Faucial diphtheria infection caused due to *Corynebacterium striatum* in a paediatric patient – A rare case report from central India

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Summary

Medically relevant *Corynebacterium species* include *Corynebacterium diphtheriae*, and non-diphtherial *Corynebacteria*. A part of the normal flora of the skin and mucous membranes, non-diphtherial *Corynebacteria,* which is frequently dismissed as a contaminant, has an important role in clinical disease. In the last decades, the pathogenicity among other *Corynebacterium spp.* has been increasingly reported.

This case report presents a rare occurrence of faucial diphtheria caused by *Corynebacterium striatum* in a 13-year-old female patient. Molecular analysis confirmed *C. striatum,* which was non-toxigenic by Elek's gel precipitation test.

This case underscores the need for heightened awareness of non-diphtherial *Corynebacteria* as emerging pathogens, their diagnosis and accurate treatment.

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Introduction

Among the omnipresent *Corynebacterium* species, *Corynebacterium diphtheriae* is a medically relevant causative pathogen for diphtheria. *C. striatum, C. amycolatum, C. minutissimum, C. xerosis,* and *C. freneyi* are grouped as non-diphtherial corynebacteria and are considered part of mucosal and epidermal flora.

Corynebacterium striatum is recognized as a true pathogen when isolated in several samples from sterile body sites or from indwelling medical devices [1].

An increasing number of invasive infections caused by *C. striatum* are reported in immunocompromised and immunocompetent individuals, including bacteraemia and sepsis, septic arthritis, endocarditis, meningitis, and others [9].

Here, we report a case of faucial diphtheria caused by *C. striatum* in a paediatric patient.

Case Report

History

A 13-year-old female patient presented with fever and chills for the last 4 days. There was difficulty in swallowing for the same duration, along with sore throat and earache. The patient developed neck swelling, predominantly on the left side. The patient also had multiple, painful skin lesions over both buttocks and left knee. There was no history of breathlessness, respiratory distress, or other co-morbidities. There was no similar family history. The patient was fully vaccinated for the Universal Immunization Program as per her age.

Examination

On admission, the patient was alert, conscious, and oriented, with stable vitals. Her tonsils were enlarged and inflamed. There was progressive submandibular swelling, more on the left side (Figure 1).

A greyish-white membrane was present over the posterior pharyngeal wall, partially covering the tonsils and uvula (Figure 2).

Multiple well-defined, tender, excoriated papules with a mild crust were present over the bilateral buttocks and the left knee.

Differential diagnoses for membrane over tonsils were: membranous tonsilitis, diphtheria, Vincent angina, and infectious mononucleosis. The provisional diagnosis was narrowed down to diphtheria because the patient had an insidious onset of symptoms and adherent membrane, which bled on removal. There were no symptoms like rashes or splenomegaly suggestive of Infectious mononucleosis. So, diphtheria was considered as the provisional diagnosis.

Figure 1. Progressive submandibular swelling, more on the left side, of the patient.

Figure 2. A greyish-white membrane was present over the posterior pharyngeal wall of the patient, partially covering the tonsils and uvula.

Investigations

Microbiological

A throat swab gave the following results: i) Gram-stain, a few pus cells, and occasional Gram-negative bacilli, and no structures morphologically resembling *C. diphtheriae* were observed; ii) a culture on Loeffler's Serum Slope (LSS), blood and chocolate agar was done. LSS was examined after 6 hours of incubation for visible growth. Yellowish, moist, smooth colonies were seen on LSS, which were subjected to Gram and Albert stains. Gram stain revealed Gram-positive bacilli (Figure 3), and Albert's stain showed green bacilli with dark blue to black-coloured metachromatic granules (Figure 4). Subcultures were made on a 1% potas-

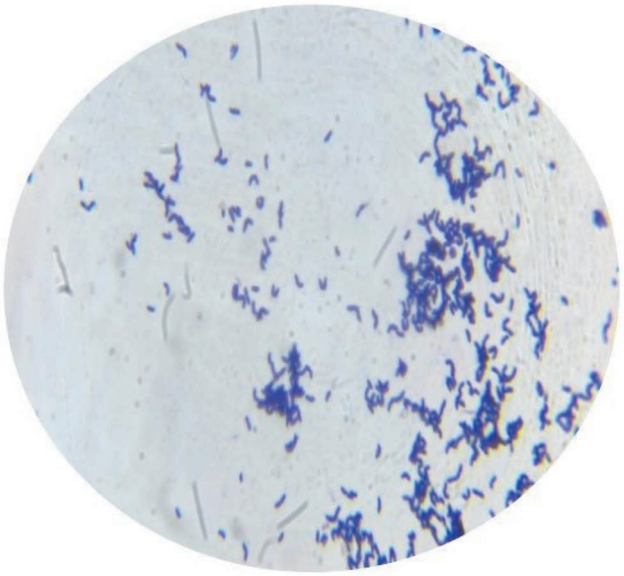

Figure 3. Gram stain revealed Gram-positive bacilli.

