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CASE REPORT

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 characterised by pulmonary infiltration along with peripheral eosinophilia and commonly follows parasitic infestation. We report a 33-year-old male patient who presented to a tertiary care hospital in eastern India in 2019 with LS that was attributed secondary to multifocal CLM. Treatment with seven-day course of oral albendazole (400 mg daily) coupled with nebulisation (levosalbutamol and budesonide) led to complete resolution of cutaneous lesions and respiratory complaints within two weeks. There was complete resolution of pulmonary pathology at four-weeks follow-up.

Keywords: Loeffler's syndrome; Peripheral Eosinophilia; Cutaneous Larva Migrans; Helminths; Albendazole; Case Report; India.

Cutaneous larva migrans (CLM) is a distinct cutaneous entity that is relatively common in the warmer tropical and subtropical regions. It is characterised 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 in Loeffler's syndrome (LS), which is characterised by migratory pulmonary infiltrates and peripheral eosinophilia.[2] We present an interesting case of LS associated with multifocal cutaneous larva migrans and review the literature on this uncommon association.

Case Report

A 33-year-old male patient presented to a tertiary care hospital in eastern India in 2019 with intense, non-productive cough for the last seven days with occasional breathlessness on exertion; he was otherwise healthy. 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, haemoptysis, wheeze, chest pain, allergic rhinitis or relevant drug intake (prescription, over the counter or illicit). His primary care physician had initiated a five-day course of oral azithromycin (500 mg daily) without any significant improvement. His medical and family history was non-contributory. On general examination, he was afebrile, normotensive (126/78 mmHg) with a saturation of 97% on room air. Bi-basilar crackles were heard on chest auscultation. Cutaneous examination revealed multiple discrete thread-like skin-coloured to erythematous serpiginous tract of various sizes (4–12 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 = 2,200 cells/μL). Stool examination for ova, parasite and cyst presence was negative. Chest radiography showed ill-defined bilateral pulmonary infiltrates. A high-resolution computed tomography of his thorax revealed the presence of ground-glass opacities mainly in the mid and lower zones 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 (400 mg) once daily for seven consecutive days along with nebulisation with levosalbutamol and budesonide as required. His respiratory symptoms and cutaneous lesions completely subsided in two weeks. There was complete radiological resolution at four weeks follow-up [Figure 2B].

Informed written consent was obtained from the patient after full explanation regarding his images

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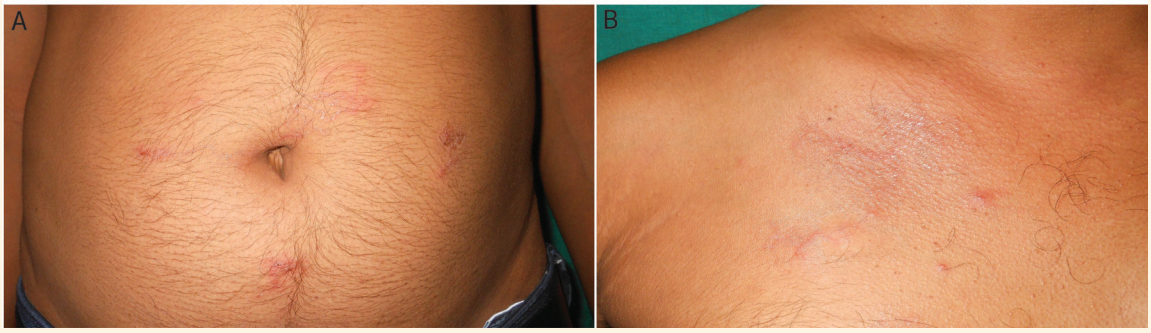

Figure 1: Photographs of the (**A**) abdomen and (**B**) chest of a 33-year-old male showing multiple discrete thread-like skin-coloured to erythematous serpiginous tracts of various sizes (4–12 cm in length).

