Corynebacterium kroppenstedtii in Cystic Neutrophilic Granulomatous Mastitis: A Case Study Highlighting Diagnostic and Therapeutic Challenges

Dr. Wail NAMOUNE, MD
Constantine University Hospital Center
Clinical Microbiology Department

Plan

1. Introduction
2. Clinical Presentation
3. Imaging Studies
4. Laboratory Tests
5. Treatment
6. Discussion
7. Conclusion

Clinical Context of Mastitis

Epidemiology:

- Mastitis is a common inflammatory breast condition, particularly affecting **parous women of reproductive age**, with an estimated incidence of 1–3% in lactating and non-lactating individuals.
- While lactation-associated mastitis is well-studied, **non-lactational mastitis** presents diagnostic and therapeutic challenges due to its varied etiologies (e.g., infection, idiopathic granulomatous inflammation).

Bacterial Pathogens:

- Traditionally attributed to *Staphylococcus aureus* or streptococci.
- **Corynebacterium spp.**, part of normal skin flora, are frequently dismissed as contaminants in breast specimens despite growing evidence of their pathogenic role in specific contexts.

2. Clinical Presentation

Patient Profile

- 37-year-old parous female : G3P1, She originates from the North-East of Algeria.
- Stopped breastfeeding 3 months prior
- No smoking, nipple piercings, or trauma. No personal/family history of breast cancer.

Presenting Symptoms

- Acute, progressive left breast pain over 2 weeks.

Lump Characteristics:

Location: Upper outer quadrant of the left breast.

Appearance: Palpable, firm, erythematous mass (~4 cm), *unchanged in size* since onset.

- No nipple discharge, fever, or systemic symptoms.

Breast Exam:

- Tender, well-defined mass with localized erythema (no peau d'orange or nipple retraction).
- No axillary lymphadenopathy.

3. Imaging Studies

Left Breast Ultrasound:

- 4.5 cm irregular,
- Hypoechoic mass
- At 10-o’clock position
- 1.5 cm from nipple with posterior acoustic shadowing.

- No microcalcifications or cystic components observed.

