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Loeffler's Syndrome and Multifocal Cutaneous Larva Migrans

Case report of an uncommon occurrence and review of the literature

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Abstract

Cutaneous larva migrans (CLM) is a zoonotic skin disease that is frequently diagnosed in tropical and subtropical countries. Loeffler's syndrome (LS) is a transient respiratory ailment characterized by pulmonary infiltration along with peripheral eosinophilia and commonly follows parasitic infestation. We report here an interesting case of a patient presenting with LS that was attributed secondary to multifocal CLM. Treatment with seven-day course of oral albendazole (400mg daily) coupled with nebulization (levosalbutamol and budesonide) led to complete resolution of cutaneous lesions and respiratory complaints in two weeks. There was complete resolution of pulmonary pathology at 4 weeks follow-up. As there are only a few reported cases of LS associated with CLM, we also reviewed the literature on this rare association.

Keywords: Loeffler's syndrome; peripheral eosinophilia; cutaneous larva migrans; multifocal; disseminated; helminths, albendazole.

Introduction

Cutaneous larva migrans (CLM) is a distinct cutaneous entity that is relatively common in the warmer tropical and sub-tropical regions. It is characterized by tortuous skin lesions attributed

to epidermal burrowing by certain helminthic larvae.[1] Apart from the cutaneous affliction, this condition is rarely uneventful. On rare occasions, CLM can culminate into Loeffler's syndrome (LS), which is characterized by migratory pulmonary infiltrates and peripheral eosinophilia.[2] Here we describe an interesting case of LS associated with multifocal cutaneous larva migrans and review the literature on this uncommon association.

Case Report

An otherwise healthy 33-year-old gentleman presented with intense, non-productive cough for the last 7 days with occasional breathlessness on exertion. The pulmonary symptoms were accompanied by abrupt onset pruritic skin eruptions over chest and abdomen for the same duration. Recently he had returned from a vacation to a nearby coastal town where he had spent a significant time on the sandy beaches. There was no history of fever, hemoptysis, wheeze, chest pain, allergic rhinitis or relevant drug intake (prescription, over the counter or illicit). His primary care physician had initiated a 5-day course of oral azithromycin (500mg daily) without any significant improvement. His medical and family history was non-contributory. On general examination, he was afebrile, normotensive (126/78 mm Hg) with a saturation of 97% on room air. Bi-basilar crackles was appreciated on chest auscultation. Cutaneous examination revealed multiple discrete thread-like skin-coloured to erythematous serpiginous tract of various sizes (4 to 12 cm in length) distributed over the chest and abdomen. **(Figure 1)** Focal excoriation and pustules were noted over few lesions. Other mucocutaneous sites were uninvolved. Evaluation of other organ systems was uneventful.

Laboratory examination was notable for peripheral eosinophilia (absolute eosinophil count 2200 cells/μL). Stool examination for ova, parasite, and cyst was negative. Chest radiography showed ill-defined bilateral pulmonary infiltrates. A high-resolution computed tomography (HRCT) thorax revealed the presence of ground-glass opacities mainly in mid and lower zone of both lungs with predominant peripheral distribution. **(Figure 2a)** Based on suggestive history, characteristic clinical presentation, laboratory and radiological findings, the final diagnosis of Loeffler's syndrome secondary to multifocal cutaneous larva migrans was established. He was treated with oral albendazole (400mg) once daily for 7 consecutive days along with nebulization with levosalbutamol and budesonide as required. His respiratory symptoms and cutaneous lesions completely subsided in 2 weeks. There was complete radiological resolution at 4 weeks follow-up. **(Figure 2b)**

An informed written consent was obtained from the patient after full explanation regarding his images being published for academic interest. The patient did not have any objection regarding use of his images which may reveal his identity and gave due permission to use them.

