

Cutaneous granulomas in a child with Ataxia telangiectasia - A rare association

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Abstract

Ataxia-telangiectasia (AT) is an autosomal recessive disorder due to defective DNA damage repair. It is characterized by progressive cerebellar ataxia, oculocutaneous telangiectasias and immune system dysregulation resulting in recurrent and progressive sino-pulmonary infections. We present a case of a 4 year old male child with delayed motor development and recurrent sino-pulmonary infections and complaints of multiple asymptomatic plaques over knees and nodules over elbows since 3 years. On investigations and genetic testing he was diagnosed as a case of AT. Biopsy of the lesion over knees showed non-infectious granulomas. We report the case owing to rarity of association of non-infectious cutaneous granuloma with AT.

Key words

Ataxia-telangiectasia, cutaneous granulomas, immune dysregulation.

Introduction

Ataxia telangiectasia (AT) is a rare multisystem disorder characterized by progressive neurologic degeneration, distinctive oculocutaneous lesions and selective immunodeficiencies.¹ The prevalence of AT has estimated to be 1 in 100,000 cases.² Till now only 22 cases of AT with cutaneous granulomas have been reported in the literature.³ Patients with AT have variable dysfunction of both humoral and cell-mediated immunity, as demonstrated by an immature thymus; low levels of IgA, IgE, IgG2, and IgG4; and a poor response to antigenic challenge. They have a high risk of cancer and have recurrent or

chronic sino-pulmonary disease.¹ Several cutaneous lesions have been described in patients with AT, especially the telangiectasias, pigmentary alterations, poliosis, and seborrheic dermatitis.^{4,5} Presence of non-infectious granulomas in patients of AT is said to be due to primary immune dysregulation.³

We report a case of 4 year old male child with the typical clinical and laboratory features of AT in whom cutaneous granulomas developed.

Case report

A 4 year old male child born out of a non-consanguineous marriage by full term normal vaginal delivery was referred to us with complaints of skin lesions over both the knees and elbows. Child was diagnosed as AT at a tertiary care paediatric hospital and was referred to us for cutaneous lesions.

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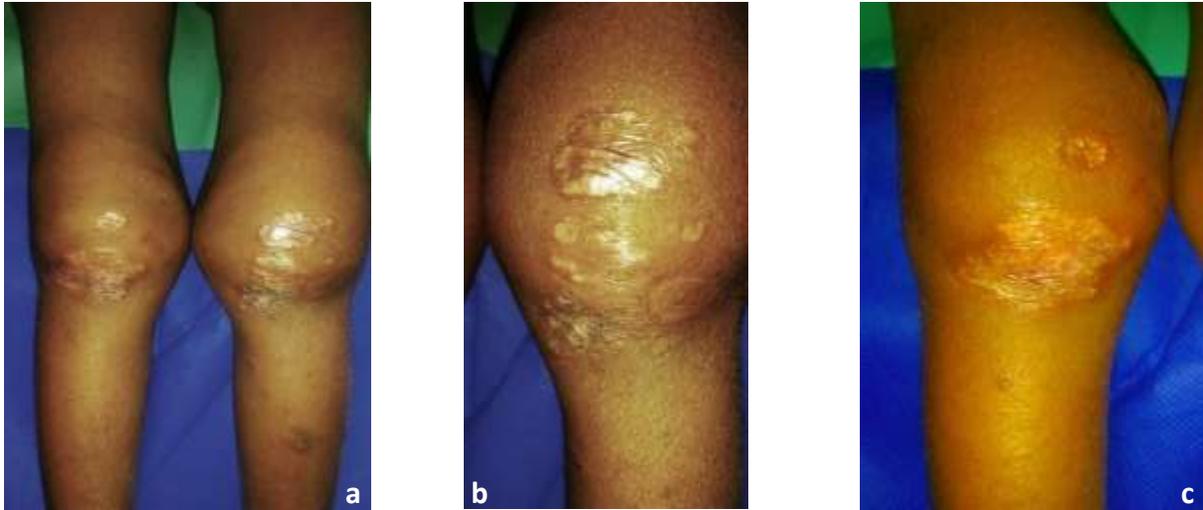


Figure 1a, 1b & 1c Well-defined annular scaly atrophic plaques on both the knees.