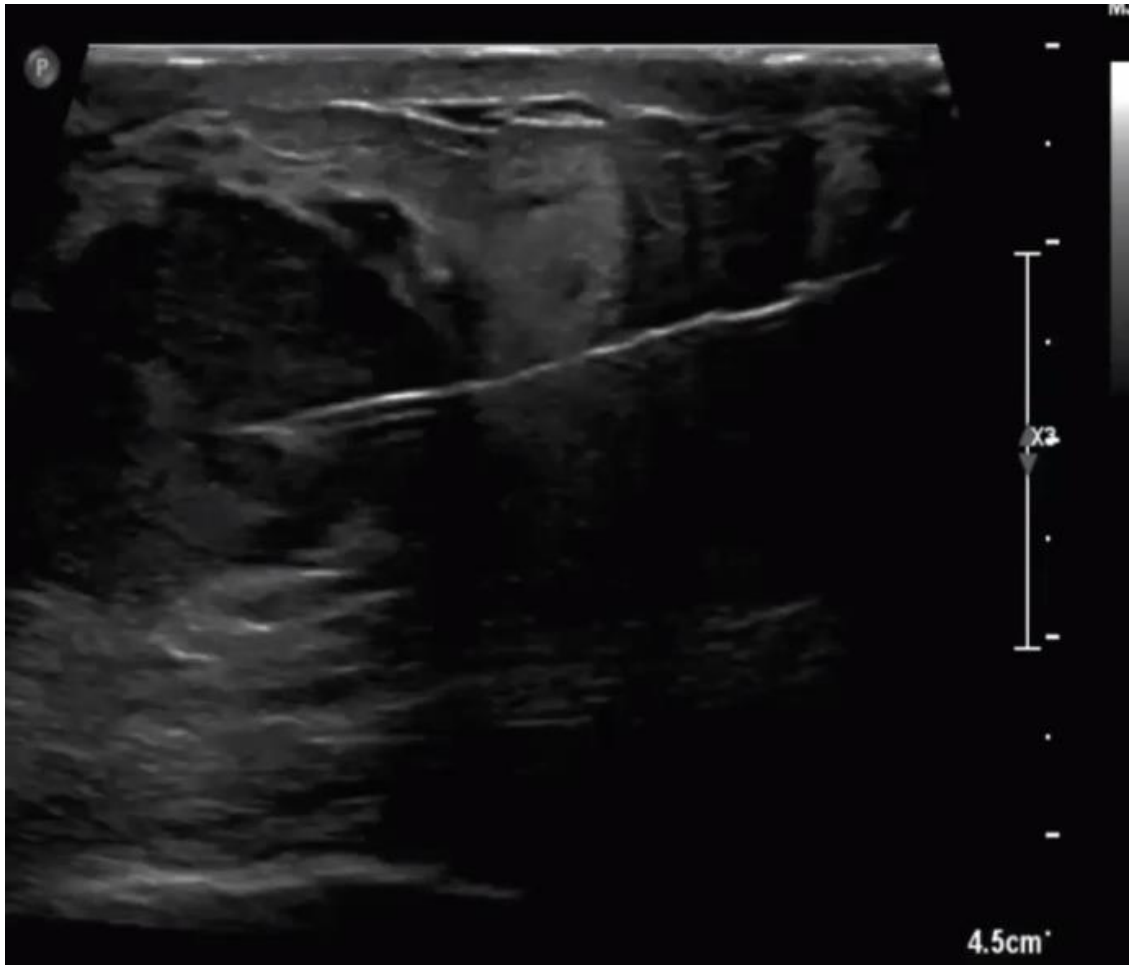

Figure 01 : US Image of the left breast

4. Laboratory Tests

- **Ultrasound guided biopsy performed**
- **Core needle Biopsy sent to surgical pathology :**

- Histological evaluation

- **Breast fluid aspirate sent to clinical microbiology department**
  - Gram Stain
  - Culture

4. Laboratory Tests

A Gram stain revealed a few gram-positive bacilli, which were consistent with coryneform bacteria.