Discussion

LS is a transient respiratory illness associated with peripheral eosinophilia as a response to parasitic infestation or medications.[3] *Ascaris lumbricoides* is most commonly implicated with the condition followed by *Trichuris*, *Strongyloides*, *Taenia saginata*, *Entamoeba histolytica*, and as a complication of chronic asthmatic states. However, it has rarely been reported with CLM. In 1946, Wright and Gold first described 26 patients with cutaneous larva migrans who developed Loeffler's syndrome.[4] Subsequently this rare complication of CLM has been reported only in handful of cases.[3, 5-16] Table 1 summarizes the previous published case report of CLM with LS.

CLM, also termed as "creeping eruption," is a parasitic infestation caused by the invasion and migration of parasitic larvae in the skin. The burrowing of the larva of *Ancylostoma braziliense*, *Ancylostoma caninum*, *Necator americanus*, *Uncinaria stenocephala* and *Strongyloides stenocephala* have been implicated in such creeping eruptions.[17] Adult hookworms infest the intestines of cats and dogs and their ova in excreta hatch under favourable conditions. These larvae then penetrate intact or abraded skin following exposure with soil contaminated with faeces. Humans act as an accidental dead-end host as the travelling parasite perishes, and the cutaneous manifestations usually resolve uneventfully within months. Warm, sandy, humid and shady fields, sandpits or sea shores are particularly favoured areas. This makes barefoot walkers, farmers, gardeners, hunters, hod carrier or beach visitors particularly susceptible to acquire the infestation. Exposed anatomical sites like hands and feet are usually affected. However, involvement of atypical locations like the buttocks, genitalia, scalp, and multifocal or disseminated lesions have also been rarely reported in the literature. Clinically an initial small reddish papule progresses to a serpiginous pruritic rash with a slow rate of progression from less than 1–2 cm/day.[1, 17-20] CLM may be complicated by secondary bacterial infection, allergic reaction, eczematisation, or very rarely LS. Concurrently or subsequently patient may develop non-productive cough, exertional breathlessness, exacerbation of pre-existing asthma which should raise the clinical suspicion of LS. Interestingly, a unique case of asymptomatic LS in CLM has been reported recently.[12]

The exact pathogenesis of pulmonary infiltrates in CLM remains poorly understood. The current understanding encompasses a systemic immunologic process in which hookworm in the skin leads to generalized sensitization. The lung reacts with the soluble larval antigen and produces the eosinophilic pulmonary infiltration. The complete resolution of pulmonary infiltrates and skin eruptions with oral anti-helminths supports this proposed mechanism.[21] Associated eosinophilia is teleologically related to the role of eosinophils in parasitic destruction. In parasitic infestation like CLM, eosinophilic chemotaxis may result from IgE-mediated reactivity against the infestant, direct chemotactic property of certain parasites, T-cell dependent mechanism, and immune-complex related.[13]

The differential diagnoses we considered for the cutaneous lesions included larva currens, migratory myasis, gnathostomiasis, cercarial dermatitis, allergic contact dermatitis, inflammatory tinea, and scabies. All the above mentioned conditions were ruled out based on history, and clinical examination. Loeffler's syndrome should be considered early in the differential diagnosis for community acquired pneumonia and asthma unresponsive to classic antibiotic therapy in individuals with associated cutaneous pruritic eruption. Pulmonary fibrosis and respiratory failure may rarely complicate LS.[3, 6, 7, 22]

The condition is primarily self-limiting but appropriate pharmacological intervention leads to faster resolution. Veraldi et al[23] reported a new therapeutic regimen of oral albendazole (400/day for 7 days) to be highly effective. Single dose therapy of oral ivermectin (200ug/kg) is equally effective with near 100% cure rates. Topical 10% thiabendazole may be used as an alternative. Opting for surgery or cryotherapy rarely proves to be effective. Sometimes supportive therapy like oxygen inhalation, systemic, or inhalational corticosteroids may be required to alleviate the respiratory symptoms.[4, 8, 9, 24]

Conclusion

In conclusion, we report this case to add to the existing literature on this rare association. LS secondary to multifocal CLM has rarely been documented previously. LS should be considered early in the differential diagnosis for respiratory complaints in association with pruritic cutaneous eruption especially in an individual having recently returned from a vacation at a tropical destination. In this era of global migration, physicians should be aware of the uncommon systemic manifestation of this uncommon tropical infestation and provide prompt treatment to avoid long-term complication.