Figure 2a Multiple skin coloured papulo-nodules present over both the elbows.



Figure 2b Lesion on left elbow was showing slight atrophy at centre and hyperpigmentation at periphery.



Figure 3 A single café au lait macule was noted on the anterior trunk.

Child started having these lesions since the age of one year. They started first as asymptomatic symmetrical papulo-nodules and slowly progressed to scaly plaques first on knees followed by lesions on elbows. There is also a history of recurrent sino-pulmonary infections and delayed milestones of motor and speech development.

Examination revealed multiple well-defined annular scaly atrophic plaques varying from 1x 2 cm to 4x 5 cm on both the knees (**Figure 1a-1c**), multiple skin coloured papulo-nodules present

over both the elbows (**Figure 2a**). Lesion on left elbow was showing slight atrophy at centre and hyperpigmentation at periphery (**Figure 2b**). A single café au lait macule was noted on the anterior trunk (**Figure 3**). Ophthalmologic examination revealed telangiectasias over both the bulbar conjunctivae (**Figure 4**). The gait was clumpy, staggering and wide based. Slight torticollis of neck was noted. Other system examination was within normal limits.

Skin biopsy of the lesion from right knee was performed which showed unremarkable

Table 1 Laboratory findings like immunoglobulin profile, serum lipid profile and thyroid function test.

	Test value	Normal values
<i>Immunoglobulin profile (g/L)</i>		
IgA	0.179	0.7-4.0
IgG	1.495	7-16
IgM	2.54	0.4-2.3
α FetoProtein	28.8ng/ml	0.0-15.0
<i>Lipid profile (mg/dl)</i>		
Cholesterol-total	126	0-200
HDL	36	35-60
LDL	41.6	70-180
VLDL	48.4	7-40
TGs	242	0-150
Total cholesterol/ HDL ratio	3.5	0-4.0
LDL/HDL	1.2	0-3.5
<i>Thyroid function test</i>		
T3	189.8 pg/ml	80-253
T4	6.59mg/dl	6.1-12.6
TSH	1.73microIU/ml	0.55-7.1



Figure 4 Ophthalmologic examination revealed telangiectasias over both the bulbar conjunctivae.

epidermis with multiple granulomas in dermis composed of epithelioid histiocytes, lymphocytic infiltrate and occasional langhans type of multinucleated giant cell with no frank necrobiotic collagen bundles (**Figure 5 & 6**). Ziehl–Neelsen stain showed no acid fast bacilli (**Figure 7**) and periodic acid schiff (PAS) and gomorri methamine silver stain (GMS) for fungus was found to be negative.

Laboratory investigations showed low IgA and IgG and IgM was slightly elevated alpha-fetoprotein levels were elevated (**Table 1**).

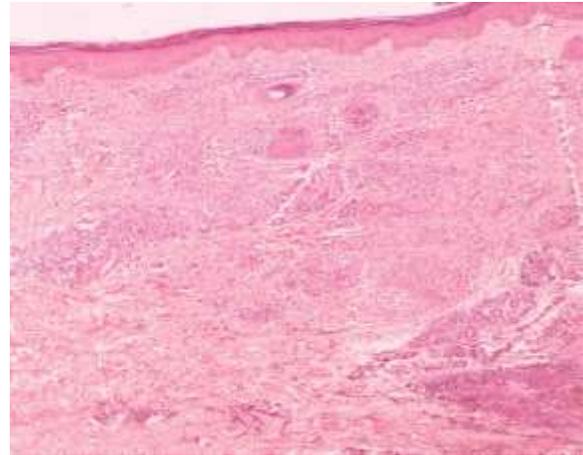


Figure 5 Low magnification view shows unremarkable epidermis with multiple granulomas in dermis (H & E, 4X).

