

## Case Report

# Delayed diagnosis of ataxia-telangiectasia in an adolescent patient

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**Ataxia-telangiectasia (AT) is a rare autosomal recessive neurodegenerative disorder characterized by cerebellar ataxia, telangiectasies, immune defects, and a predisposition to malignancy. Patients present in early childhood with progressive cerebellar ataxia and later develop conjunctival telangiectases, other progressive neurologic degeneration, sinopulmonary infection and malignancies. Underdiagnosis or diagnostic delay of AT and its pulmonary complications contribute to morbidity and early mortality. We reported a patient who, due to a delay in diagnosis of AT, presented with bronchiectasis at the age of seventeen. To reduce the morbidity associated with AT, there needs to be greater awareness of the respiratory complications. Early management and monitoring lung function can minimize pulmonary damage.**

**Key words:** Adolescent, ataxia-telangiectasia, bronchiectasis.

## INTRODUCTION

Ataxia-telangiectasia (AT) is a rare autosomal recessive multisystem disorder characterized by progressive cerebellar ataxia, oculocutaneous telangiectasia, recurrent sinopulmonary infection, variable humoral and cellular immunodeficiency, high incidence of mainly B lymphoid malignancy and hypersensitivity to ionizing radiation (Chun et al., 2004).

AT has been estimated to occur 1 in 40,000-100,000 individuals and results from mutations in a single gene, ataxia telangiectasia mutated (Bezerra et al., 2001). Ataxia-telangiectasia patients are prone to recurrent sinopulmonary infections as a result of a variety of cellular and humoral immunodeficiencies (Canny et al., 1988).

Here, we report a patient who developed bronchiectasis as a consequence of the delayed diagnosis of AT at the age of seventeen.

## CASE REPORT

A 17-year-old boy was admitted to our clinic with a 20

day history of cough. He was born term as the 6th child of healthy parents who are first cousins. Although there were several consanguineous marriages in the family, no genetic disorder was observed. His first sibling had died from unknown causes. He displayed normal early developmental milestones and walked at the age of 1 year. He had no history of recurrent or chronic sinopulmonary infections and was on no medication.

At the age of 7, he had presented with complaints of unsteady gait. 1 month after the onset of this symptom, he developed fever and vomiting and he was diagnosed with meningitis and treated with antibiotics. During his treatment at the hospital, he had additional symptoms such as impaired control of the head and neck. Ocular-motor apraxia was manifested at the age of eight years. Later, he had regression in developmental milestones, progressive ataxia and dysarthria. Ataxic walk was diagnosed at the age of 7, remaining stable until the age of 11. When it became progressive, he became accentuated at the age of 12 and was unable to walk at the age of 13.

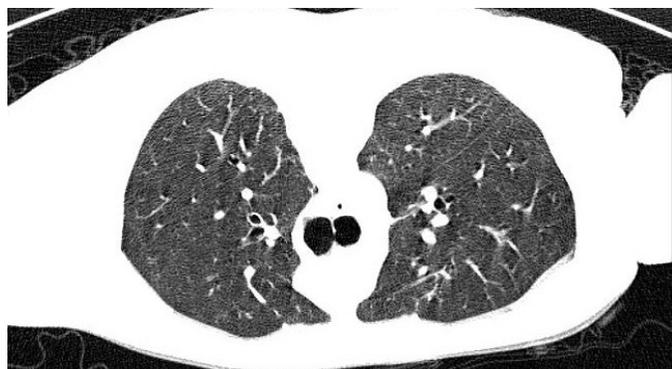
At the age of 13, ocular telangiectatic blood vessels appeared; however, the diagnosis of ataxia-telangiectasia was delayed until age seventeen.

On physical examination, the patient had a typical phenotype comprising an expressionless face and dysarthric

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**Figure 1.** Dilated blood vessels on both sides of the bulbar conjunctiva.



**Figure 2.** CT scan showing bronchiectasis.

speech. His weight was below the 3rd percentile. He had telangiectatic vessels on the bulbar conjunctivae, diminished breath sounds, crackles in the right hemithorax, pectus excavatum and disturbed cerebellar function tests (Figure 1). Neurologic examination showed ocular-motor apraxia, slurred speech with normal intellectual development. He had impaired control of the head and neck, and skilled movements. He had difficulty grasping objects because of marked dysmetria. He was unable to walk. The patellar and ankle reflexes were barely elicited, and there was severe weakness and wasting of the lower extremities.

