ORIGINAL RESEARCH PAPER
Volume-9 | Issue-1 | January-2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ATAXIA TELANGIECTASIA WITH LIVER LEIOMYOMA: A RARE OCCURRENCE

Paediatrics

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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 has 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 has 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 ($2.3\text{-}5.4\times10^9$/L). Nitroblue tetrazolium dye reduction test was normal. Immunoglobulin 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 - 25.6% (60-80%) and low CD19+ B cells- 4.05% (10-40%). 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.

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 $9.2\text{x}10^9$/L ($P_{76}L_6M_{17}E_1$), lymphopenia (absolute lymphocyte count: 0.5×10^9/L), platelets $699\text{x}10^9$/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). CD40 expression on B lymphocytes and CD40 ligand expression on T lymphocyte was normal; immunophenotyping for T, B and NK cells showed low CD3+ T cells- 16.48 % (55-78%), low CD19+ B cells- 2.06 % (10-31%) and elevated CD56+ CD16+ NK cells- 72.93 % (4-26%). His serum alpha fetoprotein was 146.6 ng/ml (<8.5). Computed tomography (CT) chest and abdomen showed collapse consolidation in bilateral lung fields with multiple hypodense lesions in liver and spleen (Fig.1). Ultrasonography (USG) abdomen showed heterogeneous hypoechoic lesion (3.2x1.8 cm) in left lobe of liver and well defined circular hypoechoic lesion (2.5x 2.5 cm) in lower pole of spleen. Ultrasound guided aspiration from these liver lesions, however, did not reveal any bacterial or fungal organism. His blood culture was sterile. Fungal

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 (cefoperazone-sulbactam, cloxacillin and amikacin) and antifungals (amphotericin B) to which he responded well. He was also initiated on anti-tubercular therapy (isoniazid, rifampicin, ethambutol and pyrazinamide).

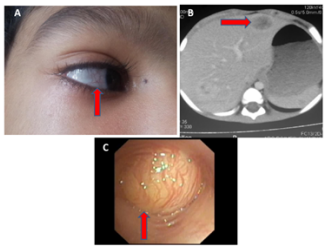
On follow-up, his cough improved but he continued to have hypodense lesions in liver and spleen despite adequate anti-tubercular therapy. He underwent an open surgical biopsy from the most superficial hypodense lesion in the liver. The histopathology examination of excised mass revealed well encapsulated tumor with elongated cells arranged in long and short fascicles with cigar shaped nuclei, conspicuous nucleoli, eosinophilic cytoplasm, frequent mitosis and tumour 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 immunoglobin 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 Surarez et al has documented cancers in 69 (24.5%) patients. Among these, acute leukemias, Hodgkin lymphoma (HL), non-Hodgkin lymphoma were seen in 8, 12 and 38 patients respectively (12). Our patient had leiomyoma of liver (Fig. 2). Laryngeal leiomyosarcoma and jejunal cellular leiomyoma (3), splenic leiomyoma (4) and leiomyoma of suprarenal gland (5) has been reported in patients of A-T but leiomyoma of liver has never been reported earlier. Primary liver leiomyoma is rare and secondary leiomyoma of liver have been reported in immunosuppressive states like patients on immunos uppressive therapy and human immunodeficiency virus infection (13,14). Surgical resection of the tumor is both diagnostic and curative with excellent prognosis (15). Our patient probably also had lung leiomyoma but due to an apparently increased vascularity of the mass as seen during bronchoscopy, a biopsy could not be done.

We conclude that, though A-T patients have predisposition for malignancies and leiomyoma of other sites of body has been reported rarely, to best of our knowledge this is the first case of liver leiomyoma associated with A-T. Liver leiomyoma should be considered as a differential diagnosis of liver lesions in A-T patients and histopathological examination of the tissue specimen is imperative for diagnosis.

FIGURES:



Figures:1 A, Telangiectasia in right eye of the child; B, Computed tomography abdomen showing heterogeneous hypoechoic lesion in left lobe of liver; C, Bronchoscopy showing mass in the opening of right middle lobe.

