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Published by Intisari Sains Medis

Colonization of *Citrobacter koseri* and *Streptococcus agalactiae* in a case of cellulitis cruris dextra et sinistra



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Received: 2022-05-24

Accepted: 2022-07-26

Published: 2022-08-08

ABSTRACT

Background: Cellulitis is a skin infection involving the deep dermis and subcutaneous tissue, characterized by localized pain, swelling, tenderness, erythema, and warmth. The most common causes of cellulitis are *group A streptococci* and *Staphylococcus aureus*. *Streptococcus agalactiae* or the so-called *group B Streptococcus* can also cause cellulitis. This case report aims to evaluate the colonization of *Citrobacter koseri* and *Streptococcus agalactiae* in a case of cellulitis cruris dextra et sinistra.

Case Presentation: A 53-year-old married woman presented to the outpatient clinic complaining of swelling and redness in her left and right legs since five days ago. At first, there was only a little redness around the calf, but it became wider and pain in that area. On examination, there were multiple erythematous macules, patches, and multiple erosional lesions, warm

palpable and tender to palpation, and the diascopy test disappeared with pressure. Based on the wound culture results, isolated *Citrobacter koseri* and *Streptococcus agalactiae* bacteria were considered colonization. Both of these bacteria were less virulent. The patient was treated with systemic and topical antibiotics, analgesics, wound care management and elevated lower limbs.

Conclusion: The diagnosis of cellulitis is based on history and physical examination. On examination of the wound culture of this case, *Citrobacter koseri* and *Streptococcus agalactiae* were found, considered as colonization. The patient showed clinical improvement at each observation after administration of antibiotics and wound care management. The patient's prognosis is dubious ad bonam.

Keywords: colonization, *Citrobacter koseri*, *Streptococcus agalactiae*, cellulitis.

Cite This Article: Sari, L.G.M.P., Fatmawati, N.N.D., Praharsini, I.G.A.A., Giantoro, M. 2022. Colonization of *Citrobacter koseri* and *Streptococcus agalactiae* in a case of cellulitis cruris dextra et sinistra. *Intisari Sains Medis* 13(2): 426-430. DOI: [10.15562/ism.v13i2.1326](https://doi.org/10.15562/ism.v13i2.1326)

INTRODUCTION

Cellulitis is a skin infection involving the deep dermis and subcutaneous tissue and is most often caused by *streptococcal* and *staphylococcal* species of bacteria. Cellulitis is characterized by localized pain, swelling, tenderness, erythema, and warmth.^{1,2}

In Utah, USA, a study found 24.6 cases per 1000 people per year. Incidence is higher in males and individuals aged 45-64 years old.^{3,4} Based on Indonesia's health profile in 2009, infectious diseases of the skin and subcutaneous tissue were the third most common disease in outpatients in hospitals, with 247,256 cases.⁵ Based on data from the Dermatology and Venereology outpatient polyclinic register at the Sanglah General Hospital from

December 2016 to June 2020, 103 cases of skin and soft tissue infections were hospitalized, including 68 patients (66%) with cellulitis.⁶

In immunocompetent adults, the most common cause of cellulitis is *group A streptococci* (*Streptococcus pyogenes*) and may also be caused by *Staphylococcus aureus*.⁷ In addition, skin and soft tissue infections that manifest as cellulitis, abscesses, foot infections, or pressure ulcers can also be caused by *Streptococcus agalactiae* or *group B Streptococcus*.⁸ The most common predilection for cellulitis is the lower extremities, about 70% – 90% of cases.⁹

In the following case study, we report a case of lower extremities cellulitis in an immunocompetent patient whose wound culture showed colonization of

Streptococcus agalactiae and *Citrobacter koseri*. It is expected to provide information about cellulitis and its treatment.

CASE REPORT

A 53-year-old married woman presented to the outpatient clinic complaining of swelling and redness in her left and right legs since five days ago. At first, there was only a little redness around the calf, but it became wider and there was a pain in that area. There were no complaints of itching and fever. From her past medical history, the patient said that she had been diagnosed with lupus in 2002 and had routine medical treatment. The patient has been off medication since 2016 as the disease is well controlled.

