

TRICHOBACTERIOSIS, ERYTHRASMA AND PITTED KERATOLYSIS – THE SPECTRUM OF NON-DIPHOTHEROID *CORYNEBACTERIA*

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Abstract

Keywords:

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The genus *Corynebacteria* or *Diphtheroids* are aerobic, non-sporulating, pleomorphic Gram-positive and catalase-positive bacilli. *Corynebacteria* are a usual part of the human microbiome, but they may cause characteristic skin diseases. *Corynebacterium minutissimum* was first isolated from erythrasma, but it is also involved in pitted keratolysis. The dominant species in trichobacteriosis (syn. trichomycosis) is *C. tenuis*. Diagnosis, differential diagnoses and treatment options are discussed in this review.

Introduction

The genus *Corynebacteria* or *Diphtheroids* are aerobic, non-sporulating, pleomorphic Gram-positive and catalase-positive bacilli. In culture, these bacteria are more uniformly stained and lack metachromatic granules. They are arranged in a palisade order.

Corynebacteria are a usual part of the microbiome of skin and mucous membranes. However, they have frequently been reported in association with nosocomial infections on chronic open wounds, with catheter sepsis or endotracheal infections, and often show antibiotic resistance (1, 2).

Corynebacterium minutissimum was first isolated from erythrasma in 1961. This bacterium is known to be responsible for erythrasma and pitted keratolysis. *C. minutissimum* has also been reported in more severe disorders such as bacteremia, meningitis, endocarditis, cellulitis, abscesses, peritonitis, pyelonephritis. The dominant species in trichobacteriosis (syn. trichomycosis palmellina) is *C. tenuis* (1, 2).

Identification

The identification of non-diphtheroid *Corynebacteria* is exemplarily described for *C. minutissimum*.

C. minutissimum can be cultivated under standard 37°C growth conditions

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on usual laboratory media. Their phenotypical identification includes Gram stain microscopy, details of the colony at 24 h, catalase and oxidase reactions and establishing whether the isolate is lipophilic or not. Lipophilia has been linked to the absence of a microbial type I fatty acid synthase gene (3).

16S rRNA gene sequencing discerns among most species in the genus *Corynebacterium*, which can be combined with sequencing of the *rpoB* gene if necessary (4). Matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) analysis is an advanced method, whereby proteins liberated from bacteria are ionized and detected by a mass spectrometer (MS), the spectrum is analyzed and its pattern is compared to entries found in a database, giving rise to a degree of match (5, 6). Full genome sequencing of *C. minutissimum* had been published in 2015 (7).

Erythrasma

Erythrasma is a localised and chronic skin infection of the intertriginous areas caused by *C. minutissimum*. The lesions are macular or plaque-like, reddish brown, often asymptomatic and well-defined in shape. Interdigital erythrasma is the most frequent type, but axillae and groins are also commonly involved (Fig. 1). The diagnosis is usually clinical, but a Wood light (320-400 nm) examination can be useful since the bacteria produce coproporphyrin III – a coral-red fluorescent compound. Erythrasma has no gender preponderance but is more commonly seen in patients with a body mass index (BMI) > 23 kg/m² and in diabetics (8, 9).

The differential diagnoses include psoriasis, tinea, candida intertrigo, and acanthosis nigricans (Fig. 1b).

Treatment is topical with antibiotics such as fusidinic acid or mupirocin, but isoconazole nitrate 1% with diflucortolone valerate 0.1% has also been

used successfully (10-12). Quality of data is limited to case reports and uncontrolled studies.

In an *in vitro* study, 24 strains of *C. minutissimum* and other *Corynebacteria* species were investigated for their susceptibility against bifonazole by an agar dilution test (13).

Bifonazole showed a very good *in vitro* activity against all tested species and strains of *Corynebacterium*. Minimal inhibitory concentration (MIC) values were in a range from 0.05 to 1.56 µg mL⁻¹ (106 cfu [colony forming units] mL⁻¹). At a higher density of bacteria (108 cfu mL⁻¹), MIC values were in a range from 0.1 to 1.56 µg mL⁻¹. In a recently published *in vitro* investigation of the antibacterial efficacy of miconazole against Gram-positive aerobic bacteria, *Corynebacteria* spp. were found to be most sensitive to miconazole (14).

