Ataxia telangiectasia (A-T) is a primary immunodeficiency disorder characterized by recurrent sinopulmonary infections, oculocutaneous telangiectasia, progressive neurodegeneration and cerebellar ataxia. It is an autosomal recessive disorder. Patients with A-T have an increased risk of malignancies including heterozygous carriers who may otherwise be phenotypically normal. Benign tumors such as leiomyoma have also been reported rarely in A-T patients. We report a young child with A-T who was followed up as combined immunodeficiency, subsequently developed ataxia, telangiectasia and later developed leiomyoma of the liver, a hitherto unreported malignancy in A-T.

ABSTRACT

Ataxia telangiectasia (A-T) is a primary immunodeficiency disorder characterized by recurrent sinopulmonary infections, oculocutaneous telangiectasia, progressive neurodegeneration and cerebellar ataxia. It is an autosomal recessive disorder. Patients with A-T have an increased risk of malignancies including heterozygous carriers who may otherwise be phenotypically normal. Benign tumors such as leiomyoma have also been reported rarely in A-T patients. We report a young child with A-T who was followed up as combined immunodeficiency, subsequently developed ataxia, telangiectasia and later developed leiomyoma of the liver, a hitherto unreported malignancy in A-T.

KEYWORDS

Ataxia Telangiectasia; Leiomyoma; Immunodeficiency; Malignancy; Pneumonia

INTRODUCTION

Ataxia telangiectasia (A-T) is a primary immunodeficiency disorder with autosomal recessive mode of inheritance. It is a multi-system disorder characterized by recurrent sinopulmonary infections, oculocutaneous telangiectasia, progressive neurodegeneration and cerebellar ataxia. Patients with A-T have an increased risk of malignancies (acute leukemia and lymphoma) including heterozygous carriers who may otherwise be phenotypically normal (1,2). Benign tumors such as leiomyoma have also been reported rarely in A-T patients (3-5). We report a young child with A-T who developed leiomyoma of the liver, a hitherto unreported malignancy in A-T.

CASE REPORT

A 2-year-old boy who had been symptomatic since the age of 1 year and he first presented to our institute in 2010. He had been failing to thrive, and had had recurrent episodes of fever, cough and loose stools. He had been worked up for cystic fibrosis – sweat chloride was 25mEq/l and Δ508 mutation was negative. He was born to a 4th degree consanguineously married parents. His elder sister had had similar complaints to which she succumbed at the age of 9 years. She had also been evaluated for a primary immunodeficiency disorder but no definite diagnosis could be established.

Investigations carried out in the index patient in 2010 showed hemoglobin 117 gm/L, total leucocyte counts (TLC) 7.6×10^9/L and absolute lymphocyte count (ALC) 0.7×10^9/L (2.3-5.4×10^9/L). Nitroblue tetrazolium dye reduction test was normal. Immunoglobin profile showed low IgG (<2.10 g/L), low IgA (<0.36 g/L) and normal IgM (0.70 g/L). Immunophenotyping showed low CD3+ T cells – profile showed low IgG (<2.10 g/L), low IgA (<0.36 g/L) and normal IgM (0.70 g/L). Immunoglobulin absolute lymphocyte count (ALC) 0.7×10^9/L (2.3-5.4×10^9/L). Hemoglobin 117 gm/L, total leucocyte counts (TLC) 7.6×10^9/L and C-reactive protein (CRP) 3.43 mg/L. Immunoglobulin profile (post IVIG) revealed IgG 9.27 gm/L (5.4-16.1), IgA 0.2 gm/L (0.5-2) and IgM 0.68 gm/L (0.5-1.8). Plasma protein revealed immunoglobulin (Ig) and complement (C3 and C4) levels were normal, IgM was normal and C-reactive protein was negative.

