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Case Report

Cutaneous Diphtheria: An Overlooked Skin and Soft Tissue Infection—A Case Series from India

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ABSTRACT

Cutaneous diphtheria is an under-recognized manifestation of an infection that is caused by Corynebacterium diphtheria (***C. diphtheriae***), particularly in endemic regions. Usually it presents as a chronic non-healing ulcer and is frequently polymicrobial origin, which may lead to misidentification as contamination. In this article, we have reported four cases of cutaneous diphtheria, including one toxigenic strain with severe clinical progression and three non-toxigenic strains associated with diabetic foot ulcers. Diagnosis of this condition was established through careful Gram stain examination, culture reports, and confirmatory testing using MALDI-TOF or PCR with Elek's test. Recognising the condition at an early stage is important for appropriate antimicrobial therapy, infection control, and prevention of transmission. In this case series, we have highlighted the continued relevance of cutaneous diphtheria in India, where underreporting remains a concern.

KEYWORDS: Cutaneous diphtheria; *Corynebacterium diphtheriae*; Chronic ulcers; Polymicrobial infection

INTRODUCTION

Cutaneous diphtheria has been recognized worldwide as a rare infectious disease, and it was documented since 1759 [1, 2]. Both toxic [3, 4, 5] and non-toxic [6, 7] strains of Corynebacterium diphtheria cause skin manifestation which can lead to **cutaneous** diphtheria. Clinically, it is characterised by progressive non-healing necrotic, persistent ulcer that commonly affect the limbs. Overcrowding [1, 2], low socioeconomic status [4], travel to endemic locations [8, 19, 11, 12], skin trauma [8, 9], pre-existing skin lesions, immunocompromised status, and contact with livestock and pets[13] are some of the various risk factors that were linked to the disease. In many cases an immunocompromised state can be due to long-term diabetes mellitus [7, 11,] and that is a major risk factor for infection by opportunistic pathogens such as C. diphtheriae.

Symptomatic infections with non-toxigenic strains of C. diphtheriae are rare but, when identified, need appropriate treatment. Due to contagious nature and prolonged shedding from chronic skin lesions it is very important to control the infection, otherwise it may contaminate the environment and spread to susceptible individuals [7-8, 12, 25]. Few case reports have been published in India [3-7,] and a considerable number of publications from other developing countries and reports following travel to endemic areas from developed countries [1, 2, 9, 12, 15, 17, 18, 20-25]. This lower number of reports from India may be due to various factors, including neglect of this pathogen as a skin commensal or growth masked by polymicrobial infection.

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In this article we have reported four cases of Cutaneous Diphtheria among which one case is due to toxigenic strain with bad prognosis. Other three strains are isolated from diabetic patients with chronic non-healing foot ulcer.

CASE SERIES

CASE 1

Demographics and comorbidities:

A 55-year-old male presented to the surgery outpatient department with a history of a chronic non-healing ulcer over the left leg for 10 years. He was a known case of chronic kidney disease for 5 years and was hemodynamically stable.

Cutaneous Lesion characteristics:

The ulcer measured 6 × 5 × 2 cm and was located over the left medial malleolus, with membranous slough **(Figure 1a).**

Microbiological findings:

Culture of exudate obtained from the depth of the ulcer showed polymicrobial growth of Corynebacterium diphtheriae and Morganella morganii. *C. diphtheriae* was presumptively identified based on colony morphology on blood agar, Gram stain, and Albert's stain (Table 1).

Antimicrobial susceptibility (AST) of Diphtheria isolate shown in Table 2 was performed as per EUCAST Standardized disc diffusion method & zone Break points interpreted as per EUCAST 2019 v.9.0 guideline. Morganella morganii (AST was performed as per CLSI guideline) susceptible to amikacin, cefepime, ciprofloxacin, and cotrimoxazole based on zone size Interpretation as per CLSI 2022 guideline. Throat swab culture showed no evidence of pharyngeal carriage of C. diphtheriae.