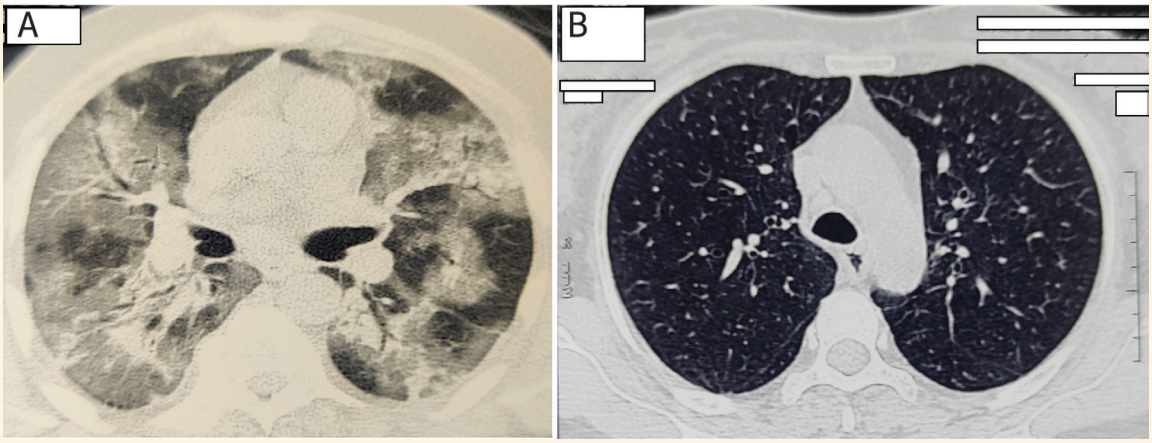

Figure 2: Chest computed tomography scan showing (**A**) the presence of ill-defined reticulonodular infiltrates in both lungs and (**B**) complete resolution after four weeks.

being published for academic purposes. The patient did not have any objection regarding use of his images which may reveal his identity and gave 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 a few cases [Table 1].[3,5–15]

CLM, also termed '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.[16] 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 such as hands and feet are usually affected. However, involvement of atypical locations such as the buttocks, genitalia, scalp and multifocal or disseminated lesions have 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.[1,16–19] CLM may be complicated by secondary bacterial infection, allergic reaction, eczematisation or very rarely LS. Concurrently or subsequently, a patient may develop non-productive cough, exertional

Table 1: Comparison of clinical characteristics of previous case reports of Loeffler's syndrome in association with cutaneous larva migrans[3,5–15]

Author and year of publication	Country	Age (gender)	Travel / exposure history	Location of CLM	Pulmonary symptoms	Absolute eosinophil count in mm^3	Imaging finding (CXR and/or CT scan)	Treatment	Outcome
Guill and Odom[9] (1978)	USA	40 (M) and his spouse 36 (F)	Vacation in Gulf of Mexico	Feet	Non-productive cough, tightness in chest, exertional dyspnoea	7,598 (male) and 2,528 (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 eight weeks from onset of symptoms
Butland and Coulson[11] (1985)	UK	58 (F)	Holiday trip to Barbados	Buttocks, legs and abdomen	Cough	3,000	Ill-defined patchy shadowing in the left upper and middle zones (CXR)	Topical thiabendazole	Complete resolution within two months
Wong-Waldamez and Silva-Lizama[13] (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 *et al.*[6] (2002)	France	41 (M)	Holiday trip to Thailand	Left foot	Intense non-productive cough	1,100	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 five days
Schaub *et al.*[10] (2002)	Switzerland	39 (M)	Holiday trip to Thailand	On the buttocks	Dyspnoea	1,616	Bilateral diffuse ground-glass opacities (CXR; further confirmed on CT scan)	Oral albendazole 400 mg for five consecutive days and a single dose of oral praziquantel (3,600 mg)	Complete resolution
Te Booij *et al.*[5] (2010)	Netherlands	27 (M)	Holiday trip to Thailand	Both feet	Exacerbation of pre-existing asthma	2,700	Small nodular granular infiltrates and linear paracardial opacities in both lungs (CXR)	Ivermectin, inhalation medication (budesonide/formoterol) and topical potent steroid	Complete resolution
Tan and Liu[7] (2010)	Singapore	47 (M)	Trip to beach holiday in Bali, Indonesia	Both feet and his right thigh and buttock	Dyspnoea, wheezing and chest discomfort	2,903	Reticulonodular infiltrates in the right middle and lingular lobes (CXR and CT scan)	Oral mebendazole (three days) followed by albendazole and intravenous hydrocortisone (five days) with oxygen supplementation	Complete remission in two weeks
Darocha *et al.*[15] (2011)	Poland	28 (M)	Trip to Sri Lanka	Both feet	Cough and dyspnoea at rest with exacerbation of asthma	3,400	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 three months

CLM = cutaneous larva migrans; CXR = chest X-ray; CT = computed tomography.