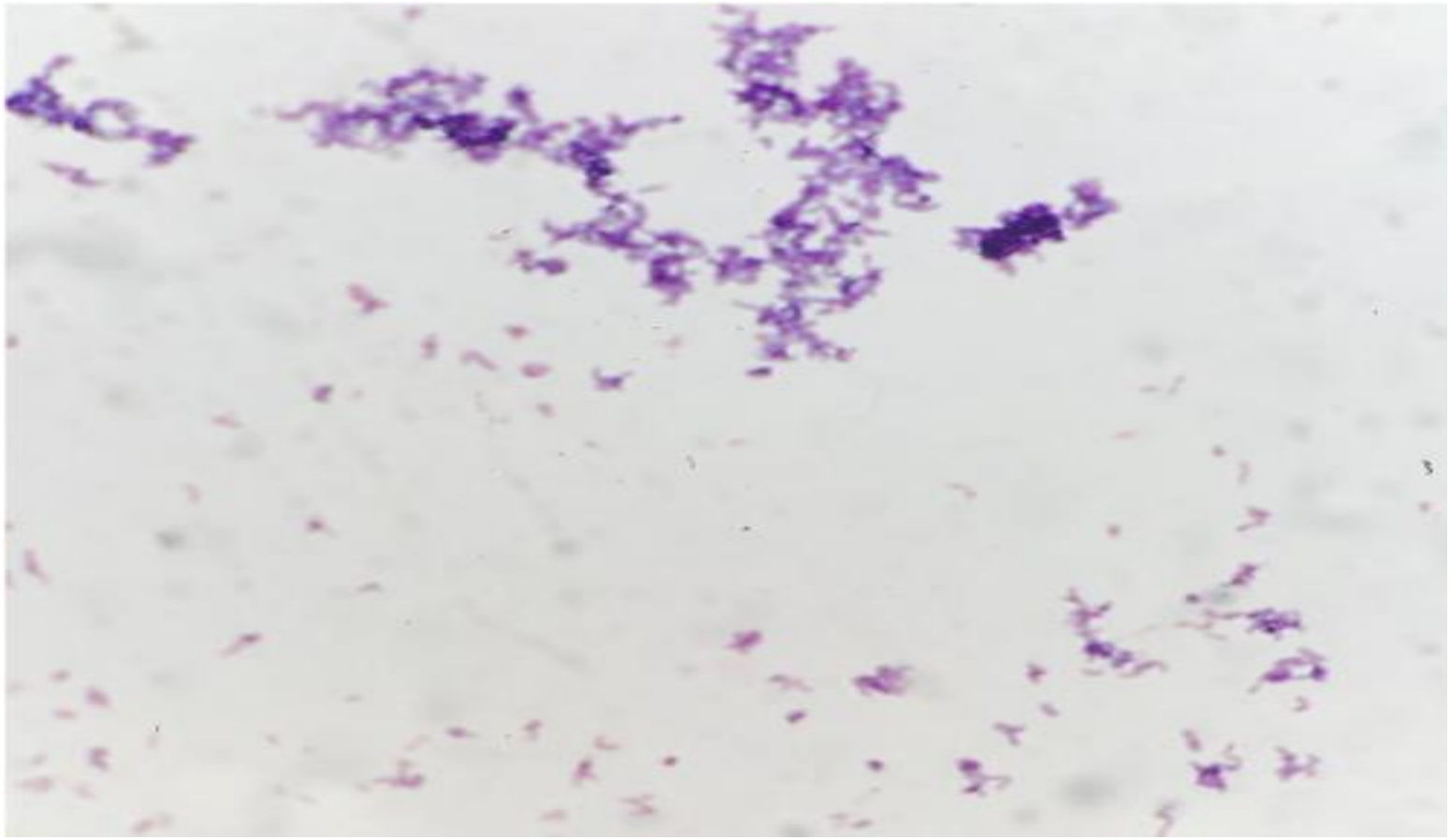

Fig. 2. Gram stain of *C. kroppenstedtii*. A single colony was selected from blood agar media and bacteria were Gram positive and displayed rod like morphology suggestive of Corynebacterium

4. Laboratory Tests

After 48 hours of incubation, a blood agar plate revealed growth of non-hemolytic, round, gray-to-white colonies measuring less than 1 mm in diameter.