On physical examination, the patient's

general condition appeared to be good. Blood pressure 100/60 mmHg, respiratory rate 20x/minute, pulse 89x/minute, axillary temperature 36.7°C, and Visual Analog Scale (VAS) 2. General status within normal limit, extremities were warm, and there was no pitting edema in both lower extremities.

The dermatological status of the cruris dextra et sinistra region showed multiple erythematous macules, well-defined borders, geographical shape, size 0.3x0.8 cm – 2x3 cm confluent. Above the lesion, multiple erosions were seen, well-defined borders, geographical shape, size 0.1x0.5 cm – 1x2 cm (Figure 1A-1C). On palpation, it was warm and there was no tenderness. On diascopy, it disappeared with pressure.

The history and physical examination showed that the patient was diagnosed with cellulitis cruris pedis dextra et sinistra. The complete blood count showed an increase in white blood cells, but the percentage of neutrophils was within the normal limit (Table 1). The clinical chemistry found that all parameters were within a normal range (Table 2).

Specimens were also taken for gram examination and wound culture. The results of the gram examination showed no epithelium was observed, leukocytes and gram-negative rod bacteria were found scanty. Wound specimens were streaked on Blood Agar and Mac Conkey media, then incubated at 37°C for 24 hours. The characteristic of the colonies that grew on blood agar were flat, opaque colonies with an irregular contour. The colony's growth on the McConkey showed gray-whitish colored pinpoint colonies (Figure 2). The colony that grew on blood agar was tested with a catalase test. The catalase test was negative, confirming that the bacteria was *Streptococcus*.

Identification of bacterial species and susceptibility testing was continued using the VITEK 2 compact (bioMérieux, Marcy L'Étoile, France). It was found that the colonies were *Streptococcus agalactiae* and *Citrobacter koseri*. Based on complete blood count results, especially neutrophil percentage combined with gram examination, both bacteria were considered colonization. Therefore, clinical microbiologists recommended



Figure 1. Clinical photo of the patient on the first day of examination. In the region of (A) cruris sinistra and (B) cruris dextra, (C) multiple erythematous macules were found.

Table 1. The hematology results during the study period.

Parameter	04/27/2021	04/29/21	Reference Range
WBC ($10^3/\mu\text{L}$)	15.06	7.86	4.10-11.00
% Ne	62.10	57.90	47.00-80.00
%Lym	29.30	30.40	13.00-40.00
%Mo	6.90	8.50	2.00-11.00
%Eo	1.30	2.70	0.00-5.00
%Ba	0.40	0.50	0.00-2.00
RBC ($10^6/\mu\text{L}$)	4.72	4.51	4.00-5.20
Hb (g/dL)	13.10	12.50	12.00-16.00
HCT (%)	40.60	38.10	36.00-46.00
MCV (fL)	86.00	84.50	80.00-100.00
MCH (pg)	27.80	27.70	26.00-34.00
MCHC (g/dL)	32.30	32.80	31.00-36.00
RDW (%)	13.20	13.10	11.60-14,80
PLT ($10^3/\mu\text{L}$)	2,299.00	284.00	140.00-440.00

WBC: White Blood Cells; RBC: Red Blood Cells; Hb: Hemoglobin; HCT: Hematocrit; MCV: Mean Corpuscular Volume; MCH: Mean Corpuscular Hemoglobin; MCHC: Mean Corpuscular Hemoglobin Concentration; RDW: Red-Cell Distribution Width; PLT: Platelet; Ne: Neutrophils; Lym: Lymphocytes; Mo: Monocytes; Eo: Eosinophils; Ba: Basophils

Table 2. The clinical chemistry result during the study period.

Parameter	04/27/2021	Reference Range
BUN (mg/dL)	10.80	8.00-23.00
Creatinine (mg/dL)	0.70	0.57-1.11
SGOT (U/L)	24.50	5.00-34.00
SGPT (U/L)	19.00	11.00-34.00

SGOT: Serum Glutamic Oxaloacetic Transaminase; SGPT: Serum Glutamic Pyruvic Transaminase; BUN: Blood Urea Nitrogen

performing wound care management instead of systemic antibiotic treatment.