**Maximum absolute eosinophil count recorded during hospital stay.*

Table 1 (cont'd): Comparison of clinical characteristics of previous case reports of Loeffler's syndrome in association with cutaneous larva migrans[3,5–15]

Author and year of publication	Country	Age (gender)	Travel / exposure history	Location of CLM	Pulmonary symptoms	Absolute eosinophil count in mm^3	Imaging finding (CXR and/or CT scan)	Treatment	Outcome
Podder *et al.*[3] (2016)	India	30 (M)	Agriculturist	Both hands	Non-productive cough occasional exertional breathlessness	5,200	Fleeting opacities (CXR)	Oral albendazole (400 mg/day) for five days	Complete resolution
Wang *et al.*[14] (2017)	China	6 (M)	Vacation in Malaysia	Left pretibial and tarsal skin eruptions	Severe cough	1,870	Bilateral small nodular infiltrates in lower lungs (CXR)	Oral albendazole (400 mg/day) for seven days	Complete resolution in two weeks
Gao and Liu[8] (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 seven days
Ng *et al.*[12] (2021)	USA	52 (M)	Working outside (barefoot in an area where feral cats frequently defecate)	Right foot, chest and abdomen	Asymptomatic	2,100	Nodular opacities bilaterally (CXR)	Oral albendazole 400 mg as a single dose	Complete resolution
Present case (2021)	India	33 (M)	Farmer	Chest and abdomen	Intense, non-productive cough with occasional exertional breathlessness	2,200	Ill-defined pulmonary infiltrates (CXR); nodular opacities bilaterally (CT scan)	Oral albendazole (400 mg) once daily for seven consecutive days along with nebulisation with levosalbutamol and budesonide	Respiratory and cutaneous lesions resolved within seven days; complete radiological resolution on four-weeks follow-up

CLM = cutaneous larva migrans; CXR = chest X-ray; CT = computed tomography.
**Maximum absolute eosinophil count recorded during hospital stay.*

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 generalised sensitisation. 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.[20] Associated eosinophilia is teleologically related to the role of eosinophils in parasitic destruction. In parasitic infestation such as CLM, eosinophilic chemotaxis may result from IgE-mediated reactivity against the infestant, direct chemotactic property of certain parasites, T-cell dependent mechanism or may be immune-complex related.[13]

In the present case, the differential diagnoses for the cutaneous lesions included larva currens, migratory myasis, gnathosto-miasis, cercarial dermatitis, allergic contact dermatitis, inflammatory tinea or scabies. However, these were excluded based on history and clinical examination. Loeffler's syndrome should be considered early as a 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.[3,6,7,21]

The condition is primarily self-limiting but appropriate pharmacological intervention leads to faster resolution. Veraldi *et al.* reported a new therapeutic regimen of oral albendazole (400/day for seven days) to be highly effective.[22] Single dose therapy of oral ivermectin (200 µg/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 such as oxygen inhalation, systemic or inhalational corticosteroids may be required to alleviate the respiratory symptoms.[4,8,9,23]

Conclusion

The current case highlights the occurrence of LS secondary to multifocal CLM and adds to the limited existing literature on this rarely documented association. LS should be considered early in the differential diagnosis for respiratory complaints in association with pruritic cutaneous eruption especially in an individual who recently returned

from a vacation in 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.