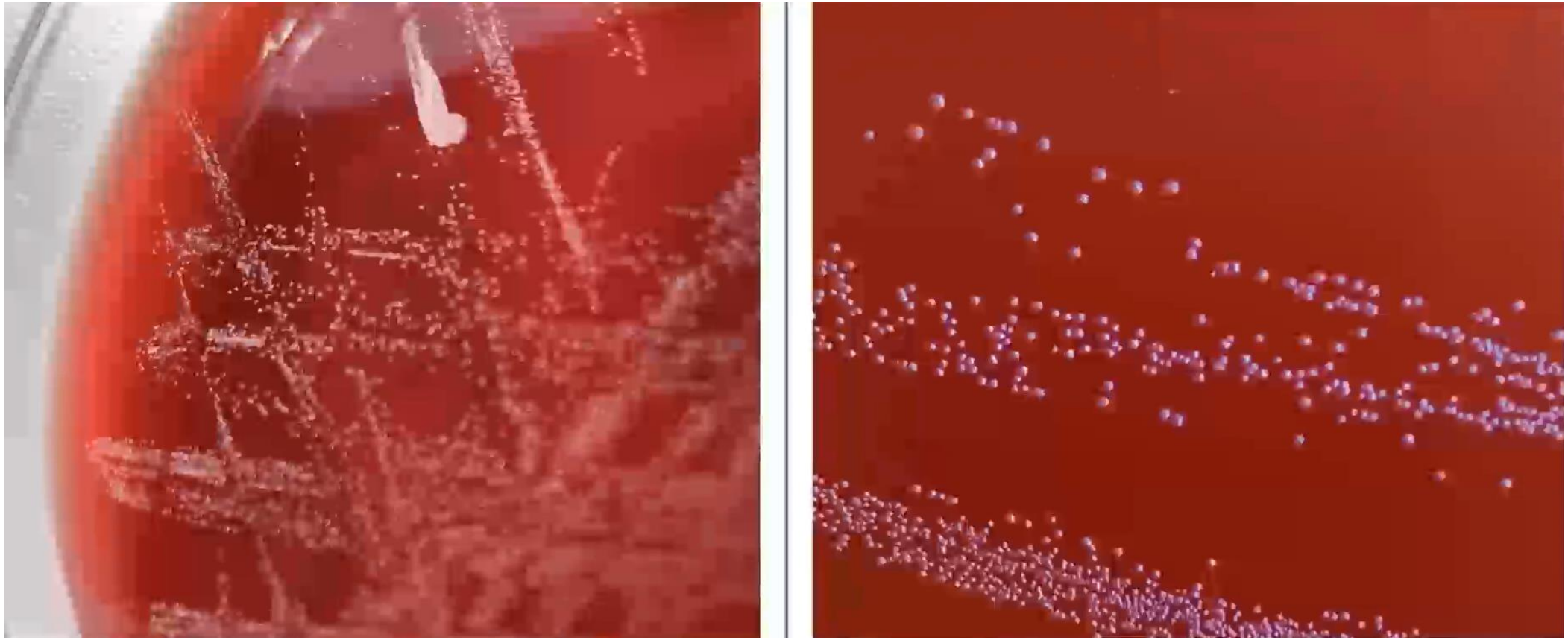

Figure 03 : 48Hours Culture on Blood Agar plate.

4. Laboratory Tests

The results obtained, using the API Coryne system identification strip (bioMérieux, Marcy-l'Etoile, France) did not match with any record in the database of the current version (V3.0).

API Strep (hippurate hydrolysis)
API NH (fructose fermentation)
API NE (assimilation of maltose, *N*-acetyl-glucosamine and phenylacetic acid) were used for the phenotypic characterization of the corynebacterial isolates.

4. Laboratory Tests

Table 01 : Phenotypic Characterizations

Test / Method	Result
Catalase	**Positive**
Oxidase	Negative
Urease	Negative
Nitrate Reduction	Negative
Pyrazinamidase	**Positive**
Alkaline Phosphatase	Weakly Positive
Esculin Hydrolysis (48h)	Weakly Positive
Gelatin Hydrolysis	Negative
β-glucuronidase	Negative
β-galactosidase	Negative
α-glucosidase	Negative
N-acetyl-β-glucosaminidase	Negative
CAMP Test	Negative
API Strep (Hippurate Hydrolysis)	**Positive**
API NH (Fructose Fermentation)	**Positive**
API NE (Maltose, NAG, Phenylacetic Acid Assim.)	Negative
Growth at 20°C on Blood Agar	**Positive**
Glucose Fermentation at 42°C	**Positive**
Lipophilia	**Positive**
Acid Production From:	
– Glucose	**Positive**
– Fructose	**Positive**
– Maltose, Sucrose, Ribose, Xylose, Lactose, Mannitol, Glycogen	Negative

4. Laboratory Tests

Using Vitek 2.0 ANC Card, *C. kroppenstedtii* was identified with 98% confidence, indicating high reliability

4. Laboratory Tests

Antibiotic susceptibility was determined by the disk diffusion method and E-test (bioMérieux, Marcy-l'Etoile, France) on Mueller-Hinton agar supplemented with 5% blood.

