

## A rare case of ankle peri-implant infection by multi drug resistant *Chryseobacterium indologenes*

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**Chryseobacterium indologenes is a rare human pathogen which is nowadays considered an emerging fearsome organism because of its upcoming antibiotic resistance. We present a quite unique case of a multi drug resistant C. indologenes surgical wound infection in a patient submitted to cannulated screw fixation of a displaced medial malleolus fracture. The microorganism was identified only after three months of attempts to treat pharmacologically the unhealed wound, by removing the osteosynthesis device and sonicating it, and the surgical wound progressively restored by second intention.**

**Keywords:** Chryseobacterium indologenes, medial malleolus fracture, surgical site infection.

### INTRODUCTION

Chryseobacterium indologenes is a rare human pathogen, which is not normally part of the human microflora although widely distributed in nature, but nowadays it is considered an emerging fearsome organism because of its upcoming antibiotic resistance<sup>1,2</sup>. C. indologenes, previously known as Flavobacterium indologenes, is a yellow-pigmented, non-motile, oxidase positive, glucose non-fermentative, Gram-negative rod-shaped bacterium, which is ubiquitous in nature and can be found in soil, food products and water source, despite adequate chlorination<sup>3,4</sup>.

The majority of human infections have been reported from Taiwan and increasing cases have been registered from Australia, India, USA and Europe<sup>5,6</sup>.

Immunocompromised patients, such as patients with diabetes mellitus, malignancies and neutropenia, and those exposed to prolonged antibiotic treatments, are mainly affected. The preference of the organism to wet or humid surfaces makes both exudative surgical wounds and tubes in contact with fluids (i.e. feeding tubes, central venous catheters, tracheostomy tubes) potential sources of nosocomial infections<sup>7,8</sup>. The ability of the bacterium to build biofilm on foreign materials and produce proteases, combined with its emerging multi drug resistance, despite its own low virulence, makes this kind of infection an ominous disease and a great challenge for clinicians<sup>9</sup>.

Despite it has been quoted in infectious disease textbooks as a potential surgical site pathogen, no case of C. indologenes orthopedic wound infection has been reported in literature.

Therefore, we present a quite unique case of a multi drug resistant C. indologenes surgical wound infection in a patient submitted to cannulated screw fixation of a displaced medial malleolus fracture, at the Department of Orthopedics and Traumatology of C.T.O. Hospital in Naples.

### CASE REPORT

A 50-year-old man suffered from a closed displaced medial malleolus fracture (AO/OTA 44A2.1), because of a car accident, and was submitted to open reduction and double cannulated screw fixation surgery, under pre-operative intravenous administration of Cefazolin 2g, which was continued for the following two days post-op (Fig. 1).

He was a heavy smoker and had a medical history of aortic valve mechanical replacement, therefore he was under warfarin therapy, which was switched pre-operatively to low molecular weight heparin. Dressing change was performed daily during hospitalization and no early complications at the surgical site have been reported.

He was discharged one week after the surgery, with a prescription of keeping out of load the injured



*Fig. 1 — X-rays of a 50-year-old man, affected by displaced closed medial malleolus fracture (AO/OTA 44A2.1).*

ankle and renewing the dressing every week, at the outpatient, paying attention to keep it dry and clean.

Despite the suggestions, the patient quite immediately resumed his work at an oriental cuisine restaurant and did not fully comply with the hygiene rules to preserve the dressing clean. Furthermore, he skipped the outpatient follow-up checks the coming weeks.

Finally, at one-month post-op, he came to the outpatient with a superficial wound dehiscence, medial malleolus erythematous swelling and leg edema, despite the absence of fever or malaise. No evident signs of cannulated screw heads exposures could be appreciated (Fig. 2).

Promptly, a wound swab culture was performed and an empirical therapy with Trimethoprim/sulfamethoxazole was started. The patient was prescribed with dressing changes three times a week, at the outpatient, in order to exclude possible secondary exposure of the osteosynthesis device.