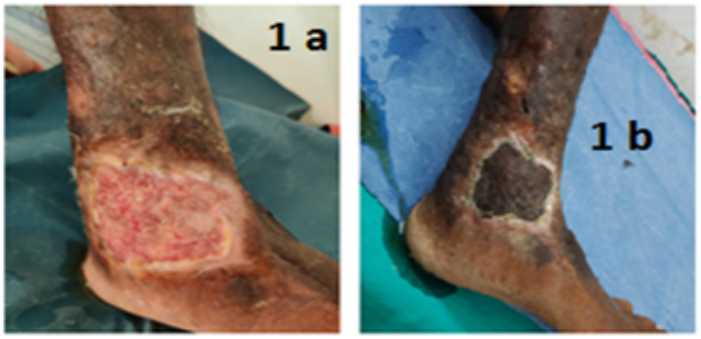
Confirmation of Corynebacterium *diphtheriae*

: The isolate was confirmed as a non-toxigenic strain of *C. diphtheriae* by MALDI-TOF at a reference laboratory (Coimbatore).

Treatment and outcome:

The patient was treated with intravenous ciprofloxacin and cefepime for two weeks along with daily wound care and then he underwent split-skin grafting, and a significant wound healing was observed on follow-up **(Figure 1b).**

Figure 1a & 1b: Chronic leg ulcer of case-1 (before & after SSG)



CASE 2

Demographics and comorbidities:

A 40-year-old male presented with swelling over the left eye and forehead for four days and swelling of the right eye for one day. He had sustained a traumatic injury to the left eye eight days earlier. He had no history of diabetes mellitus or tuberculosis and was hemodynamically stable.

Cutaneous Lesion characteristics:

Examination revealed diffuse periorbital swelling, sloughing of the left eyelid with purulent discharge, facial skin excoriation, conjunctival chemosis, and palpable left submandibular lymph nodes **(Figure 1 c).**

Fig 1 c: Fulminant orbital & frontal cellulitis (Case-2)

Microbiological findings:

Culture of pus from the affected site showed polymicrobial growth of Corynebacterium diphtheriae and Streptococcus pyogenes. C.diphtheriae was presumptively identified by colony morphology, Gram stain, and Albert's stain (Table 1). Antimicrobial

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susceptibility is detailed in Table 2. Antimicrobial susceptibility of Diphtheria isolate shown in Table 2 was performed as per EUCAST Standardized disc diffusion method & zone Break points interpreted as per EUCAST 2019 v.9.0 guideline. S. pyogenes (AST performed as per CLSI guideline) was susceptible to Penicillin, Ampicillin, and Clindamycin based on zone size Interpretation as per CLSI 2022 guidelines.

Confirmation of *Corynebacterium diphtheriae* : The isolate was confirmed as a toxigenic strain of C. diphtheriae by PCR and Elek's test at Christian Medical College, Vellore.

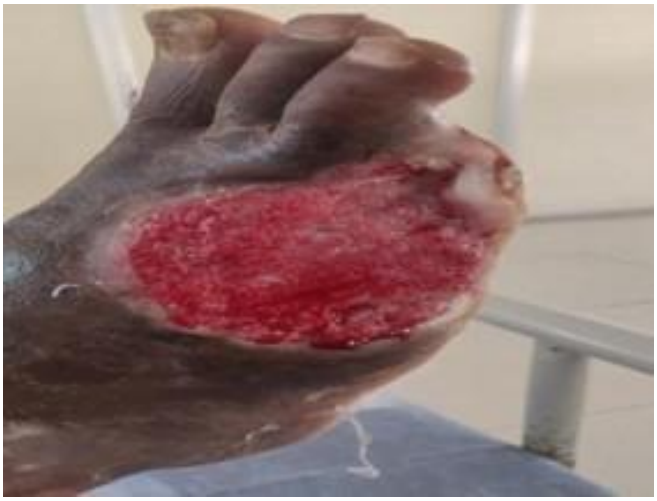
Treatment and outcome:
The patient received intravenous cefoperazone–sulbactam for seven days, ciprofloxacin for six days, and topical mupirocin. Due to fulminant clinical progression, he was referred to a higher ophthalmic center before confirmatory results were received. Follow-up could not be obtained.