4. Laboratory Tests

Antibiotiques	Concentrations critiques (mg/L)			Charge du disque (µg)	Diamètres critiques (mm)			Notes Chiffres : commentaires généraux ou portant sur les concentrations critiques Lettres : commentaires portant sur les diamètres critiques
	S ≤	R >	ZIT		S ≥	R <	ZIT	
Pénicilline G[1]	0,001	1		**1 unité**	50	12		**1**. Les souches catégorisées « sensibles à forte posologie » à la pénicilline G peuvent être rendues « sensibles à posologie standard » à l'amoxicilline. Pour les souches « résistantes » à la pénicilline G, la sensibilité de l'amoxicilline peut être évaluée par détermination de la CMI, en interprétant les résultats en fonction des concentrations critiques PK/PD. **2**. Une résistance inductible à la clindamycine peut être observée chez les corynébactéries. Elle peut être mise en évidence sur l'antibiogramme par une image d'antagonisme entre la clindamycine et l'érythromycine (D-test), mais son impact clinique n'est pas connu. **3**. La tétracycline peut être utilisée pour le dépistage des résistances aux autres cyclines. Si le test de dépistage est négatif (diamètre ≥ 24 mm ou CMI ≤ 2 mg/L), les souches peuvent être catégorisées « sensibles » à la doxycycline et à la minocycline. **4**. Le ratio triméthoprime-sulfaméthoxazole est de 1:19. Les concentrations critiques sont exprimées en concentrations de triméthoprime.
Ciprofloxacine	0,001	1		**5**	50	25		
Moxifloxacine	0,5	0,5		**5**	25	25		
Clindamycine[2]	0,5	0,5		**2**	20	20		
Linézolide	2	2		**10**	25	25		
Rifampicine	0,06	0,06		**5**	30	30		
Tétracycline (dépistage)[3]	2	2		**30**	24	24		
Triméthoprime-sulfaméthoxazole[4]	1	2		**1,25-23,75**	19	16		
Vancomycine	2	2		**5**	17	17		

CA - SFM genus-level standards were applied due to lack of species-specific breakpoints

4. Laboratory Tests

The results are shown in Table 2. At present, there are few recommendations about the Corynebacterium genus but none about this specific species *C. kroppenstedtii*.

Table 02: Disk diffusion method an E-test MICs results of our Isolate

Amoxicilline	S	45 mm	Céfotaxime	S	40 mm
Penicilline G	S	35 mm	Gentamicine	S	40 mm
Kanamycine	S	35 mm	Minocycline	S	33 mm
Trimethoprime/Sulfamethoxazole	R	6 mm	Fosfomycine	R	6 mm
Erythromycine	S	40 mm	Pristinamycine	S	40 mm
Rifampine	S	45 mm	Vancomycine	S	32 mm
Penicilline G	S	0.125 mcg/ml	Amoxicilline	?	0.125 mcg/ml
Céfotaxime	S	0.032 mcg/ml	Clindamycine	S	26 mm

4. Laboratory Tests

Histopathological correlate in surgical pathology specimens is Cystic Neutrophilic Granulomatous Mastitis (CNGM)

Which is ….

