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Multidrug-Resistant *Corynebacterium Striatum* Strains: The Villain with the Angelic Face

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ABSTRACT

Corynebacterium striatum is a gram-positive bacterium part of common flora of the human skin and mucous membranes. Plethora of data worldwide registers the pathogen a potent causative agent of invasive infection and nosocomial outbreaks in both immunocompromised and immuno-competent patients. Limited virulence factors of C. striatum have been reported in literature. C. striatum multidrug-resistant strains are here to stay. They provoke nosocomial invasive infections and outbreaks. The plasticity of the microorganism to acquire resistance via mobilizable resistance genes renders C. striatum a potent reservoir for naïve strains of other species. The ability to form biofilms is extra armor of the bacterium.

Keywords

Corynebacterium striatum, Resistance genes, Multidrug resistance.

Introduction

Corynebacterium striatum is a gram-positive bacterium part of common flora of the human skin and mucous membranes. Plethora of data worldwide registers the pathogen a potent causative agent of invasive infection and nosocomial outbreaks in both immunocompromised and immunocompetent patients [1]. However, limited virulence factors of *C. striatum* have been reported in literature [2].

Predisposing factors for invasive infections are skin lesions, medical devices, prosthetic devices, long period of parenteral antibiotic administration, underlying disease, immunosuppression [2]. The tolerance of the bacterium to common antiseptics regarding biofilm formation needs further elucidation [3-6].

Main Text

Virulence factors: *C striatum* strains can form biofilm at 37◦C on all the abiotic surfaces and on all types of tracheostomy tubes [7]. *C. striatum* strains isolated from invasive human infections can adhere to human epithelial cells via pili encoded by *Spa DEF* genes [7].

The first world reported case of *C. striatum* invasive infection was reported in 1976 in the United States of America (USA) by Bowstead and Santiago regarding an acute and fatal pleuropulmonary infection in a patient with history significant for hematologic malignancy [5]. In 1993, the microorganism was firstly reported as the culprit of nosocomial outbreak infection. The mechanism was transmission from patient to patient via the hands of the hospital staff [8].

Before 2000, all *C. striatum* strains isolated from invasive infections involved immunocompromised patients. From 2000 onwards, the microorganism is involved in nosocomial infections related to intravenous catheters, endoscopic devices, and respiratory tract colonization in the Intensive-Care Unit (ICU), in immunocompetent patients also [5,9].

Multidrug-resistant strains (MDRs) have been reported worldwide. Japan: Till 2020 all strains reported had high levels of resistance for erythromycin, tetracycline, rifampicin, and ciprofloxacin.

All strains were susceptible to vancomycin [5,10]. Spain: Till 2020 all reported nosocomial strains isolated were MDRs. Of those, 11% were susceptible only to vancomycin [5,11]. South America: To our knowledge, available data regarding MDR *C. striatum* infections are only available in Brazil [5,12,13]. Korea: The first MDR *C. striatum* strain was described by Yoo et al. in 2015 from a patient with bacteremia [14]. China: Between 2017 and 2018, 95.3% of *C. striatum* strains were multidrug-resistant [15]. Turkey: All *C. striatum* strains reported were resistant to penicillin, cefotaxime, ciprofloxacin, and tetracycline. All strains were susceptible to vancomycin and linezolid [16]. Tunisia: Half of the isolated strains showed MDR phenotype. All strains were susceptible to vancomycin, linezolid, and daptomycin [17]. Italy: MDR phenotype was attributed to clonal spread of a specific strain [18,19]. USA: MDR strains have been reported as case reports [20]. Greece: MDR strains have been reported as case reports [21-23].

Regarding *C. striatum* infections related to prosthetic devices, MDR strains reported were mainly susceptible to vancomycin, linezolid, and daptomycin [6]. Mechanisms involved in antimicrobial resistance in MDR *C. striatum* strains:

a) Long period of parenteral antibiotic administration is related to *C. striatum* infections [9].

b) Genes of resistance detected on MDR strains: The *erm(X)* gene, encoding resistance to erythromycin and clindamycin has been reported in *C. striatum* strains isolated from invasive infections [5,18]. Resistance is the result of a modification in the binding region of the antibiotics [17]. *TetA* and *tetB* genes, encoding resistance to tetracycline, oxytetracycline, and oxacillin. *Cmx* and *aphA1* genes, encoding resistance to aminoglycosides and chloramphenicol via an efflux pump [5,18,24]. The *aac(3)-XI* gene is related to aminoglycoside resistance [25]. The *bla* gene that encodes class A beta-lactamase is responsible for penicillin resistance 16]. The *amp C* gene that encodes class C beta-lactamase is responsible for cefotaxime resistance [16]. Quinolone resistance was found to be associated with point mutations in the gyrase subunit A structural gene region. Thus, resistance is the outcome of mutations in chromosomal genes [24, 26-27]. High level resistance to ciprofloxacin and moxifloxacin has been linked to double mutations in the *gyrA* gene in positions 87 and 91 [17].

Mobile genomic elements like transposons and plasmids are related to resistance to macrolides, tetracyclines, beta-lactams, and aminoglycosides [24]. The most common mechanism for aminoglycoside resistance has been reported to be the enzymatic inactivation of the antibiotic molecule [16]. The *sul* genes give sulfamethoxazole resistance [15]. The *aphA1* gene is responsible for resistance to chloramphenicol [18].

c) Development of high level daptomycin resistance: High level daptomycin resistance (MIC > 256 μg/mL), after exposure of the isolates to the antibiotic for 24 hours period, has been proved in vitro. In nosocomial settings high level daptomycin resistance has been reported for doses ranging from 6 to 8 mg/kg. Daptomycin activity on *C. striatum* strains is dependent on the concentration of the bacterial cell membrane phosphatidylglycerol (PG). A single mutation leads to loss of function of phosphatidylglycerolsynthase (pgsA2). As a result, the membrane content of PGs decreases, as they are removed from the cell membrane. This alteration leads to resistance to daptomycin [28-31].

d) Acquired mobilizable resistance genes localized to common chromosomal regions provoke resistance to aminoglycosides, macrolides, lincosamides, and tetracyclines to naïve strains [25]. These characteristic renders *C striatum* a potent source to provoke mobilizable resistance to susceptible strains of other species [25].

Conclusion

C. striatum multidrug-resistant strains are here to stay. They provoke nosocomial invasive infections and outbreaks. The plasticity of the microorganism to acquire resistance via mobilizable resistance genes renders *C striatum* a potent reservoir for naïve strains of other species. The ability to form biofilms is extra armor of the bacterium.

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