References

1. Brenner MA, Patel MB. Cutaneous larva migrans: The creeping eruption. Cutis 2003; 72:111–15.
2. Ekin S, Sertogullarindan B, Gunbatar H, Arisoy A, Yildiz H. Loeffler's syndrome: An interesting case report. Clin Respir J 2016; 10:112–14. https://doi.org/10.1111/crj.12173.
3. Podder I, Chandra S, Gharami RC. Loeffler's syndrome following cutaneous larva migrans: An uncommon sequel. Indian J Dermatol 2016; 61:190–2. https://doi.org/10.4103/0019-5154.177753.
4. Wright DO, Gold EM. Löffler's syndrome associated with creeping eruption (cutaneous helminthiasis). Arch Intern Med (Chic) 1946; 78:303–12. https://doi.org/10.1001/archinte.1946.00220030050003.
5. Te Booij M, de Jong E, Bovenschen HJ. Löffler syndrome caused by extensive cutaneous larva migrans: A case report and review of the literature. Dermatol Online J 2010; 16:2.
6. Del Giudice P, Desalvador F, Bernard E, Caumes E, Vandenbos F, Marty P, et al. Loeffler's syndrome and cutaneous larva migrans: A rare association. Br J Dermatol 2002; 147:386–8. https://doi.org/10.1046/j.1365-2133.2002.48102.x.
7. Tan SK, Liu TT. Cutaneous larva migrans complicated by Löffler syndrome. Arch Dermatol 2010; 146:210–12. https://doi.org/10.1001/archdermatol.2009.392.
8. Gao YL, Liu ZH. Cutaneous Larva Migrans with Löeffler's Syndrome. Am J Trop Med Hyg 2019; 100:487–8. https://doi.org/10.4269/ajtmh.18-0406.
9. Guill MA, Odom RB. Larva Migrans Complicated by Loeffler's Syndrome. Arch Dermatol 1978; 114:1525–6.
10. Schaub N, Perruchoud AP, Buechner S. Cutaneous larva migrans associated with Löffler's syndrome. Dermatology 2002; 205:207–9. https://doi.org/10.1159/000063917.
11. Butland RJ, Coulson IH. Pulmonary eosinophilia associated with cutaneous larva migrans. Thorax 1985; 40:76–7. https://doi.org/10.1136/thx.40.1.76.
12. Ng J, Lee D, Kryzstofiak M. A Unique Case of Cutaneous Larva Migrans and Asymptomatic Löeffler's Syndrome. Cureus 2021; 13:e15960. https://doi.org/10.7759/cureus.15960.
13. Wong-Waldamez A, Silva-Lizama E. Bullous larva migrans accompanied by Loeffler's syndrome. Int J Dermatol 1995; 34:570–1. https://doi.org/10.1111/j.1365-4362.1995.tb02957.x.
14. Wang S, Xu W, Li LF. Cutaneous Larva Migrans Associated With Löffler's Syndrome in a 6-Year-Old Boy. Pediatr Infect Dis J 2017; 36:912–14. https://doi.org/10.1097/INF.0000000000001593.
15. Darocha S, Wawrzyńska L, Oniszh K, Dziewulska B. [Eosinophilic pneumonia in response to cutaneous larva migrans syndrome--a case report]. Pneumonol Alergol Pol 2011; 79:365–70.
16. Sil A, Mukherjee GS, Bhanja DB, Panigrahi A. Multiple curvilinear lesions on a patient's back. Neth J Med 2020; 78:92.
17. Das A, Panigrahi A, Bhanja DB, Sil A, Biswas SK. Pruritic genital rash. J Paediatr Child Health 2021; 57:302. https://doi.org/10.1111/jpc.1_15165.
18. Sil A, Panigrahi A, Pramanik J. Isolated cutaneous larva migrans over the scalp in a hod carrier. Br J Dermatol 2021; 185:e157. https://doi.org/10.1111/bjd.20589.
19. Sil A, Panigrahi A, Bhanja DB, Chakraborty S. Cutaneous Larva Migrans Over Penis. Urology 2020; 140:e6–7. https://doi.org/10.1016/j.urology.2020.03.004.
20. Gandullia E, Lignana E, Rabagliati AM, Penna R. [Visceral larva migrans caused by Ancylostoma caninum]. Minerva Pediatr 1981; 33:917–23.
21. Panigrahi A, Sil A, Bhanja DB. Pruritic curvilinear track over penis. Paediatr Child Health 2020; 26:268–9. https://doi.org/10.1093/pch/pxaa059.
22. Veraldi S, Bottini S, Rizzitelli G, Persico MC. One-week therapy with oral albendazole in hookworm-related cutaneous larva migrans: A retrospective study on 78 patients. J Dermatolog Treat 2012; 23:189– 91. https://doi.org/10.3109/09546634.2010.544707.
23. Caumes E. Treatment of cutaneous larva migrans. Clin Infect Dis 2000; 30:811–14. https://doi.org/10.1086/313787.