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# Kerstersia Gyiorum causing Chronic Oti Media: Where a Quinolone Does not Work

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## Abstract

Chronic otitis media (COM) is an inflammatory disease which affects the mucosal and bone structures of the medium ear, insidiously, slowly progressive, prone to persist and to produce severe sequelae. *Staphylococcus aureus* followed by gram negative bacillus as *Proteus spp.*, *Klebsiella spp.*, *Escherichia spp.* and *Haemophilus influenza* are common pathogens causing COM. Recently some cases of COM produced by less known bacteria have been described. This is the case of the genus *Kerstersia* which has emerged in the literature causing bacteremia and urinary infection, as well as a causative pathogen of chronic otitis.

We have reviewed five cases as well as our own experience with an 88-year-old man transferred to our hospital suffering from persistent otorrhea, finally diagnosed as COM caused by *Kerstersia gyiorum* resistant to quinolones. *Kerstersia* genus belongs to the family *Alcaligenaceae*. A sample from the ear of our patient was taken and gram-negative rods were observed in the Gram stain. After incubation for 24 h, in all media, abundant slightly convex colonies with extended edges, colorful, were isolated and identified by MALDI-TOF (matrix-assisted laser desorption ionization time-of-flight) Biotyper 3.1 as *Kerstersia gyiorum* (score of 2.3. *K. gyiorum* identification was confirmed by sequencing of the rRNA 16S gene and comparing of the sequence obtained with those deposited in GenBank with the NCBI BLASTn algorithm. Our case would be the third case resistant to quinolones reported in the literature.

**Keywords:** Kerstersia; Chronic otitis; Ciprofloxacin resistant

## Introductio

Chronic otitis media (COM) is an insidious, slowly progressive inflammatory disease affecting the mucosal and

bone structures of the medium ear and prone to persist and to produce severe sequelae [1].

Suppurate COM is known as chronic ear discharge through a tympanic drilling, lasting for at least 6 weeks with periods of inactivity [1]. Well-known risk factors for developing a COM are overcrowded living conditions, recurrent respiratory tract infections and smoking [2].

*Staphylococcus aureus* followed by gram negative bacillus as *Proteus spp.*, *Klebsiella spp.*, *Escherichia spp.* and *Haemophilus influenza* are common pathogens causing COM. *Bacteroides spp.* and *Fusobacterium spp.* are the anaerobes more frequently isolated. There are also mixed infections and several cases of COM produced by less known bacteria as *Bordetella*, *Achromobacter*, *Alcaligenes* and *Kerstersia* [2-5] have been described.

We presented a case of COM by *Kerstersia gyiorum*, the third case described resistant to ciprofloxacin.

## Case Presentatio

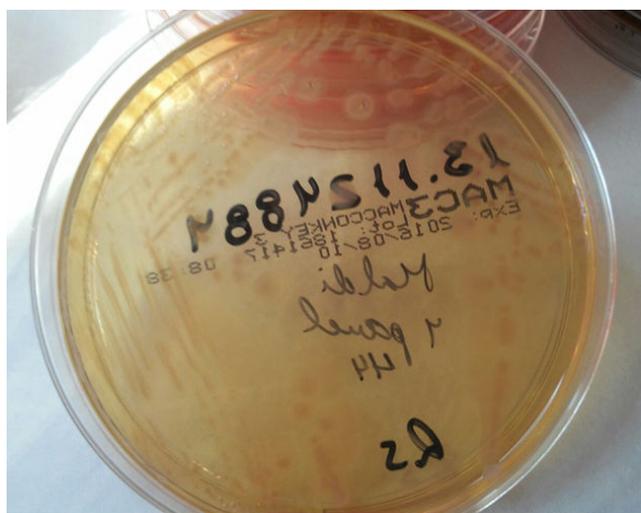
The case is a male patient, 88 years old, with a history of type 2 diabetes mellitus, hypertension, dyslipidemia, chronic renal failure, chronic heart failure and prostatic hypertrophy. In 2004, he was diagnosed a right tympanic perforation and otorrhea with good clinical outcome after medical treatment.

In May 2016, the patient went to his family doctor complaining of a right otalgia and otorrhea for three weeks and being referred to an ENT specialist. Then, the presence of a foreign body (cotton) in the right ear canal and a tympanic perforation already known was shown. The foreign body was removed and topical corticosteroids (solution dipropionate/cloquinol beclomethasone; Menaderm eardrops® 0.25 mg/10 mg/ml, 3 drops tid, 7 days) were prescribed and monthly reviews were scheduled.