Consistent with previously described histological patterns of CNGM

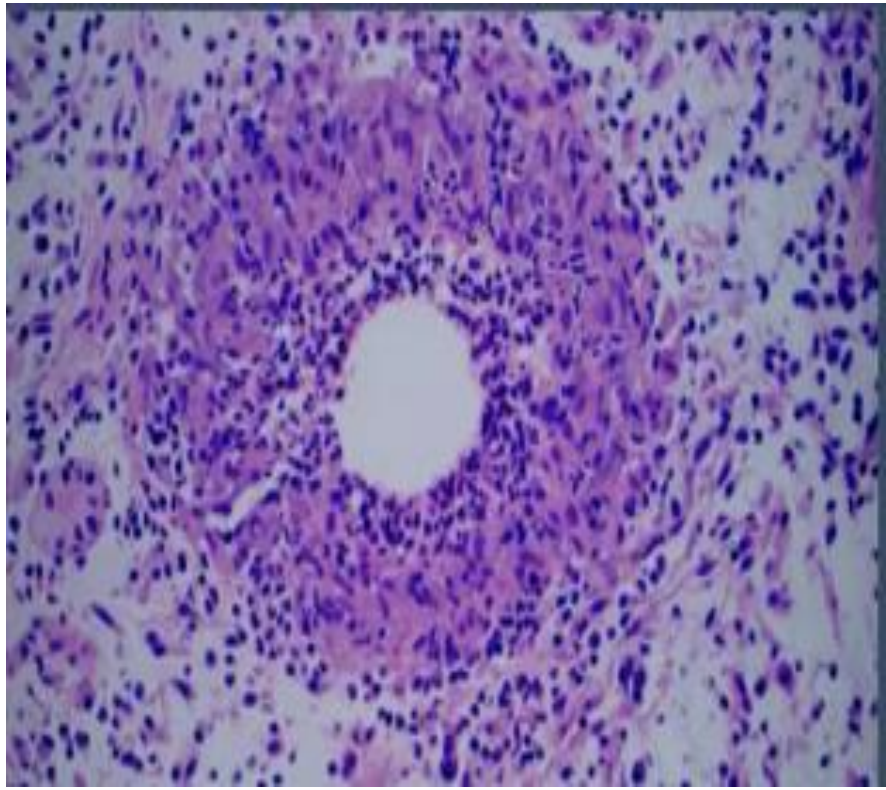

Fig 4 : Hematoxylin and esosin stain of cystic neutrophilic granulomatous mastitis. Breast parenchyma with granulomatous inflammation and cystic spaces rimmed by neutrophils.[1]

[1]Tana, C., Lue, F.-I., Aftanas, P., Tsang, K. K., Mubareka, S., Chan, A., & Kozak, R. (2023). *Whole genome sequence of Corynebacterium kroppenstedtii isolated from a case of recurrent granulomatous mastitis*. *New Microbes and New Infections*, **54**, 101122. https://doi.org/10.1016/j.nmni.2023.101122

5. Treatment

There are various approaches to CNGM

Alone or in combination : Antibiotics (which is the most common route), steroids and/or Surgery

- Can be very challenging to treat

- Women can suffer from long term complications including fistula tract formation, abscess and recurrence

- And for that reason antimicrobial susceptibility testing is warranted

The patient required surgical intervention in combination with prolonged antibiotic therapy (amoxicillin). To date, no recurrence has been observed.

6. Discussion

Cystic neutrophilic granulomatous mastitis (CNGM):

- Rare and underrecognized form of **chronic mastitis**.

Corynebacterium kroppenstedtii :

- Is a **significant and increasingly reported** pathogen [2][3].
- **Lipophilic**, **Gram-positive**, **non-spore-forming bacillus**.
- **Lacks mycolic acids**, distinguishing it from other corynebacteria.
- Often **overlooked or misclassified** as a contaminant in clinical samples.
- Strongly associated with **CNGM**.
- Common in **non-lactating women** presenting with **subacute or chronic breast masses** [4][5].

Antimicrobial susceptibility testing:

Findings are **consistent with previously reported susceptibility profiles** of *C. kroppenstedtii* [8][9].

[2]Taylor GB, et al. "Cystic neutrophilic granulomatous mastitis: a clinicopathologic study of 34 cases." *Am J Surg Pathol.* 2003;27(7):932–939.
[3] Paviour S, et al. "Corynebacterium species isolated from breast tissue." *J Clin Microbiol.* 2002;40(10):3596–3601.
[4] Dobinson HC, et al. "Corynebacterium kroppenstedtii: a rare cause of granulomatous mastitis." *ANZ J Surg.* 2015;85(12):979–983.
[5] Riegel P, et al. "Corynebacterium kroppenstedtii isolated from an infection of the breast: a case report." *J Clin Microbiol.* 2004;42(4):1737–1739.
[8] Moubarak M, et al. "Antimicrobial susceptibility of Corynebacterium kroppenstedtii." J Glob Antimicrob Resist. 2017;10:78–80.
[9] Alqumber MA, et al. "Corynebacterium kroppenstedtii as a cause of granulomatous mastitis: a case series and review." IDCases. 2020;21:e00842.

6. Discussion

Therapeutic management of CNGM remains challenging. While antibiotics are often initiated empirically, the chronic granulomatous nature of the disease may require prolonged treatment, corticosteroids, or surgical drainage in refractory cases. Notably, lipophilic antibiotics such as doxycycline or macrolides are preferred given the lipophilic cell wall structure of *C. kroppenstedtii* [10].

[10] Reddy KM, et al. "Granulomatous mastitis: a review with focus on rare infectious etiologies." *Clin Breast Cancer.* 2020;20(3):e335–e342.

6. Discussion

- This case underscores the diagnostic complexity of non-lactational mastitis and highlights the need for heightened clinical suspicion for rare pathogens such as *C. kroppenstedtii*, particularly in granulomatous mastitis.

- Early recognition and targeted antimicrobial therapy can prevent unnecessary surgical interventions and reduce recurrence.

