Ataxia telangiectasia with abnormal cellular immunity

Omar M Alakloby, Saeed A Al-Ghamdi, Abdullah M Al-Adnan, Mohammad H Al-Qahtani, Raidah S Al-Baradie, Obied E Obeid

ABSTRACT

Introduction: Ataxia telangiectasia (AT) is an autosomal recessive syndrome characterized by progressive cerebellar ataxia, immunodeficiency, which usually takes the form of sinopulmonary infections, oculocutaneous telangiectasia, X-ray hypersensitivity, and predisposition to lymphoid malignancies. Case Report: A case of ataxia telangiectasia in a Yemeni boy with cerebellar atrophy, mottled pigmentation, scarring, recurrent sinopulmonary infections, and elevated alpha-fetoprotein. Conclusion: Ataxia telangiectasia should be suspected in the presence of progressive gait deterioration, recurrent sinopulmonary infections, inverted T4/T8 ratio, reduced B-cell count and ocular/oculo-cutaneous telangiectasia and abnormal cellular immunity. Elevated alpha-feto protein is a confirmatory test and should be done in all patients with AT.

Keywords: Ataxia Telangiectasia, Immunodeficiency, Alpha-feto protein, Cellular immunity

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INTRODUCTION

Ataxia Telangiectasia is an autosomal recessive multisystem disease characterized by progressive cerebellar ataxia, oculocutaneous telangiectasia, X-ray hypersensitivity, predisposition to lymphoid malignancies, variable immunodeficiency and susceptibility to sinopulmonary infection. The probable incidence of ataxia-telangiectasia is about 1 case in 100,000 births [1]. Mutated gene is localized on chromosome, 11q22-23 [2]. Cells of AT patients have chromosomal instability and hypersensitivity to DNA-damaging agents such as X-rays and radiomimetic agents such as bleomycin [3]. AT is classified into four types: Type I is the classical syndrome with all manifestations, Type II lacks some of the typical findings but shows radiosensitivity, Type III has the classic clinical findings but is not radiosensitive and Type IV shows only some clinical features and is not radiosensitive.

CASE REPORT

A 7-year-old Yemeni boy was admitted to the pediatric ward of King Fahd Hospital of the University
Al-Khobar, Saudi Arabia, with bronchopneumonia and failure to thrive.

This patient had a history of frequent hospital admissions because of bronchopneumonia. He had also recurrent otitis media and progressive gait deterioration since he was two years old. No history of similar problems was present in the family, and his parents were first degree relatives.

There was a history of severe varicella infection three years prior to presentation which required two weeks of hospital admission.

On examination patient has respiratory distress with decreased chest expansion bilaterally with inspiratory and expiratory crackles. He has conjunctival telangiectasia (Figure 1), abnormal gait, paper like atrophic scars involving most of his skin, mottled pigmentation on the trunk and extremities (Figure 2), cautery marks on the abdominal wall (Figure 3) as it is one of the most ancient forms of therapy used by the Arabs over centuries for various recalcitrant diseases, and facial hypertrichosis.

Laboratory investigations showed leukocytosis with predominant neutrophils (73%); flow cytometry analysis shows inverted CD4/CD8 ratio (820/2067) with increased T cell count. B cell count was markedly decreased with CD19 marker being 74 cells/μl (1%) (reference range: 300–500/μl) (Table 1); there was high expression of DR on CD3+, denoting T cell activation; immunoglobulins levels were within normal limits except high levels of IgG as a result of secondary immune response to infection (Table 2); there was abnormal expression of gamma/delta TCR on CD3+; high level of alpha-fetoprotein (408 ng/ml); brain MRI showed mild cerebellar atrophy (Figure 4) and chest CT scan showed cystic changes in the lung due to bronchiactatic and fibrotic changes resulting from repeated pulmonary infection.

**DISCUSSION**

Boder and Sedgwick [4] coined the term Ataxia-Telangiectasia when they defined the disease as a distinct syndrome in 1957. Ataxia is presenting symptom in this syndrome, being evident when the child begins to walk at the end of the first year of life, manifesting ataxic gait and truncal movements [5]. Our patient started walking late at 20 months of age. He started to have truncal ataxia which gradually worsened with age, but now he walks with support. His Magnetic resonance imaging (MRI) demonstrated a mild cerebellar atrophy. A selective atrophy involving lateral portions (middle cortex) of the hemispheres was favored by Tavani et al. who also suggested that the neurological deterioration is correlated to the degree of atrophy [6].