An X-rays exam, performed at 40 days after surgery, showed a good progression of fracture healing, without any signs of screws mobilization or peri-implant osteolysis (Fig. 3). A venous doppler ultrasound of the lower limb showed a deep and superficial venous system with normal flow and compressibility (negative



*Fig. 2 — At 1 month post-op: superficial wound dehiscence, medial malleolus erythematous swelling and leg edema.*



Fig. 3 — X-rays at 40 days after surgery: good progression of fracture healing, without any signs of screws mobilization or peri-implant osteolysis.

CUS-test). A blood sample reported a week increase in white blood cell count (11,19 mm<sup>3</sup>) and C-reactive protein (1,1 mg/dl).

The swab cultures revealed a methicillin-sensitive *Staphylococcus aureus* (MSSA) and a *Staphylococcus lugdunensis* isolation, both sensitive to tetracyclines, therefore, under the prescription of the infectious disease consultant, the trimethoprim/sulfamethoxazole was suspended after 7 days and switched to minocycline hydrochloride, which was continued for 14 days.

At almost three weeks after the discovery of a surgical wound infection, thanks to the combination of advanced medications every two days and targeted antibiotic therapy, the size of the dehiscence had reduced but the bottom of the lesion was still frankly fibrinous and the edges hard and discolored (Fig. 4). The patient started to complain week general malaise and heavy discomfort with the complete weight bearing over the ankle. Other two delayed wound swabs were performed, both for bacteria and fungi, together with two blood culture sets and naso-rectal swabs as in look up for *Acinetobacter*, *Pseudomonas*, *Enterobacteria*, but all the results were negatives.

However, the previously reported isolation of *Staphylococci* had disappeared in the following



Fig. 4 — At almost three weeks after the discovery of a surgical wound infection the size of the dehiscence had reduced but the bottom of the lesion was still frankly fibrinous and the edges hard and discolored.

cultures. On a new blood sample, the count of white blood cells was within the ranges (9,69 mm<sup>3</sup>), except for a slight eosinophilia (6,9%).

As infectious disease consultant suggested, new targeted antibiotic therapy was attempted with Amoxicillin/clavulanate three times a day for 14 days.

At three months after the osteosynthesis procedure, in consideration of the fact that bone healing was completed while the surgical wound had continued to look like infected, the patient was re-admitted and subjected to a wound extensive debridement and cannulated screws removal, sending the osteosynthesis device to the microbiology laboratory for sonication.

Surprisingly, the culture obtained from the sonication revealed an isolation of more than 200 colony-forming units of *C. indologenes*, which was resistant to almost all antimicrobials except meropenem and piperacillin/tazobactam, despite its high minimal inhibitory concentration (MIC) (Tab. I).

Based on the susceptibility report and under prescription of an infectious disease specialist, Amoxicillin/clavulanate was discontinued and Dalbavancin treatment was started, as a single administration at a dosage of 1500 mg, infused in 500 cc of 5% glucose solution in 30 minutes<sup>10</sup>.

Already 72 hours after the removal of tibial cannulated screws and the Dalbavancin infusion, the patient’s clinical findings improved, so at one-week post-op the patient was discharged and the wound completely healed within two weeks. No further complications have been reported and the functional outcomes of the patients were above expectation.

**DISCUSSION**

Infection at the surgical site is one of the most common post-operative complications in orthopedics, with a prevalence of about 4%. According to demographic data, males are most affected (62,4%) and the tibia is the second most common surgical site of infection (28%), followed by the knee (29,3%)<sup>11-14</sup>.

Due to the high prevalence of orthopedic surgery site infection, it is crucial to differentiate the pathogens and their bacterial resistance, therefore bacterial strains are the most important weapons to target correctly the antimicrobial therapy.

According to most studies, *Staphylococcus* is the most common organism causing infection in orthopedic patients, followed by Gram-negative bacilli, coagulase-negative *Staphylococci*, *Enterococcus* species and *Escherichia coli*<sup>15,16</sup>. However, in case of a difficult unhealing surgical wound, other etiologic hypothesis needs to be considered and different specimens have to be obtained.