CASE 3

Demographics and comorbidities: A 70-year-old female presented with a left leg ulcer of 15 days' duration. She was a newly diagnosed case of diabetes mellitus and had no history of tuberculosis. Vital signs were stable.

Cutaneous Lesion characteristics: The ulcer measured 6 × 3 × 2 cm and was located on the anterior aspect of the middle third of the leg. The ulcer was foul-smelling, covered with slough, and infested with maggots **(Figure 1 d).**There was no radiological evidence of osteomyelitis.

Fig 1 d : Leg ulcer (Case-3)



Microbiological findings: Culture report shows polymicrobial growth of C. diphtheriae, Pseudomonas aeruginosa, and Proteus mirabilis. C. diphtheriae was presumptively identified by standard staining and culture characteristics (Table 1).Antimicrobial susceptibility is shown in Table 2 was performed as per CLSI guideline for broth dilution and zone Break points interpreted as per CLSI 2023 MIC Breakpoint**.** The accompanying Gram-negative isolates were susceptible to cefepime, piperacillin–tazobactam, gentamicin, and carbapenems based on zone size Interpretation as per CLSI 2023 guidelines

Confirmation of *Corynebacterium diphtheria* : The isolate was confirmed as a non-toxigenic strain of C. diphtheriae at Christian Medical College, Vellore.

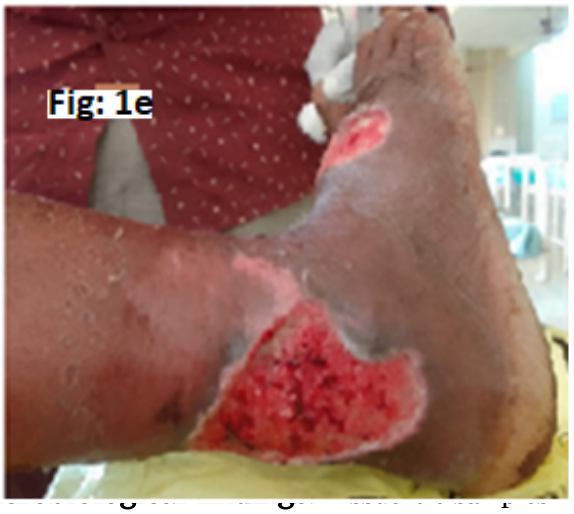
Treatment and outcome: The patient was treated with intravenous cefotaxime for two days and discharged on request with advice for wound care and oral antibiotics.

CASE 4

Demographics and comorbidities: A 65-year-old male with hypertension and poorly controlled diabetes mellitus presented with right leg ulcers of 10 days' duration following minor trauma.

Cutaneous Lesion characteristics: Two ulcers were present: one measuring 4 × 3 × 2 cm over the right medial malleolus and another measuring 3 × 3 × 2 cm over the anterior aspect of the right foot. Both ulcers had serous discharge, warmth, tenderness, and maggot infestation **(Figure 1 e).**

Fig 1 e: Chronic leg ulcer of Case-4(Before Wound debridement)



M ım both ulcers showed pure growth of *Corynebacterium*

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diphtheriae. Presumptive identification was based on Gram stain, Albert's stain, and colony morphology (Table 1**; Figures 1 f-j).** Antimicrobial susceptibility is detailed in Table 2 was performed as per CLSI guideline for broth dilution & interpreted as per CLSI 2023 MIC Breakpoint.