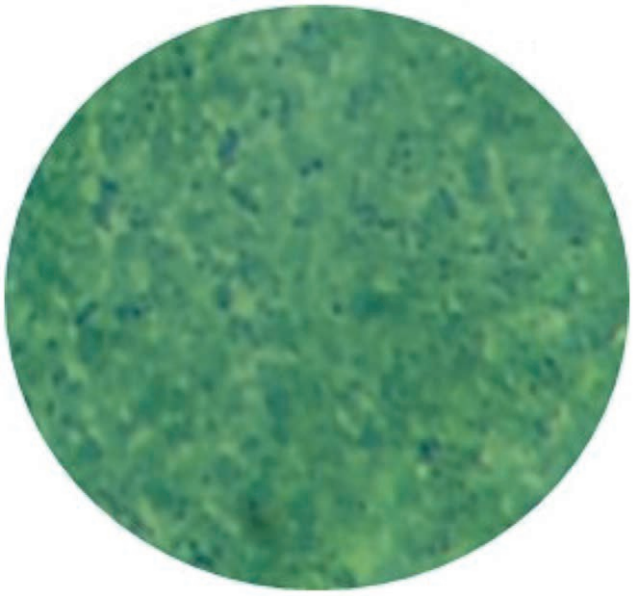

Figure 4. Albert's stain shows green bacilli with dark blue to black-coloured metachromatic granules.

sium tellurite medium that revealed black-coloured colonies after 48 hours of incubation (Figure 5).

Non-microbiological

Complete blood count showed mild lymphocytosis and severe anaemia. Electrocardiogram (ECG) showed T wave inversion on V3, V4, III & AVF leads, suggesting myocarditis secondary to diphtheria. Ultrasonography (USG) of the neck revealed cervical lymphadenopathy and cellulitis. With this diagnostic workup, the patient was diagnosed as a case of membranous tonsillitis due to *C. diphtheriae* associated with severe anemia and myocarditis.

Toxigenicity and confirmatory tests gave the following results: i) Elek's gel precipitation test was negative for toxin production; ii) Real-Time Polymerase Chain Reaction (RT-PCR) was positive for *C. striatum*; iii) RTPCR for the *tox* gene was negative.

Regarding real-time PCR methodology, the description of the primer and number of cycles was not disclosed by the Institute (CMC, Vellore, India).

Treatment

The patient was initiated on Diphtheria Antitoxin (DAT), 80,000 IU after performing sensitivity testing, injectable penicillin G 6,00,000 IU QID for 14 days and erythromycin 500 mg QID. Supportive treatment for fever, rashes, and anaemia was given. The patient was shifted to an isolation ward with close monitoring. To the best of our knowledge, no evidence-based guidelines have been proposed until now to support adequate antibiotic therapy for *C. striatum* infections [6]. As per the World Health Organization (WHO) recommended guidelines for faucial *C. diphtheriae*, penicillin G and erythromycin have been recommended, which were administered to the patient empirically based on clinical judgment. After 14 days of treatment, the patient improved clinically and was discharged with regular follow-up advice.

Figure 5. Subcultures were made on a 1% potassium tellurite medium that revealed black-coloured colonies after 48 hours of incubation.

Discussion

The Corynebacterium genus has more than 132 highly diversified species and 11 subspecies, with at least 50 species already recognized for their medical, veterinary, and biotechnological relevance [8].

Although isolation of non-diphtheria *Corynebacteria* may represent contamination with skin flora, many case reports have been published regarding these organisms as pathogens [4,10].

In recent years, *C. striatum* has been recognized as an emerging pathogen causing increasing infections [2]. Factors like prolonged hospitalizations, repeated antibiotic exposures, and prolonged use of invasive medical devices have been frequently linked to *C. striatum* infections [9]. But, in the present case report, the patient had no such risk factors. *C. striatum* has also been cultured from cases of the native valve and pacemaker-related endocarditis, bacteraemia, meningitis, and occasionally fatal pulmonary infections in clinical diagnostics [7]. However, in the present case report, *C. striatum* was isolated from a throat swab of a patient with pseudomembrane.

In a mini-review by Giorgio Silva□Santana et al., they conducted a worldwide survey of *C. striatum* from 1976-2020. They reported 14 *C. striatum* cases of human infections and/or nosocomial outbreaks from India, and none of the strains was isolated from a faucial site or diphtheria-like illness [9].

To the best of our knowledge, this is the first case of faucial diphtheria infection caused by *C. striatum* (a non-toxigenic non-diphtheric corynebacteria) from India.

Conclusions

Corynebacterium species were misidentified in the past due to complex biochemicals, but the advent of modern diagnostics has made their identification quicker and more accurate [3]. Previously reported Polymerase Chain Reaction (PCR) assays can have low diagnostic sensitivity or give species misidentifications among clinical isolates. The development of combined real-time PCR assays based on the *tox* based on the tox gene, has made detection and differentiation of toxigenic and nontoxigenic corynebacteria more accurate [5].

Further studies are required to explore virulence factors of non-diphtheric non-toxin producing Corynebacterium that can cause serious human infections.

As *C. striatum* infection is easily transmissible, especially in crowded places, identification is of the utmost importance. Since ADT is not effective and expensive for *C. striatum,* speciation has gained importance. Hence, advocating the use of combined real-time PCR assays with multiple target genes should be preferred.

The treatment with penicillin G and erythromycin can be effective for *C. striatum* infections.

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