6. Discussion

ELSEVIER

La Revue de Médecine Interne

Volume 27, Issue 7, July 2006, Pages 550-554

Communication brève

Mastite granulomateuse récidivante chez une jeune femme : rôle potentiel de « *corynebacterium kroppenstedtii* »

A young woman with granulomatous mastitis: a corynebacteria may be involved in the pathogenesis of these disease

P. Kieffer [a], R. Dukic [a], M. Hueber [a], C. Kieffer [b], M. Bouhala [a], P. Riegel [c], J.-M. Wilhelm [a]

6. Discussion

Corynebacterium kroppenstedtii Is an Emerging Cause of Mastitis Especially in Patients With Psychiatric Illness on Antipsychotic Medication

Sally C. Y. Wong,[1,2] Rosana W. S. Poon,[1,2] Jonathan H. K. Chen,[1,2] Herman Tse,[2] Janice Y. C. Lo,[3] Tak-Keung Ng,[4] Jonathan C. K. Au,[4,a] Cindy W. S. Tse,[6] Ingrid Y. Y. Cheung,[6] Man-Ting Yuk,[6] Wei-Kwang Luk,[5] and Kwok-Yung Yuen[1,2]

[1]Queen Mary Hospital, Hong Kong; [2]The University of Hong Kong; [3]Centre for Health Protection, Department of Health, Hong Kong; [4]Princess Margaret Hospital, Hong Kong; [5]Tseung Kwan O Hospital, Hong Kong; and [6]Kwong-Wah Hospital, Hong Kong

This retrospective study of patients with *Corynebacterium kroppenstedtii* infections revealed a predominance of mastitis and a potential association with psychiatric illnesses. At least one third of our patients with *C kroppenstedtii* mastitis had psychiatric illness, and >92% received antipsychotic medications. Drug-induced hyperprolactinemia may be an important modifiable risk factor in these patients.

Keywords. *Corynebacterium kroppenstedtii*; granulomatous mastitis; infection; antipsychotics agents; hyperprolactinaemia.

6. Discussion

Médecine et Maladies Infectieuses
Volume 39, Supplement 1, June 2009, Page S71

Divers

R-06 Mastite granulomateuse à *Corynebacterium kroppenstedtii* traitée avec succès par une antibiothérapie prolongée par amoxicilline

D. Andriamanantena, C. Rapp, A. Merens, G. Hatem, F. Mechai, P. Imbert, J.-D. Cavallo

6. Discussion

CLINDAMYCIN: AN EFFECTIVE TREATMENT FOR GRANULOMATOUS MASTITIS CAUSED BY *CORYNEBACTERIUM KROPPENSTEDTII* IN A PREGNANT PATIENT

Elmustafa Abdalla, Ahmed Elmudathir, Ahmed H. Ahmed, Bashir Ali, Mohamed Elhadi Ali, Noheir M. Taha, Fahmi Y. Khan

Hamad Medical Corporation, Doha, Qatar

7. Conclusion

Accurate identification of *C. kroppenstedtii*:

- Essential in **CNGM cases**.
- Increasingly recognized as a **true pathogen**, not just a contaminant.

Diagnostic approach:

Requires **integration of**:

- **Imaging**
- **Histopathological examination**
- **Advanced microbiological diagnostics**

Clinical importance:

Critical for differentiating **CNGM** from other breast conditions such as:

- **Malignancies**
- **Idiopathic granulomatous mastitis**.

7. Conclusion

Importance of timely and targeted therapy:

- Guided by **antimicrobial susceptibility testing**.
- Helps prevent chronic complications such as:
  - **Recurrent abscesses**
  - **Fistula formation**
  - **Unnecessary surgeries**

Case implications:

- Highlights the value of a **multidisciplinary approach** in managing **atypical mastitis**.
- Emphasizes the need for **increased awareness** of **emerging pathogens** in **breast infections**.

Take home messages

- Advocate for **advanced identification techniques** (e.g., MALDI-TOF, PCR 16S RNA) when *Corynebacterium* is isolated from breast specimens.

- Push for development of **species-specific breakpoints**, as current reliance on genus-level standards may be suboptimal.

THANK YOU FOR YOUR ATTENTION ☺