderate clubbing. She weighed 12kg, head circumference-48cm, HR-100/min, RR-60/min and bilateral eyes showed congestions from the corners to the limbus. Systemic examination revealed fine crackles on both sides of chest with generalised hypotonia, power of grade 3 and 5 in bilateral lower and upper limbs respectively with bilateral plantar flexor and positive cerebellar signs

Eye examination revealed a horizontal nystagmus with fast component to the right along with oculomotor apraxia in both horizontal movements. Sensory system and cranial nerves were normal with no signs of meningeal irritation.



Fig 2-Clubbing

She was admitted and started on antibiotics but did not improve with 5 days of antibiotics and in the meanwhile, was investigated. The complete blood count revealed normal parameters except for an ESR of 60mm/hr. Sputum for acid fast bacilli turned to be positive; Mantoux was negative; chest X ray showed opacities bilaterally. Serum alpha feto protein was elevated [253.77ng/ml] and serum IgA by immunoturbidimetry revealed a selective deficiency

of IgA(<10mg/dl).The definitive diagnosis of A-T by genetic analysis of ATM gene could not be done due to financial constraints of the patients and lack of facilities in the hospital.

Table1 -Relevant investigations

TEST	OBSERVED VALUE	NORMAL VALUE
ESR(mm/hour)	60	<10
Mantoux(mm)	3	Positive if >10
Serum Alpha feto protein(ng/ml)	253.77	<10
Serum IgA(mg/dl)	<10	45-250

The child was started on anti-tubercular drugs; showed signs of improvement after 5 days and was discharged with advice for regular follow up and explanation of the prognosis. The child was thriving well at follow up after 1 month .



Fig 3-Chest X-ray of the patient

**DISCUSSION**

Ataxia-telangiectasia (A-T) is an autosomal recessive disorder that has multisystem manifestations including motor impairments secondary to a neurodegenerative process, oculocutaneous telangiectasia, progressive immunodeficiency, chronic sinopulmonary infections, increased risk of lympho-reticular cancer, and hypersensitivity to ionizing radiation. The disease is heterogeneous, both clinically and genetically, as shown by the existence of four complementation groups (A, C, D, E).AT is a rare disease with a prevalence estimated to be less than 1

in 100 000.[2-4]. Death typically occurs in early or middle adolescence, usually from broncho-pulmonary infection. The lifetime risk of cancer among patients with A-T has been estimated to be 10-38% which is about 100-fold more than the population rate; however, in the absence of chronic broncho-pulmonary disease and lymphoreticular malignancy, A-T is consistent with survival into the fifth or sixth decade.

*Ataxia:* Ataxia has its onset in infancy, becoming apparent when the child begins to walk and is relentlessly progressive ultimately leading to an inability to ambulate by the second decade.

*Telangiectasia:* These are dilated vessels usually found at the corners of eyes, or on the surface of the ears and cheeks exposed to sunlight. They are noticed after age 3-6 years and sometimes not until adolescence. The mechanism of developing telangiectasia is still unknown.

*Immunodeficiency:* It affects 70% of AT patients. Deficient levels of IgA, IgG2, IgG4 and IgE are found and render them prone to sinopulmonary infections.

*Predisposition to Cancer:* Lymphoma and leukemias are particularly common. A-T heterozygote is at increased risk of breast cancer.

The diagnostic criteria formulated by Ataxia-Telangiectasia Clinical Center at the Johns Hopkins Medical Institutions, is as follows[5]: Ataxia or significant motor inco-ordination with raised alpha fetoprotein (AFP) (>2x) +3 of the following four *characteristic clinical features*:

- Inco-ordination of head and eyes in lateral gaze deflection
- Ocular telangiectasia
- Gait ataxia associated with an inappropriately narrow-base
- Immunoglobulin deficiencies

Patients with less than three of these characteristics were required to have the diagnosis confirmed by the finding of radiation-induced chromosomal breaks in lymphocytes. Siblings of known patients with AT who are older than 1 year of age and had ataxia only needed to have an elevated AFP.

The index case having fulfilled the criteria was diagnosed to have A-T and the sputum testing for AFB and radiographic evidence clinching further to an added event namely pulmonary tuberculosis.

The child was initially diagnosed as a case of A-T with bronchiectasis; the clubbing and the history of recurrent infections pointing against pulmonary TB; however she failed to improve with broad spectrum antibiotics; in addition the prolonged history of symptoms and the sputum test revealing acid fast bacilli was the turning point in ascertaining the diagnosis of pulmonary TB.

The negative reading of mantoux was not a surprise since the child was immune-compromised with deprivation of both B and T cell mediated immunity. The child was treated with anti-tubercular drugs, according to the national regimen as a sputum positive case and was discharged. She was better at the next follow up visit at the end of 1 month of anti-TB medications

## CONCLUSION

A-T with tuberculosis is an eye opener to all clinicians and it can be concluded that any patient with respiratory infection and features suggestive of A-T should not be confined to the mere diagnosis of bronchitis or bronchiectasis, rather the entity of tuberculosis which is often missed should not be overlooked to ensure the avoidance of delay in the proper intervention measures. A-T is mainly a clinical diagnosis and unnecessary, expensive investigations should be avoided. Management includes genetic counseling, examination of all the family members,

identification of A-T homozygote and providing appropriate care, regular surveillance of the heterozygote for malignancy.

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