Figure-1 f -Direct Gram stain –Case 1

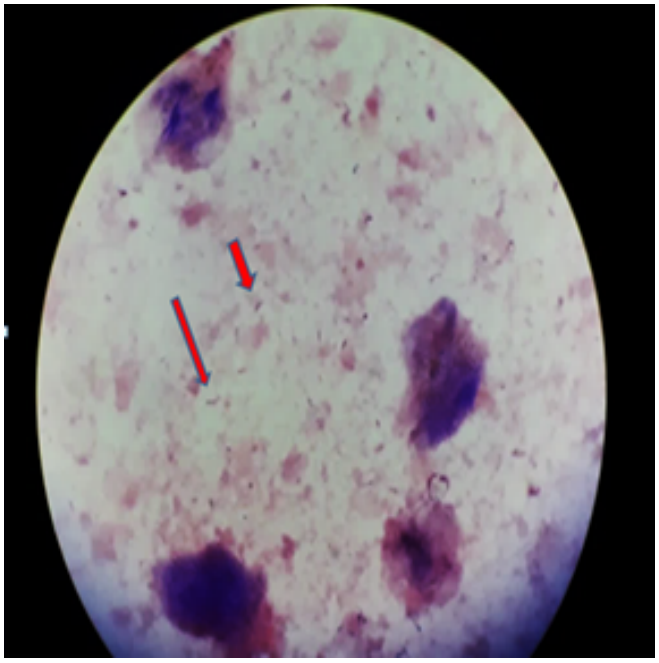


Figure-1 g: Colony growth on Blood agar and AST on Blood Agar

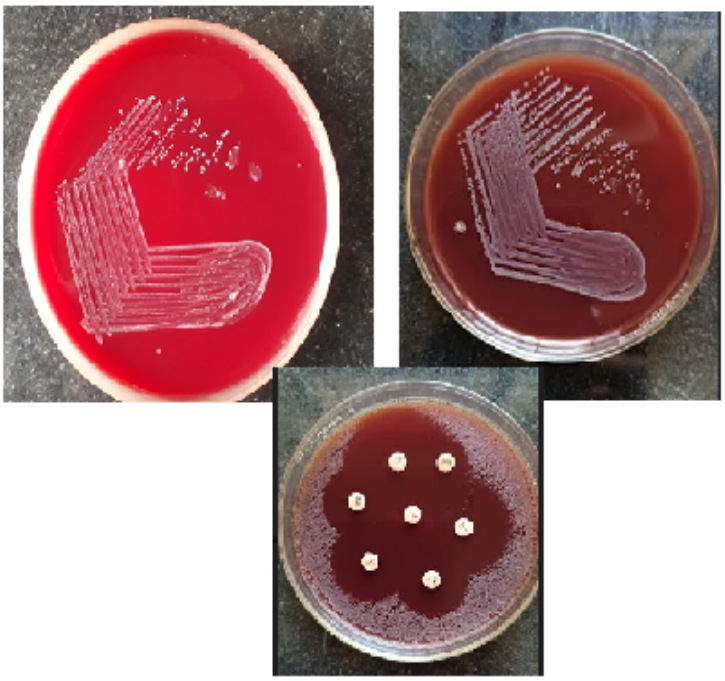


Figure 1 h & i: Colony Gram staining

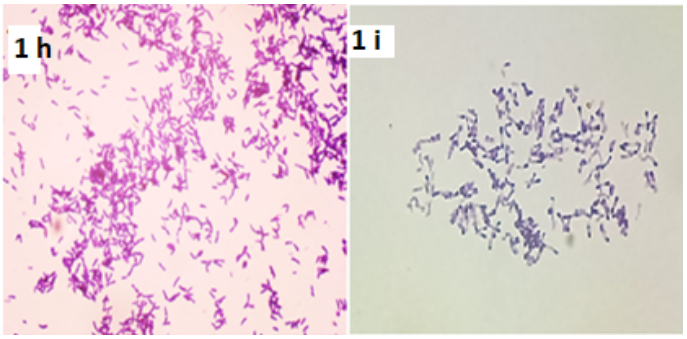
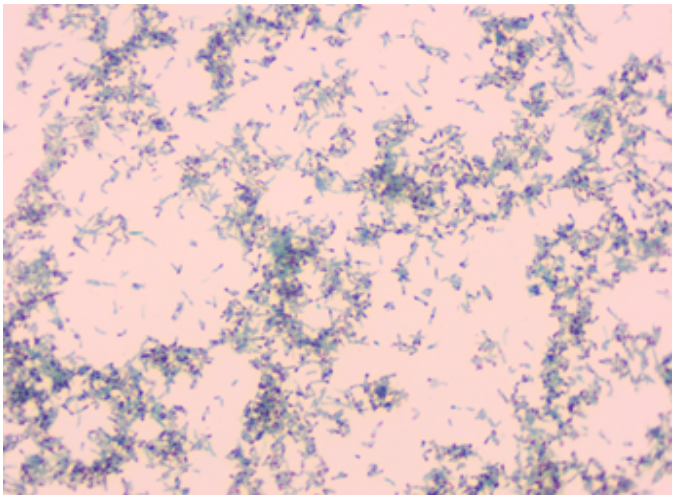


Figure-1 j: Colony Alberts stain



Confirmation of *Corynebacterium diphtheriae* : The isolate was confirmed as a non-toxigenic strain of *C. diphtheriae* at Christian Medical College, Vellore.

Treatment and outcome: The patient received intravenous ceftriaxone for five days along with surgical debridement and regular wound care. Marked wound healing was observed on follow-up **(Figure 1 k).**

Figure-1 k : Chronic leg ulcer of Case-4(after Wound debridement)

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Table-1: Results of Microbiological Investigation

Case	Direct Gram stain Findings	Culture Characteristics	Microscopic / Special Stain findings	Culture Confirmation (Method and Lab)
Case 1	Many pus cells, Moderate epithelial cells, Few Gram-Positive bacilli and Gram-negative bacilli	Small greyish -white, non-haemolytic colonies on blood agar[1]	Gram stain: Gram positive bacilli with clubbed ends arranged in V and L forms [2] Albert Stain: Green bacilli with bluish-purple metachromatic granules arranged in V and L forms [3]	Non toxigenic *diphtheriae* confirmed by MALDI-TOF. Reference laboratory, Coimbatore
Case 2	Many pus cells, Few epithelial cells, Moderate Gram-Positive bacilli and Gram-positive cocci in chains	Growth resistant with *C. Diphtheriae* on blood agar	Gram stain and Albert stain consistent with *C.Diphtheriae* morphology	Toxigenic *C.Diphtheriae* confirmed by PCR AND Elek's test. Department of Microbiology, CMC Vellore