Telangiectasia is a second major clinical manifestation of the disease. It usually has a later onset than ataxia, occurring between two and eight years of age usually on ocular sclera [5]. In our patient telangiectasia was first noticed at seven years of age and it involved the bulbar area and extended to the corneal border. Other ophthalmologic examination was unremarkable.

By reviewing the literatures, the cutaneous changes seen in patients with Ataxia Telangiectasia include cutaneous telangiectasias, mottled hyperpigmentation

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**Figure 1:** Conjunctival telangiectasia.

**Figure 2:** Paper like atrophic scars and mottled pigmentation.

**Figure 3:** Cautery marks on the abdominal wall.
AT is a highly variable primary immunodeficiency, involving both cellular and humoral immunity [11]. Although early publications correlated AT with the selective deficiency of IgA, the immunity disorders that these patients can show are very diverse and do not always correlate with the clinical expression of the immunodeficiency [10, 12]. Our patient had normal immunoglobulin level except IgG elevation as a result of secondary immune response to infection; he had frequent sinopulmonary infections and otitis media, the most frequently isolated infection was streptopneumonia as in other studies [12]. The repeated infections seen in our patient could be explained by the low level of B-cells and the inverted CD4/CD8 ratio.

Over expression of DR on CD3+ T cells is a sign of T cell activation as a result of infection.

Patients with ataxia-telangiectasia have an elevated incidence of cancers, approximately 100-fold in comparison to the general population. In children, more than 85% of neoplasms are acute lymphocytic leukemia or lymphoma. In adults with ataxia-telangiectasia, solid tumors are more frequent [13].

**CONCLUSION**

Ataxia telangiectasia should be suspected in the presence of ataxia, ocular/oculo-cutaneous telangiectasia and abnormal cellular or humeral immunity in early childhood. Immunological abnormalities in AT are inconsistent and could involve B-cells or any T-cell subtype both qualitatively or quantitatively. Elevated alpha-feto protein is a confirmatory test and should be done in all patients with AT.

**Author Contributions**

Omar M Alakloby – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Saeed A Al-Ghamdi – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Abdullah M Al-Adnan – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Mohammad H Al-Qahtani – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Raidah S Al-Baradie – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

and hypopigmentation, a poikilodermatous appearance [7]. Other pigmentary changes include Café au Lait spots, multiple ephelides and vitiligo. Hypertrichosis, alopecia areata, multiple verrucae, atopic dermatitis, keratitis pilaris and acanthosis nigricans have also been described in patients with AT. Scalp hair often becomes coarse and brittle with diffuse graying [8].

There was no cutaneous telangiectasia in our patient, but he has mottled pigmentary changes on the trunk and extremities and atrophic scars with variable sizes involving wide areas of the skin. It is difficult to tell whether the atrophic scars related to the previous varicella infection or an independent finding, but according to parents the scars following varicella were limited.

Alfa-fetoprotein (AFP) level was high (408 nm/ml) which is a confirmatory test that support our diagnosis of AT. AFP is a human fetal serum protein is found at levels of <10 ng/ml in children more than one year of age [9]. Elevated serum alpha fetoprotein (AFP) is seen in more than 95% of patients with AT [11]. AFP testing has been recommended by some researchers in all toddlers and children with undiagnosed progressive ataxia [9–10].

**Table 1:** Laboratory investigations.

| **Complete blood count Normal Range** |  |
|--------------------------------------|--|
| Leukocyte count | 85.4x10³/µl | 5–15x10³/µl |
| Neutrophils | 87% | 8.5% – 71.5% |

**Table 2:** Immunoglobulin levels.

| **Immunoglobulin** | **Result** | **Normal range** |
|---------------------|------------|------------------|
| IgA | 257 mg/dL | 70–400 mg/dL |
| IgG | 1830 mg/dL | 700–1600 mg/dL |
| IgE | 1.11 IU/ml | 0–52 IU/ml |
| IgM | 164 mg/dL | 40–230 mg/dL |

Figure 4: Brain MRI showed mild cerebellar atrophy.

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Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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