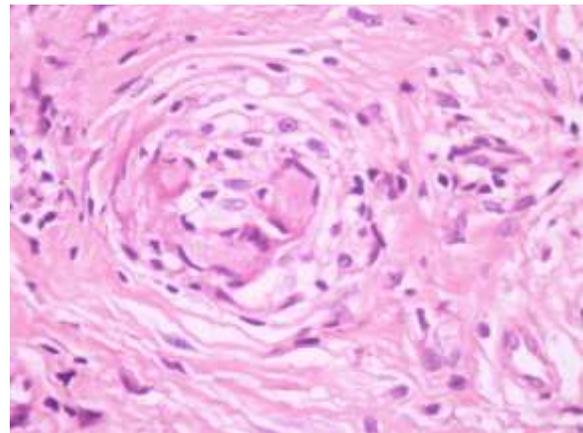


Figure 6 Higher magnification shows granulomas composed of epithelioid histiocytes, lymphocytic infiltrate and occasional langhans type of multinucleated giant cell with no frank necrobiotic collagen bundles (H & E, 40X).

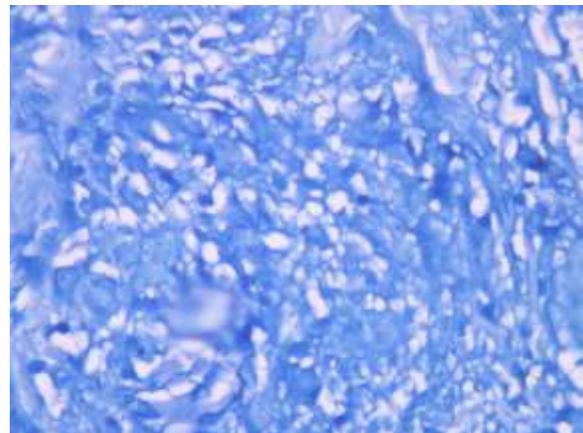


Figure 7 Ziehl–Neelsen stain showed no acid fast bacilli (Z-N stain, 40X).

Routine investigations like complete blood count, liver and renal function were normal. Mantoux test was negative. Thyroid profile was normal. Chest radiograph was normal and screening test for metabolic disorders was negative. Plain Magnetic Resonance Imaging (MRI) of brain showed no abnormality. Radiograph of bilateral hands with wrists showed increased peri-auricular soft tissue density in inter-phalangeal joints. Chromosomal analysis showed mutation in ATM gene on chromosome 11 thus confirming the diagnosis of AT.

Discussion

Ataxia telangiectasia also called as Louis-Bar syndrome is a rare autosomal recessive disorder caused by a disruption at chromosome 11q22-23, which encodes the ATM protein and is involved in DNA damage repair.³ It is characterized by progressive cerebellar ataxia, oculocutaneous telangiectasia, immunodeficiency, predisposition toward malignancy, elevated 1-fetoprotein levels and increased radiosensitivity.⁸

Characteristic cutaneous finding in AT are mucocutaneous telangiectasias seen on bulbar conjunctiva and on cutaneous are most prominent in facial areas. Other cutaneous findings include premature greying of hairs, café-au-lait spots and pigmentary changes like vitiligo, hypopigmented macules and poikilodermas.⁶

Cutaneous granulomas with unknown etiology are also been reported in association with AT.⁸

Cutaneous granulomas with unknown aetiology not related to infectious or systemic diseases occur uncommonly in various primary immunodeficiencies (PIDs).⁸ These granulomas are postulated to be due to impaired wound

healing, as evidenced by propensity of lesions to develop on trauma prone areas coupled with unopposed activity of CD T-cells or NK cells and immune dysregulation of macrophages due to the absence of naive T-cells.⁸

No therapy has proven effective in treating these lesions in patients of AT. Various topical treatments like steroids^{8,9}, tacrolimus¹⁰, antibiotics⁽¹⁾ and intralesional steroid¹⁰ but only limited or no improvement was seen.

Other treatments which have been tried in treatment of cutaneous granulomas in PIDs with inconsistent results are oral antifungals,^{8,10} thalidomide,¹⁰ etanercept and infliximab.¹⁰

In one case report lesions were completely healed after 6 week regimen of IVIG and topical steroid application.⁵

We present the interesting and rare case of a child with AT presenting with non-infectious cutaneous granuloma as a primary cutaneous manifestation of AT.

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