Case 3	Many pus cells, few epithelial cells, few Gram positive bacilli and moderate Gram-negative bacilli	Polymicrobial growth including C.Diphtheriae	Gram stain and Albert stain consistent with *C.Diphtheriae*	Non-Toxigenic *C.Diphtheriae* confirmed by PCR AND Elek's test. Department of Microbiology, CMC Vellore
Case 4	Many pus cells, no epithelial cells, few Gram positive bacilli and Occasional Gram positive cocci in pairs	Pure growth of C.Diphtheriae	Gram stain and Albert stain consistent with *C.Diphtheriae*	Non-Toxigenic *C.Diphtheriae* confirmed by PCR AND Elek's test. Department of Microbiology, CMC Vellore

Footnotes

- **Figure 1 g:** Colony morphology on blood agar
- **Figures 1 h & 1i:** Gram stain showing club-shaped bacilli in V and L arrangement
- **Figure 1 J:** Albert stain showing metachromatic granules

Note:

***PCR :** Polymerase chain reaction

****CMC :** Christian Medical college-Vellore

TABLE-2: Antibiotic susceptibility of Diphtheria isolates (EUCAST 2019 zone Break points * and CLSI 2023 MIC Breakpoint **)

R-Resistant, S-Susceptible

Diphtheria isolate	Penicillin	Erythromycin	Clindamycin	Tetracycline	Ciprofloxacin	Linezolid	Vancomycin
Isolate-1* (Cse-1)	R	S	T	S	S	S	S
Isolate 2* (Case 2)	R	S	S	S	S	S	S
Isolate 3** (Case 3)	R	S	S	R	S	S	S
Isolate 4** (Case 4)	S	S	S	S	S	S	S

Infection Control Measures: Following presumptive identification of *C. diphtheriae*, all patients were isolated, and appropriate droplet precautions were implemented to prevent transmission.