Authors' Contribution

AS, DBB and AC drafted the manuscript. AS and SKB contributed to patient management, review of literature and critical revision of the manuscript. All authors approved the final version of the manuscript.

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191 **Table 1:** Comparison of clinical characteristics of previous case reports of Loeffler's syndrome
192 in association with cutaneous larva migrans

Case report (year)	Country	Age, sex	Travel / Exposure history	Location of CLM	Pulmonary symptoms	Absolute eosinophil count(mm^3)	Imaging finding (chest X-ray and/or CT scan)	Treatment	Outcome
Guill MA et al (1978)	USA	40,M and his spouse 36,F	Vacation in Gulf of Mexico	Feet	Non-productive cough, tightness in chest, exertional dyspnoea	7598 (male) and 2528 (female)*	Multiple patchy consolidations in lung fields (CXR)	Thiabendazole oral suspension, 0.1% triamcinolone acetonide cream (four times daily), symptomatic management for respiratory symptoms	Resolution after 8 weeks of onset of symptoms
Butland RJ et al (1985)	UK	58,F	Holiday trip to Barbados	Buttocks, legs and abdomen	Cough	3000	Ill-defined patchy shadowing in the left upper and middle zones (CXR)	Topical thiabendazole	Complete resolution within 2 months
Wong-Waldamez A et al (1995)	Guatemala	21,M	None	Disseminated bullous lesions over trunk and extremities (especially lower)	None	710	Diffuse miliary infiltrate in both lung fields (CXR)	Single dose albendazole (400 mg)	Resolution in one week
Del Giudice P et al (2002)	France	41,M	Holiday trip to Thailand	Left foot	Intense non-productive cough	1100	Ill-defined reticulonodular infiltrates in both lungs (CT scan)	Oral thiabendazole (25 mg/kg) twice daily for 10 days; oral corticosteroids 1 mg/kg daily	Complete resolution within 5 days
Schaub N et al (2002)	Switzerland	39, M	Holiday trip to Thailand	On the buttocks	Dyspnoea	1616	Bilateral diffuse ground-glass opacities (CXR; further confirmed on CT scan)	Oral albendazole 400 mg on 5 consecutive days and a single dose of oral praziquantel (3600 mg)	Complete resolution
TeBooij M et al(2010)	Netherlands	27, M	Holiday trip to Thailand	Both feet	Exacerbation of pre-existing asthma	2700	Small nodular granular infiltrates and linear paracardial opacities in both lungs (CXR)	Ivermectin, inhalation medication (budesonide/formoterol) andtopical potent steroid	Complete resolution
Tan SK et al (2010)	Singapore	47,M	Trip to beach holiday in Bali, Indonesia	Both feet and his right thigh and buttock	Dyspnea, wheezing and chest discomfort	2903	Reticulonodular infiltrates in the right middle and lingular lobes (CXR and CT scan)	Oral mebendazole (3 days) followed by Albendazole and intravenous hydrocortisone (5 days) with oxygen supplementation	Complete remission in 2 weeks
Darocha S et al (2011)	Poland	28,M	Trip to Sri Lanka	Both feet	Cough and dyspnoea at rest with exacerbation of asthma	3400	Multiple poorly defined consolidations and ground-glass attenuation areas, some of them peripherally involving bilateral upper and lower lobes (CT scan)	Salbutamol, nebulisation with budesonide, prednisolone, topical albendazole	Complete resolution on scheduled follow-up after 3 months
Podder I et al(2016)	India	30,M	Agriculturist	Both hands	Non-productive cough	5200	Fleeting opacities (CXR)	Oral albendazole (400 mg/day) for 5 days	Complete resolution