Initial laboratory workup revealed the following: peripheral blood smear was normal, hemoglobin 13.2 g/dL, white blood cell count  $26,100/\text{mm}^3$ , platelets  $262 \times 10^3/\text{mm}^3$ , normal urinalysis and blood biochemistry panel. Serum Alfa Fetoprotein (AFP) was elevated (262

ng/ml, normal 0-4). Immunoglobulin (Ig) G1 (4.46 g/l), G2 (0.405 g/l), G4 (0.0707 g/l) levels were low according to the age. Ig G3 (0.33 g/l), Ig E (18.3 IU/mL), Ig A (1.84 gr/l), IgM (1.77 gr/l) levels were normal. Magnetic resonance imaging of brain under sedation was normal. Echocardiography was also normal.

The diagnosis of ataxia telangiectasia in our patient was made by clinical and laboratory findings. The patient was hospitalized with the initial diagnosis of pneumonia. The patient was started on ceftriaxone two times daily intravenously (75 mg/kg), plus clarithromycin two times daily orally (15 mg/kg) for pneumonia. Treatment with intravenous gammaglobulin 400 mg/kg for 3 weeks was started. Chest computed tomography showed minimal pneumothorax, a subpleural bullous lesion measuring  $1 \times 1$  cm on the right lung apex, cystic bronchiectatic changes on the basal segments of the right lung and consolidation area on the inferior posterobasal segment of the right lung (Figure 2). He was discharged after the successful treatment of pneumonia. The patient was started on prophylactic infusions of intravenous immunoglobulin 400 mg/kg every 3 weeks.

## DISCUSSION

Ataxia-telangiectasia is characterized by a wide variety of progressive clinical features: neurodegeneration, sinopulmonary manifestations, oculo-cutaneous telangiectasis, progeric hair and skin change, growth retardation, endocrine abnormalities including diabetes and ovarian-digenesis, susceptibility to lymphoreticular neoplasm, immunodeficiencies, clinical and cellular radio sensitivity, and chromosomal instability (Cabana et al., 1998). The

clinical diagnosis of AT can be problematic before the appearance of telangiectases. Oculomotor apraxia is a useful aid to early clinical diagnosis. Elevated levels of AFP and carcinoembryonic antigen are the most useful readily available markers for confirmation of the diagnosis of AT (Swift et al., 1991). Serum AFP is increased in 90 to 95% of the cases in AT but generally not beyond the range of 300-400 ng/mL and is considered a disease marker, suggesting immaturity of the liver (Regueiro et al., 2000). Dysgammaglobulinemia, decreased cellular immune responses, and peripheral lymphopenia are supportive findings for AT. Our patient diagnosed AT through symptoms and findings: ataxia, telangiectasies, Ig G subgroup deficiency and increased AFP level.

The most common humoral immunological defects in AT are diminished or absent serum IgA and IgG2 and impaired antibody responses to vaccines (Canny et al., 1988). 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 (Popa et al., 2002). Increased IgM levels and gammopathy may occur in AT (Nowak-Wegrzyn et al., 2004).

Pulmonary infections in AT are usually caused by viruses during the first two years of life, and by common bacterial pathogens in later childhood, such as *Hemophilus influenzae*, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*. These common infections are often correlated with the severity of humoral defect, and hence are the rationale for using gamma-globulin (Popa et al., 2002). However, the treatment chosen for our patient was intravenous gammaglobulin administration every three weeks which is commonly recommended. The development of safe and effective intravenous preparations of immune globulin represents a major advance in the treatment of patients. The overall consensus is that high-dose IVIG (at least 400/mg/kg/month) is superior to lower doses and most clinicians aim to maintain trough Ig G levels above an arbitrary level of 5 g/l. The annual cost of intravenous preparations of immune globulin at a dose of 400 mg/kg/month is about £4500 for a 70kg adult and about £650 for a 10 kg infant. (Haeney, 1994).

Recurrent pneumonia results in progressive bronchiectasis and advanced lung disease (Nowak Wegrzyn et al., 2004). Pulmonary status is a prognostic factor for AT: 50% of patients die in adolescence from overwhelming bronchopulmonary disease (Canny et al., 1988).

Under-diagnosis or diagnostic delay of AT and its pulmonary complications contribute to morbidity and early mortality (Cabana et al., 1998). This disease needs to be managed by a specialist multi - disciplinary team whose members work in close coordination (Bott et al., 2006). Bronchiectasis has emerged in our patient because of diagnostic delay of AT.

Like in other common variable immune deficiency, morbidity of AT is most commonly due to acute-chronic respiratory infections, leading to respiratory failure (Popa et al., 2002). Improved assessment of pulmonary status can prevent some complications in AT (Bott et al., 2006). There has been emphasis on the role of intravenous immunoglobulin treatment in reducing acute infections and improve lung function in variable immune deficiency (Popa et al., 2002)

In conclusion, to improve morbidity and mortality in AT, there needs to be heightened awareness amongst physicians and involvement of respiratory expertise at an early stage. Hence, the development of irreversible pulmonary changes may be limited and early mortality due to lung disease in AT may be decreased.

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