DISCUSSION

Diphtheria is a re-emerged public health concern in several regions, including resource-rich settings, with a notable rise in both respiratory and cutaneous forms over the past decade[1, 2, 13, 23, 25]. *Corynebacterium diphtheriae* and *Corynebacterium ulcerans* are the commonest reported causative agents of cutaneous Diphtheria. Respiratory diphtheria is the commonest and severe clinical form. The recent increasing reports of cutaneous diphtheria highlight its significance epidemiologically[6,7,10–25]. Cutaneous diphtheria usually presents as non-specific, chronic ulcers, commonly involving in the extremities and frequently developing at sites of prior skin trauma, as observed in Cases 2 and 4 of the present series [8,9,13].

Multiple risk factors can cause the development of cutaneous diphtheria, which includes diabetes mellitus, skin trauma, poor wound hygiene, overcrowding, and compromised socioeconomic conditions. In our case series, diabetes mellitus was the commonest

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predisposing factor. This highlights the role of diabetes mellitus in impairing host defenses and facilitating opportunistic infection. Microbiologically it was reported that cutaneous diphtheria is often polymicrobial, with *C. diphtheriae* isolated alongside other bacterial pathogens. *Streptococcus pyogenes* and *Staphylococcus aureus* are commonly reported co-pathogens, but in our case series we have observed a predominant Gram-negative co-infection, and this highlights the regional and clinical variability [4,10–14,18–20,22,24,25]. Particularly, one case in this series yielded a pure isolate of *C. diphtheriae*, highlighting that monomicrobial infection can occur and should not be overlooked.

Both toxigenic and non-toxigenic strains of *C. diphtheriae* are capable of causing cutaneous infection. Although systemic complications are uncommon with cutaneous disease, toxigenic strains may be associated with severe local disease and poor outcomes, as illustrated by the fulminant clinical course in one patient in this series. Importantly, non-toxigenic strains are not clinically benign; they can cause persistent infection, delay wound healing, and serve as reservoirs for prolonged bacterial shedding, thereby posing infection-control challenges. Factors such as migration, poverty, overcrowding, and geopolitical conflicts particularly in settings with poor hygiene—continue to facilitate the persistence and re-emergence of cutaneous diphtheria worldwide [1,2,4,10,19].

CONCLUSIONS

Among patients with chronic non-healing ulcers, particularly in those with diabetes or a history of trauma Cutaneous diphtheria should be considered. A thorough microbiological evaluation should be done for Gram-positive bacilli instead of dismissing them as contaminants. Early diagnoses, appropriate antimicrobial therapy, along with strict infection-control measures are essential to prevent transmission and complications.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interests

SOURCE OF FUNDING

None

ETHICS STATEMENT INCLUDING PATIENT CONSENT

This study got IEC approval & Number is AMCH/IEC/Proc.No.56/2024 Dated 17-4-24.

AUTHORS' CONTRIBUTIONS

NS V: Conceptualization, Supervision and Guidance, Review and editing , Data collection and sorting, Analysis, Writing draft

BU: Conceptualization, Review and editing

KS: Conceptualization, Review and editing , Data collection

AI DECLARATION

No AI tool was used to generate research data, perform data analysis, interpret findings, formulate scientific conclusions, or make editorial decisions. All AI-assisted content was critically reviewed, verified, and revised by the authors. The authors take full responsibility for the accuracy, originality, integrity, and final content of the manuscript.

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