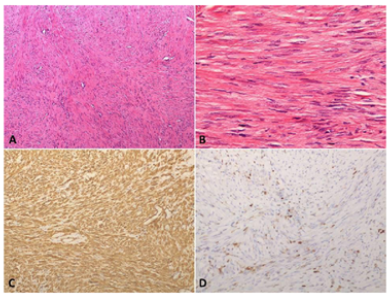


Figure 2: A,Cellular tumor with cells arranged as long and short intersecting fascicles (H&E, 100X); B, The tumor cells are spindle shaped with cigar shaped nuclei with blunt ends and densely eosinophilic cytoplasm (H&E, 400X); C, The tumor cells are positive for smooth muscle actin (IHC, 200X); D, Ki67 immunostain highlilghts increased mitotic activity by the tumor cells (IHC, 200X).

ACKNOWLEDGEMENT:

First authors: Dr. Sandesh Guleria, Dr Ankur kumar Jindal, Dr. Ankur Dharmani

REFERENCES

1. Swift M, Reitnauer PJ, Morrell D, Chase CL. Breast and other cancers in families with ataxia-telangiectasia. N Engl J Med 1987;316:1289–94.
2. Easton DF. Cancer risks in A-T heterozygotes. Int J Radiat Biol 1994;66: 177–82.
3. Reyes C, Abuzaitoun O, De Jong A, Hanson C, Langston C. Epstein-Barr virus-associated smooth muscle tumors in ataxia-telangiectasia: a case report and review. Hum Pathol 2002;33:133-6.
4. Coşkun M, Aydingöz U, Tacal T, Ariyürek M, Demirkazik F, Oğuzkurt L. CT and MR imaging of splenic leiomyoma in a child with ataxia telangiectasia. Pediatr Radiol. 1995; 25:45-7.
5. Mouchet F, Ninane J, Gosseye S, Verellen C, Bonnier C, Evrard P, et al. Leiomyoma of the suprarenal gland in a child with ataxia-telangiectasia. Pediatr Hematol Oncol 1991; 8:235-41.
6. European Society for Immunodeficiency, 2005. http://esid.org/Resources/Ataxia-Telangiectasia (accessed December 29, 2015).
7. Lavin MF, Shiloh Y. The genetic defect in ataxia-telangiectasia. Annu Rev Immunol 1997;15:177-202.
8. Kastan MB, Lim DS. The many substrates and functions of ATM. Nat Rev Mol Cell Biol 2000;1:179-86.
9. Ersoy F, Berkel AI, Sanal O, Oktay H. Twenty-year follow-up of 160 patients with ataxia-telangiectasia. Turk J Pediatr 1991;33:205-15.
10. Sanal O, et al. Impaired IgG antibody production to pneumococcal polysaccharides in patients with ataxia-telangiectasia. J Clin Immunol 1999;19:326-34.
11. Peterson RD, Cooper MD, Good RA. Lymphoid tissue abnormalities associated with ataxia-telangiectasia. Am J Med 1966;41:342-59.
12. Suarez F, Mahlaoui N, Canioni D, Andriamanga C, Dubois d'Enghien C, Brousse N, et al. Incidence, presentation, and prognosis of malignancies in ataxia-telangiectasia: a report from the French national registry of primary immune deficiencies. J Clin Oncol 2015;33:202-8.
13. Penn, "Malignancies associated with immunosuppressive or cytotoxic therapy," Surgery, vol. 83, no. 5, pp. 492–502, 1978.
14. Lee ES, Locker J, Nalesnik M, Reyes J, Jaffe R, Alashari M, et al., "The association of Epstein-Barr virus with smooth-muscle tumors occurring after organ transplantation". N Engl J Med 1995; 332:19–25.
15. Omiyale AO. "Primary leiomyoma of the liver: a review of a rare tumour," HPB Surgery 2014, Article ID 959202, 8 pages, 2014. doi:10.1155/2014/959202.