In the case reported of a complicated surgical wound, despite the initial identification of MSSA and *S. lugdunensis* at a superficial wound swab culture, the prolonged antibiogram-guided therapy had eradicated the pathogens, without obtaining a successful healing effect on the wound. The explication proposed was likely of a *Staphylococci* over-colonization in a subset of wet environment below the dressing, caused by the sero-purulent secretions. The *Staphylococci* identified in the specimen, according to the sensitivity spectrum, were common extra-nosocomial bacteria which had acted as opportunists, but it could not be possible to consider them responsible of a subacute infection. Actually, after hardware removal and sonication, beyond all expectations, a biofilm of *C. Indologenes* had been detected over the cannulated screw threaded edge. It was the first case of *C. Indologenes* infection identified in our hospital, therefore it was not presumably a nosocomial infection. Furthermore, the peri-operative antibiotic prophylaxis had been correctly accomplished, according to the guidelines available in the literature<sup>17</sup>.

**Table I.** — Hardware sonication culture: isolation of more than 200 colony-forming units of *C. indologenes*, which was resistant to almost all antimicrobials except meropenem and piperacillin/tazobactam, despite its high minimal inhibitory concentration (MIC).

IDENTIFICATION			
Microorganism :			<i>Chryseobacterium indologenes</i>
Bacterial load :			200 cfwml
ANTIBIOGRAM			
Antibiotic			
Amikacin	> 32 (R)	Meropenem	1 (S)
Cefepime	16 (R)	Piperacillin/Tazobactam	8 (S)
Ceftazidime	2 (S)	Ceftazidime/Avibactam	> 8 (R)
Ciprofloxacin	0,5 (I)	Ceftolozane/Tazobactam	> 16 (R)
Gentamicin	> 8 (R)		
S = Susceptible - I= Sensitivity related to increased exposure to the drug - R = Resistant - IE = Insufficient Evidence NI = Non Interpretable - MIC = Minimum Inhibitory Concentration [mcg/ml] ANTIBIOGRAM INTERPRETATIVE CRITERION according to EUCAST 2023.			



The possible cause of contamination of the surgical wound could be found in the bad behavior hold by the patient, soon after the discharged, consisting of careless management of dressing and immediate weight bearing despite different prescription, and the work environment (an oriental cuisine restaurant) into which the patient would have been gotten in touch with potential carrier of the microorganism, soon after the operation.

Biofilm production over foreign materials and protease activity play an important role in *C. indologenes* virulence, especially in patients with indwelling devices<sup>4</sup>.

Moreover, the multi drug resistance of this pathogen had completely protected it from the multiple antimicrobials administered to the patient (i.e. trimethoprim/sulfamethoxazole, minocycline hydrochloride, amoxicillin/clavulanate). Beside the administration of Dalbavancin, a long-lasting second-generation lipoglycopeptide antibiotic with bactericidal activity against a very wide range of microorganisms, the real resolution therapy was the removal of the biofilm together with the hardware<sup>10</sup>.

The case report we present could be an example of how the stubbornness of treating an infected surgical wound with antibiotic therapy alone can be, sometimes, a wrong choice because it can hide the presence of germs that are difficult to identify or eradicate, germs occasionally so rare as to be unique, according to the literature.

## CONCLUSION

Despite the worldwide increasing of *C. indologenes* nosocomial infections, the pathogen is still little known in western countries as a possible source of post-operative infection, even more so in case of appropriate risk factors. It should be considered as differential diagnosis in surgical wound infection non responding to empiric antibiotic treatment, until a confirmatory culture report is obtained.

Furthermore, there aren't guidelines or gold standards of management of this pathogen, and the antibiotic treatment is strictly dependent of the antibiogram. The antimicrobials commonly used to treat Gram-negative organisms, such as cephalosporins, aminoglycosides and quinolones, have been reported to be ineffective and, in addition, it is dramatically rising the resistance to trimethoprim-sulfamethoxazole and ampicillin-sulbactam, to which *C. indologenes* had shown susceptibility in the recent past.

Because of lack of appropriateness in antibiotic choice and according to the case report presented, hardware subjacent a *C. indologenes* infected wound should be removed, in order to remove potential biofilm adherent to the device.

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