He presented again in 2015 at the age of 6 years with tachypnea and cough. On examination, he was found to have pallor, generalized lymphadenopathy (largest node, posterior cervical 2x1 cm), clubbing (grade 3), oral thrush, onychomycosis, telangiectasia on bilateral bulbar conjunctiva and right pinna (Fig.1) and cerebellar ataxia. Rest of the examination was unremarkable. Laboratory investigations revealed hemoglobin 125 gm/L, TLC 9.2x10^9/L (P, L, M, E), lymphopenia (absolute lymphocyte count: 0.5-10^9/L), platelets 699x10^9/L and C-reactive protein (CRP) 3.43 mg/L. Immunoglobulin profile (post IVIG) revealed IgG 9.27 gm/L (5.4-16.1), IgA 0.2 gm/L (0.5-2) and IgM 0.68 gm/L (0.5-1.8). CD40 expression on B lymphocytes and CD40 ligand expression on T lymphocyte was normal; immunophenotyping for T, B and NK cells were normal.

Possibility of combined immunodeficiency was considered. Cotrimoxazole prophylaxis was initiated and monthly IVIg infusions were advised. The parents, however, were unable to continue the prescribed treatment due to financial constraints.

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serology and serum galactomannan were negative. Scraping from nail on KOH mount showed mycelial elements. Bronchoscopy showed two masses in the opening of right middle and left upper and lingular lobe openings (Fig. 1). Broncho alveolar lavage fluid examination revealed acid fast bacilli.

He was empirically initiated on broad spectrum antimicrobials (cefoprazone-sulbactam, cefoxolin and amikacin) and antifungals (amphotericin B) to which he responded well. He was also initiated on anti-tubercular therapy (isoniazid, rifampicin, ethambutol and pyrazinamide).

On follow-up, his cough improved but he continued to have hypodense lesions in liver and spleen despite adequate anti-tubercular therapy. He underwent an open surgical biopsy from the most superficial hypodense lesion in the liver. The histopathology examination of excised mass revealed well encapsulated tumor with elongated cells arranged in long and short fascicles with cigar shaped nuclei, conspicuous nucleoli, eosinophilic cytoplasm, frequent mitosis and tumor cells positivity for smooth muscle actin (SMA). These findings were consistent with atypical leiomyoma (Fig. 2). No specific treatment was given for leiomyoma and he was continued on cotrimoxazole, itraconazole and isoniazid prophylaxis and monthly replacement IVIg infusions. Six months later, he suffered an episode of severe pneumonia and he succumbed to this illness.

**DISCUSSION**

A-T is a relatively rare multisystem autosomal recessive primary immunodeficiency disorder. Our patient had recurrent episodes of diarrhea and pulmonary infections, ataxia, oculo-cutaneous telangiectasia and high serum alpha fetoprotein. As per the European Society for Immunodeficiency (ESID) diagnostic criteria (6), index child is probable case of A-T. He also had profound and persistent lymphopenia with low T and B lymphocytes and low IgG and IgA immunoglobulin levels. The protein encoded by ATM gene has multiple functions like signal transduction, intracellular protein transport, and cell cycle control (7,8). Due to defect in V(D)J recombination of immunoglobulin(Ig) and T-cell receptor genes, both humoral and cell mediated immunodeficiencies have been recognized in patients with A-T. Studies have shown that A-T patients can have decreased or absent serum immunoglobulins, impaired antibody response, lymphopenia and impaired lymphoproliferative response (9-11). A-T patients have predisposition for benign as well as malignant tumors (1,2). A retrospective large cohort study on 279 A-T patients by Suraz et al has documented cancers in 69 (24.5%) patients. Among these, acute leukemias, lymphoma, germ cell tumors (including testicular cancer), breast cancer, and Ewing's sarcoma were the most common malignancies. In a recent study (12), A-T patients have been shown to have decreased or absent serum immunoglobulins, impaired antibody response, lymphopenia and impaired lymphoproliferative response (9-11). A-T patients have predisposition for benign as well as malignant tumors (1,2). A retrospective large cohort study on 279 A-T patients by Suraz et al has documented cancers in 69 (24.5%) patients. Among these, acute leukemias, lymphoma, germ cell tumors (including testicular cancer), breast cancer, and Ewing's sarcoma were the most common malignancies. In a recent study (12), A-T patients have been shown to have decreased or absent serum immunoglobulins, impaired antibody response, lymphopenia and impaired lymphoproliferative response (9-11).

**REFERENCES**