The working diagnosis, in this case, was cellulitis cruris pedis dextra et sinistra. This patient was treated with cefadroxil

1000 milligrams tablets every 12 hours intraorally for 7 days, paracetamol 500 milligrams tablets every 8 hours intraorally if pain or fever, wound toilet with 0.9% NaCl every 8 hours for 10-15 minutes on erosional lesions. Sodium fusidate 2% cream every 12 hours topically on erosional lesions. In addition, the patient was educated to do elevation of lower



Figure 2. Bacterial growth on Blood Agar and MacConkey media.



Figure 3. Clinical photo of the patient at the time of the first follow-up observation (fifth day of treatment), multiple erythematous-hyperpigmented macules were found, well defined, geographical shapes on the right and left cruris.

limbs 30°. The patient is informed about the disease and lesion expansion, wound care, medication regimen, and control within five days.

On the fifth day of observation, the patient's condition was better than before. Dermatological status of the cruris dextra et sinistra region showed multiple erythematous-hyperpigmented macules-patches, well-defined borders, geographical shape, size 0.3x0.8 cm–2x3 cm, multiple erosions with a well-defined border, geographical shape size 0.1x0.5 cm – 1x2 cm (Figures 3).

The working diagnosis was followed up of cellulitis cruris dextra et sinistra on day 5 (improved). The management given was to continue previous therapy. On the seventh day, the patient's condition was better than before. The lesion became drier. The dermatological status of the cruris dextra et sinistra region showed multiple erythematous-hyperpigmented macula-patches, well-defined borders, geographical shape, size 0.3x0.8 cm – 1x3 cm (Figures 4). The white blood cells became normal on laboratory examination on April 29th, 2021 (Table 1).

The diagnosis was follow-up cellulitis cruris dextra et sinistra on day 7 (improved). The oral antibiotic continued until the seventh day and the patient was given information to maintain personal hygiene.

DISCUSSION

Cellulitis is an infection of the deep dermis and subcutaneous tissue, most commonly caused by bacteria.¹ Although cellulitis is more common in the lower extremities, cellulitis can also occur in other areas such as the upper extremities, face, ears, and trunk.⁴ Other studies have found that the incidence of cellulitis is higher in individuals older than 45 years.^{10,11}

Cellulitis can be established based on history and physical examination. In this case, the patient complained of swelling and redness of the right and left legs which were getting wider and the pain was felt in the area of redness. Laboratory tests are not required to evaluate uncomplicated cellulitis in the absence of comorbidities. Markers of bacterial infection such as leukocytosis, neutrophilia, lymphopenia, and elevated inflammatory markers such

as C-Reactive Protein (CRP) can be found but are not specific.¹²⁻¹⁴

In almost 70% of cases, there was no growth of microorganisms from wound or tissue cultures. If found, the most common isolates were *Staphylococcus aureus*, *Streptococcus beta-hemolyticus* Group A, and group B.¹²

In a study conducted by Cranendonk et al., 1 patient had *S. aureus*, *S. agalactiae* wound cultures, 1 patient had *S. aureus*, and *C. koseri* from 13 patients with positive wound cultures. However, this study showed that there was no difference between the microbiota in the extremities with cellulitis and those without cellulitis and that the presence of the microbiota did not affect the outcome of cellulitis patients.¹⁵

Streptococcus agalactiae is also known as Lancefield group B *Streptococcus* (GBS).^{8,16} GBS is a gram-positive pathogenic bacterium that is part of the normal microbiota found in the gastrointestinal and genitourinary tracts in healthy women, 10-30% of pregnant women are estimated to have GBS colonization that is high and can be dangerous for newborns.^{17,18}

S. agalactiae can be classified into 10 different serotypes (Ia, Ib, and II to IX), with Ia, II, III, and V serotypes being the main causes. In a study in Thailand, the clinical manifestations of *S. agalactiae* in cellulitis were 2.2%, where serotype III was the most common cause.¹⁶