After persistent otorrhea, two regimens of topical ciprofloxacin (Cetraxal ótico® 1.2 mg/0.4 ml solution ear drops, 3 drops tid, 7 days) are prescribed. So this torpid evolution the patient was again referred to an ENT specialist on July. After his physical exam, a profuse suppuration inside the right ear

was observed and a sample of the exudate was taken for microbiological studies.

Direct Gram stain showed Gram-positive *Cocci* and Gram-negative *Bacilli* but no leukocytes. After incubation for 24 h, a few colonies of *Staphylococcus aureus* were isolated on Columbia agar (Oxoid, Germany) and Chocolate agar (Chocolate Agar Base, GC Medium, BD Difco™, Beckton Dickinson, US). In all media including MacConkey agar (No. 3, Oxoid, Germany), abundant slightly convex colonies with extended edges, colorful from gray hue to clear lavender (Figure 1), oxidase and catalase negative and indol positive were isolated. In the Gram stain from the grown colonies, gram-negative *bacilli* were observed and then identified by mass spectrometry using the technique of MALDI-TOF (matrix-assisted laser desorption ionization time-of-flight) Biotyper 3.1 (Bruker Daltonic GmbH, Bremen, Germany) as *Kerstesia gyiorum* with a score of 2.1.



**Figure 1** Growing colonies of *Kerstesia* over blood agar plate and MacConkey agar.

Antibiotic susceptibility test (Table 1) was performed by broth microdilution method using the automated system MicroScan WalkAway® (Siemens Healthcare, Spain currently Beckman Coulter) and the MicroScan® panels (Neg MIC Panel Type 44) were used. The interpretation of the minimum inhibitory concentration (MIC) was performed according to the breakpoints for non-*Enterobacteriaceae* gram-negative *bacilli* set by CLSI (Clinical and Laboratory Standards Institute) [6].

Isolates were susceptible to cefotaxime  $\leq 1$   $\mu\text{g/ml}$ , ceftazidime  $\leq 1$   $\mu\text{g/ml}$ , cefepime  $\leq 1$   $\mu\text{g/ml}$ , gentamicin  $\leq 2$   $\mu\text{g/ml}$ , tobramycin  $\leq 2$   $\mu\text{g/ml}$ , amikacin  $\leq 8$   $\mu\text{g/ml}$ , piperacillin-tazobactam  $\leq 8$   $\mu\text{g/ml}$ , tetracycline  $\leq 4$   $\mu\text{g/ml}$ , trimethoprim-sulfamethoxazole  $\leq 2/38$  g/ml, meropenem  $\leq 1$   $\mu\text{g/ml}$ , imipenem  $\leq 1$   $\mu\text{g/ml}$  and resistant to ciprofloxacin  $>2$   $\mu\text{g/ml}$  and levofloxacin  $>4$   $\mu\text{g/ml}$ .

*K. gyiorum* identification was confirmed by sequencing the 16S rRNA gene. The sequence was 99.8% identical to *K. gyiorum* type strain LMG ..... using the NCBI 16S rRNA gene database.

**Table 1** Antibiotic susceptibility profile.

Antibiotic	MIC ( $\mu\text{g/ml}$ )	Interpretation <sup>a</sup>
Cefotaxime	$\leq 1$	S
Ceftazidime	$\leq 1$	S
Cefepime	$\leq 1$	S
Gentamicin	$\leq 2$	S
Tobramycin	$\leq 4$	S
Amikacin	$\leq 8$	S
Piperacillin-tazobactam	$\leq 8$	S
Trimetoprim-sulfamethoxazol	$\leq 2/38$	S
Meropenem	$\leq 1$	S
Imipenem	$\leq 1$	S
Ciprofloxacin	$>2$	R
Levofloxacin	$>4$	R

After antibiotic susceptibility report was known, the patient was treated with topical gentamicin (gentamicin/dexamethasone eye drops solution Colircusi Gentadexa® 1/3 / 0.5 mg, 3 drops tid) plus oral cloxacillin (cloxacillin 500 mg, 1 tablet tid) for 7 days. After that, a clinical improvement and otorrhea dry up was clearly observed.