Pitted keratolysis

The disease has originally been described as keratoma plantare sulcatum with crater-like pits and malodor (Castellani, 1910). The age peak is about 25 years. Males are 8-times more affected than females. Pressure-bearing areas are the common sites of infection (15) (Fig. 2). Plantar hyperhidrosis is an important comorbidity and treatment with botulinum toxin A has been successful in pitted keratolysis (16). *C. minutissimum* has been related to pitted keratolysis (17). However, Mikx and de Jong (1987) failed to demonstrate keratolytic activity of a sample they analyzed (18), which argues for mixed infections by *C. spp.* The differential diagnosis includes tinea pedis and keratodermas.

Topical treatment with mupirocin 2% ointment or other topical antibiotic ointments like fusidinic acid, erythromycin or clindamycin has been recommended in conjunction with improved hygiene measures; however, evidence is of poor quality (19, 20). Since more than 90% of affected patients suffer from plantar bilateral hyperhidrosis,

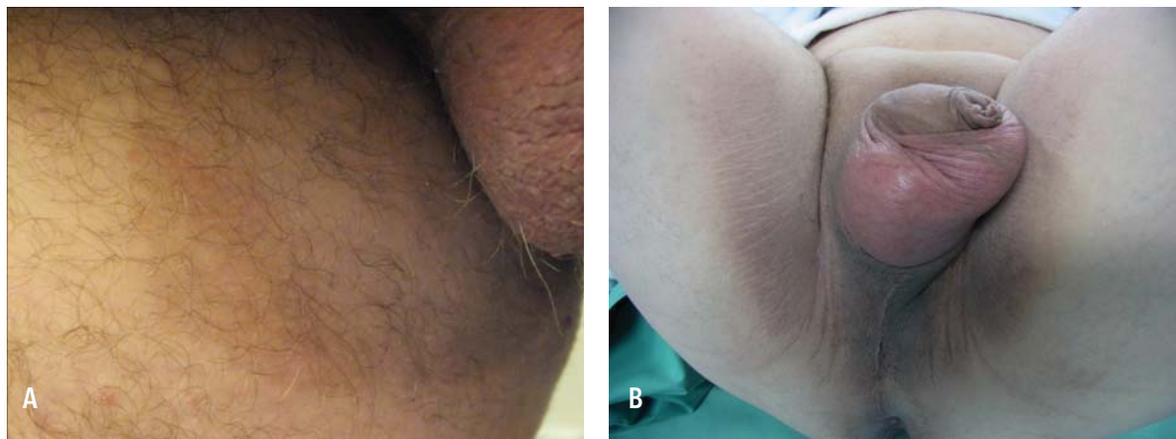


Figure 1. Erythrasma. (A) Well-defined erythematous lesions of the groins. (B) Atypical erythrasma with acanthosis nigricans in obesity



Figure 2. Pitted keratolysis

antihidrotic treatment should be considered as well (21).

Trichobacteriosis

Trichobacteriosis (Syn: trichomycosis) is a cutaneous infection of the hair, mainly of young adults. There is a strong males preponderance. The most common site is the axillary hair, but pubic hair and capillitium may also be affected (22-24).

The most common clinical variant is trichobacteriosis flava (yellowish pigmentation, while red) and black variants occur much less frequently. The causation of trichobacteriosis flava is due to *C. spp.* with *C. tenuis* as the dominant species. The other variants of trichobacteriosis have been related to *Micrococcus spp.* and *Serratia spp.* (22).

The hair becomes not only discoloured but also thickened due to bacterial growth (Fig. 3). The hair shaft is usually not penetrated, but damage of the underlying cuticular and cortical keratins has



Figure 3. Trichobacteriosis

been described. Malodor may be present. Focal hyperhidrosis is the most important comorbidity (25). The most important differential diagnosis is white piedra - a superficial fungal infection of the hair caused by *Trichosporon asahii* (26).

The treatment consists of hair shaving, antifungal or antibacterial topical therapy and control of hyperhidrosis (22, 27).

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