The main surface of GBS that plays a role in the virulence of this bacteria is protein C, namely Ca (bca gene), Rib (rib gene) and C β (bac gene), which mediate adhesion to host cells; cyl operon encoding -hemolysin is a toxin that plays a role in tissue trauma and systemic spread such as meningitis; a polysaccharide capsule that prevents the elimination of pathogens by the immune system; C5a peptidase which is a serine protein that inactivates the human C5a protein so that it can inhibit neutrophil recruitment and help reduce the host inflammatory response.¹⁶⁻¹⁸ *Citrobacter* species are opportunistic pathogenic bacteria involved in nosocomial infections and community-acquired infections. *Citrobacter* belongs to the Enterobacteriaceae family's genus, an anaerobic, gram-negative rod-shaped bacterium that does not form spores.



Figure 4. Clinical photo of the patient at the time of the second follow-up observation (7th day of treatment). Multiple erythematous-hyperpigmented macules-patches were found better than before.

Citrobacter species are found in water, soil, and colonize the gastrointestinal tract. Although the *Citrobacter* strains that colonize the human gastrointestinal tract are generally considered to be less virulent, they can cause various diseases of the urinary tract, respiratory tract, bone, peritoneum, endocardium, meninges, intestines, bloodstream, and central nervous system, especially in infants, young children, and adults with impaired immunity. *Citrobacter koseri* is frequently isolated from clinical material among the *Citrobacter* genus and has been known to cause meningitis and brain abscesses in neonates and immunocompromised individuals.¹⁹

The principle of cellulitis management is an antibiotic regimen. Antibiotics given should have a specific target on the causative organism. Empirical therapy can be given early in treatment by looking at the known pathogens and underlying conditions. Patients with mild infections can be treated with oral antibiotics.^{1,20}

Therapy can be given, such as cefadroxil 1 gram every 12 hours per day or cefalexin 1 gram every 8 to 6 hours per day. Cefadroxil is slightly advantageous because it has a longer half-life.²¹ Topical therapies like sodium fusidate can also be given.²² The duration of antimicrobial therapy is 5-10 days in uncomplicated cases and 7-14 days in immunocompromised patients. Bed rest and leg elevation can reduce edema.¹

In this case, the wound culture showed colonization of *Streptococcus agalactiae* and *Citrobacter koseri*. Both of these bacteria are less virulent. Based on complete blood count results, especially neutrophil percentage combined with gram examination, both bacteria were considered colonization. Therefore, clinical microbiologists recommended performing wound care management instead of systemic antibiotic treatment. Inappropriate use of antibiotics can induce bacterial resistance to antibiotics.

The patient was treated with cefadroxil 1000 milligrams every 12 hours intraorally,

sodium fusidate 2% cream every 12 hours topically on erosional lesions, and was given education for bed rest, elevating the lower extremity position by approximately 30 degrees, and wound care was performed.

The prognosis of cellulitis depends on the control of predisposing factors and adequate antibiotics. Cellulitis can develop into a serious disease with uncontrolled spread, including through the lymphatic or circulatory system. Associated conditions or complications include lymphangitis, abscess formation, and gangrenous cellulitis or necrotizing fasciitis. The most common complication is recurrence.²³ This case report does not explain possible causes or risk factors for cellulitis in the patient.

CONCLUSION

A case of colonization of *Citrobacter koseri* and *Streptococcus agalactiae* has been reported in a case of cellulitis cruris dextra et sinistra. The diagnosis of cellulitis is based on history and physical examination. On examination of the wound culture, *Citrobacter koseri* and *Streptococcus agalactiae* were found. These bacteria are considered colonization. Patients showed clinical improvement after administering antibiotics and wound care management at each observation. The patient's prognosis is dubious ad bonam.

CONFLICT OF INTEREST

There is no competing interest regarding the manuscript.

ETHICAL CONSIDERATION

This case report has obtained informed consent from the patient regarding the publication of their respective medical data in medical journal articles.

FUNDING

None.

AUTHOR CONTRIBUTION

All authors are responsible for the study from the conceptual framework, literature/data gathering, analysis, and implementation of scientific publication.

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