					occasional exertional breathlessness				
Wang S et al (2017)	China	6,M	Vacation in Malaysia	Left pretibial and tarsal skin eruptions	Severe cough	1870	Bilateral small nodular infiltrates in lower lungs (CXR)	Oral albendazole (400mg/day) for 7 days	Complete resolution in 2 weeks
Gao YL et al (2019)	China	26, F	A trip to Sabah, Malaysia	Right upper and lower extremity	Non-productive cough and occasional breathlessness	Mild eosinophilia	Showed ill-defined reticulonodular infiltrates in both lungs (CT scan)	Oral albendazole 400 mg for seven consecutive days	Complete resolution within 7 days
Ng J et al (2021)	USA	52, M	Working outside - barefoot in an area where feral cats frequently defecate	Right foot, chest and abdomen	Asymptomatic	2100	Nodular opacities bilaterally (CXR)	Oral albendazole 400 mg single dose	Complete resolution
Present case (2021)	India	33, M	Farmer	Chest and abdomen	Intense, non-productive cough with occasional exertional breathlessness	2200	Ill-defined pulmonary infiltrates (CXR); nodular opacities bilaterally (CT scan)	Oral albendazole (400mg) once daily for 7 consecutive days along with nebulization with levosalbutamol and budesonide	Respiratory and cutaneous lesions resolved within 7 days; complete radiological resolution on 4 weeks follow-up

193 **The maximum absolute eosinophil count recorded during hospital stay*

194 *Abbreviations: M=male, F=female, CXR=chest X-ray, CT=computed tomography scan*

Figure 1: Multiple discrete thread-like skin coloured to erythematous serpiginous tract of various sizes (4 to 12 cm in length) distributed over the abdomen (a) and chest (b)

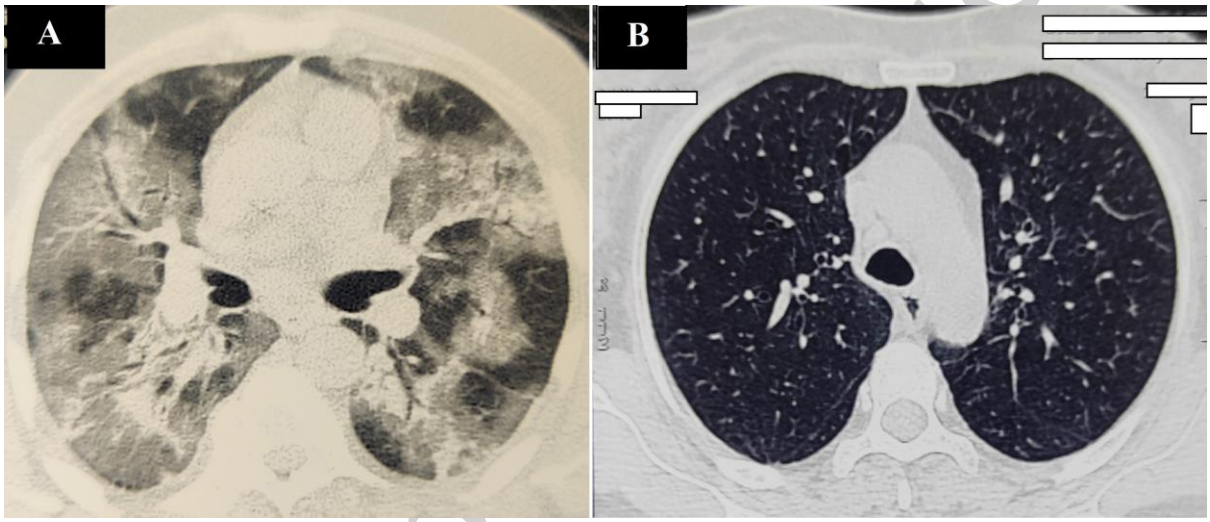

Figure 2: (a) Computed tomography of chest showed the presence of ill-defined reticulonodular infiltrates in both lungs; (b) Complete resolution after 4 weeks