## Discussion

*Kerstesia* genus belongs to the family *Alcaligenaceae*. It includes two kinds of species (*Kerstesia gyiorum* and *Kerstesia similis*). It is a gram-negative, small (1-2  $\mu\text{m}$ ), coccobacilli in pairs or short chains. It grows well on standard culture media between 28 and 42°C. On nutrient agar, the colonies are flat or slightly convex with smooth edges and white to light brown. They are strict aerobes, non-fermenter, catalase positive [7,8]. The biochemical features of our strain were similar to those reported in the literature.

*K. gyiorum* appears as a human pathogen described in the literature reviewed in nine occasions, being isolated from urine samples [9], ulcers [10,11] sputum [12] and causing chronic otitis in five cases [2-5].

The first isolation associated with chronic otitis was reported in 2012 by Almuzara et al. It was in a 16 years-old-male patient diagnosed with chronic otitis media associated to *cholesteatoma* [2]. In the other cases *K. gyiorum* has been isolated together with other microorganisms, being difficult to

determine its pathogenic role attributable solely to *K. gyiorum* (Table 2).

**Table 2** Summary of reported cases of chronic otitis media caused by *K. gyiorum*.

Reference	Age	Background	Isolation in culture	Ciprofloxacin (MIC µg/mL)	Directed therapy	Outcome
[2]	16	- AOM and retroauricular abscess -Overcrowding and unhealthy conditions	Monomicrobial	1(S)	Ceftriaxone 2 g iv then Ciprofloxacin 500 mg bid po plus Amoxicilin/clavulanic, 1 g bid po	Favourable
[3]	55	- Otorrhoea in childhood -Smoking -Bilateral mastoid surgery	Polymicrobial Corynebacterium amycolatum	>32(R)	Trimetoprim/sulfametoxazol	Favourable
[4]	53	- Chronic otorrhea in adulthood -Smoking	Polymicrobial Proteus mirabilis	1 (I)	Topical ciprofloxacin	Favourable
[4]	33	- Chronic otorrhea in adulthood	Polymicrobial Staphylococcus aureus E. coli	1 (I)	Topical ciprofloxacin	Favourable
[5]	25	- Otorrhoea In childhood	Polymicrobial Pseudomonas aeruginosa	>2 (R)	Imipenem 500 mg/qid iv, 10 days	Favourable
Present Case	88	- Chronic otorrhea in adulthood - Tympanum drilling	Polymicrobial Staphylococcus aureus	>2 (R)	Topical gentamicin Cloxacilin po 500 mg tid 7 days	Favourable

In our case, *Staphylococcus aureus* was also isolated however we considered *Kerstersia gyiorum* as a true pathogen in view of the chronicity of the disease, the poor response to treatment with ciprofloxacin, the observation of *bacilli* in the Gram stain and, the abundant growth into the inoculated plates. The cases reported so far in literature, were patients with chronic ear disease, as our patient, so it is deducible *K. gyiorum* has a pathogenic role in these patients. In our case there was no history of smoking or overcrowded conditions, described by other authors [2-4].

Currently, the identification of new species by MALDI-TOF and 16S rRNA sequencing are essential for microbiological diagnosis.

There are no cutoffs of antibiotic susceptibility in CLSI or EUCAST (European Committee on Antimicrobial Susceptibility Testing) specific to this genus. We used the CLSI criteria for non-*Enterobacteriaceae*.

According to Harris et al. [13] about the use of quinolones and aminoglycosides in the treatment of chronic suppurative otitis media, quinolones are bactericidal allowing different routes of administration and therefore outpatient treatments. They also are less ototoxic than aminoglycosides and have the same efficacy in resolving otorrhea all of which makes them a first-line option in chronic otitis, especially in cases with tympanic perforation.

*Kerstersia* isolates are generally susceptible to ciprofloxacin and cefotaxime [8] although recently there have been described two strains resistant to ciprofloxacin [3,5]. Treatment failure is considered when otorrhea persists approximately three weeks after medical therapy. Causes of failure include the presence of resistant microorganisms, the presence of *cholesteatoma* or a poor adherence to treatment, being therefore necessary a microbiological analysis including an antibiotic susceptibility study [14].

Our case would be the third case resistant to ciprofloxacin reported in the literature. The prior long treatment with ciprofloxacin may be the clue of further selection of resistant strains.

In summary, *K. gyiorum* is therefore a novel pathogen to be considered in the differential diagnosis of microorganisms causing chronic otitis media.

Microbiological diagnosis is the important key to guide the antimicrobial treatment because of the lack of homogeneity in its antibiotic susceptibility.

## Conflic of Interest

The authors declare not to have an association that might pose a conflict of interest.

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