

# *Granulicatella adiacens* as a Cause of Bacteremia in Immunocompromised Patients: A Case Report

**Basma Sherif, Yasmeen M. Mahmood**

Department of Clinical Pathology department, Faculty of Medicine Ain Shams University, Cairo, Egypt

Corresponding Author  
Basma Sherif

Mobile:  
01113151814

E mail:  
dr.basma.sherif@gmail.com  
basma@med.asu.edu.eg

Key words:  
Bacteremia,  
Granulicatella  
adiacens, Nutritionally  
deficient  
Streptococcus,  
Septicemia.

*Granulicatella* species were previously known as nutritionally variant streptococci, which are now classified in two new genera, the *Abiotrophia* and *Granulicatella*. *Granulicatella adiacens* (*G. adiacens*) is a part the normal commensals of human mucosal surfaces, including oral cavity, urogenital and gastrointestinal tract and rarely causing disease. They grow in Gram-positive cocci in pairs and chains, difficult to be identified by conventional methods, since this species require pyridoxal-supplemented culture media for optimal growth. We report a case of bacteremia caused by *G. adiacens* in an elderly male

suffering from hepatocellular carcinoma. The infection was diagnosed, the patient was treated successfully and eventually discharged. *G. adiacens* is an opportunistic infection in immunocompromised patients especially neutropenic or patients with comorbid conditions as diabetes or other systemic illnesses, particularly if they required long hospitalization and intensive care unit admission. Infection rate may be underestimated either unidentified or misidentified, since the organism necessitates automated identification.

## INTRODUCTION

*Granulicatella adiacens* (*G. adiacens*) belong to the genus *Granulicatella* which belong to nutritionally variant *Streptococcus* (NVS). *G. adiacens* colonies are alpha-hemolytic on sheep-blood agar, Gram-positive cocci, facultative anaerobe, catalase-negative, oxidase-negative, nonmotile and non-spore forming, optochin resistant and vancomycin susceptible [1]. Despite being a part of the normal flora, *G. adiacens* is able to induce serious infections as bacteremia, endocarditis and device associated infections in immunocompromised patients especially neutropenic or patients with comorbid conditions as diabetes or other systemic illnesses, particularly if they required prolonged hospitalization and intensive care unit treatment. Critically ill patients have multiple predisposing factors for infection such as impaired cortisol metabolism, increased levels of various cytokines, disrupted mucosal barrier function paving the way for commensals to invade the

bloodstream and unspecific decline of the immune response [2].

This organism is able to attach the host extracellular matrix, which may explain its ability to cause infections as endocarditis. *Granulicatella* also bind to fibronectin, facilitating intravascular infections. *G. adiacens* diagnosis may be under-reported either missed or misidentified as *Streptococcus* due to difficult identification by conventional methods [3]. Because of its tendency to cause serious life-threatening infections, being fastidious in addition to the slow growth, great attention is needed [4]. Clinical & Laboratory Standards Institute (CLSI) guidelines (M45) for Antibiotic susceptibility testing for NVS recommends broth microdilution method (BMD) using cation-adjusted Mueller–Hinton broth supplemented with 2.5%–5% lysed horse blood and 0.001% pyridoxal HCl [5]. However, due to the absence of disc diffusion breakpoints and scarcity of BMD in clinical laboratories, reporting the susceptibility

pattern of *G. adiacens* represent great challenge [6].

*Granulicatella* species (spp) are usually susceptible to penicillin, cephalosporins, and carbapenems. For treatment of endocarditis, penicillin or ceftriaxone represents the treatment of choice as recommended by the American Heart Association (AHA), however, resistance to penicillin, macrolide and cephalosporins has been described and should be taken into account when considering empirical therapy [7].

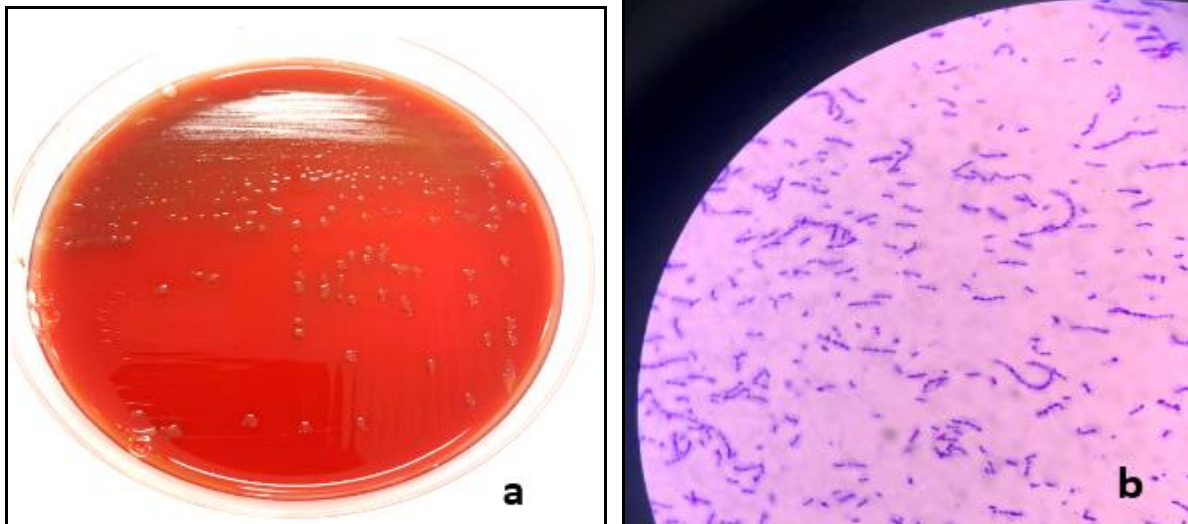
### Case Report:

**History:** 64 years old male patient presented to the emergency department (ED) complaining of difficult breathing and inability to lie down flat. The patient was previously diagnosed with hepatocellular carcinoma and he reported that he had received his chemotherapy treatment Tecentriq and Avastin two days before admission.

**Physical Examination:** the patient was dyspneic with increased respiratory rate and diminished lung sounds. However, lungs were free, heart rate was normal with a regular rhythm. There was no abdominal distension, ascites or lower limb edema.

**Laboratory and Radiological Investigations:** In the ED, chest X-ray was done which revealed pleural effusion, the patient was transferred to the Oncology department for follow up. After one day, dyspnea worsened, oxygen saturation dropped to 85% and the patient developed marked pleural effusion, upon which, he was transferred to intermediate care unit, where he underwent thoracentesis by the intermediate care unit team, with removal of about 3 Liter (L) of clear, yellowish fluid. Pleural fluid specimens were sent for chemical analysis, revealed glucose 149 mg/dL, total protein 2.3 g/dL, and albumin 1.3 g/dL, which indicated the presence transudate. Microbiological analysis revealed no bacterial growth. Cell count showed 150 WBC/uL. Gram staining showed a few cells with

no organism. Leishman stain revealed that the cells were predominantly lymphocytes. Routine laboratory workup was ordered. The results were as follows: Hemoglobin: 9.2 g/dL, total leukocytic count (TLC): 5700/uL, Neutrophils: 4200/uL, platelets: 122/uL. Elevated CRP: 18.8 mg/dL (Reference range: 0-0.5 ng/ml), and Procalcitonin 1.23 ng/ml (Reference range: <0.5 ng/ml), ammonia: 84 umol/L (Reference range: 16-60 umol/L), high total bilirubin: 2.7 mg/dl (Reference range: 0.2-1.2 mg/dl), Conjugated bilirubin: 1.4 mg/dl (Reference range: up to 0.3 mg/dl), Albumin: 3.2 g/dl (Reference range: 3.5-5.2 mg/dl). Septicemia was suspected and the intermediate care unit consultant ordered blood culture, then started Meropenem /Ceftriaxone antibiotic therapy. The blood culture gave positive signal after 24 hours, specimen was inoculated on blood agar, chocolate agar, and MacConkey agar plates and incubated at 37°C for 24 hours, anaerobic culture was done on another blood agar plate and incubated anaerobically for 48 hours. Also, gram staining was done from blood culture bottle which showed Gram positive (GP) cocci singly and in small chains. After 24 hours incubation, blood agar plate showed growth of mucoid, transparent,  $\alpha$ -hemolytic colonies. Catalase and oxidase tests were negative. Optochin was resistant, and bile esculin was negative. Gram staining of colonies showed Gram positive cocci /coccobacilli in pairs or short chains. Vitek 2 compact® (BioMerieux, France) identified the isolate as *G. adiacens* using GP identification (ID) card with 98% confidence. Minimum inhibitory concentration (MIC) was determined using antimicrobial susceptibility (AST) ST01 card of Vitek. The isolate was susceptible to penicillin, cefotaxime, ceftriaxone, erythromycin, clindamycin, levofloxacin, and vancomycin. Five days later, the patient condition improved, oxygen saturation was restored, CRP and Procalcitonin became within the reference range and the patient was discharged.



**Figure a: Blood agar plate shows round smooth alpha hemolytic colonies; (b): Gram stained film shows Gram positive cocci in short chain.**

## DISCUSSION

Nutritionally variant streptococci (NVS) show better growth on media supplemented with thiol or pyridoxal. With the increased use of automated blood culture bottles that contain pyridoxal and L-cystein, their isolation rate has increased. *G. adiacens* is an uncommon cause of infection, usually related to endocarditis or indwelling device related infection or surgery with the organism being isolated from brain abscess, CSF, joint space. However, literature has reported cases of bacteremia with *Granulicatella* spp without endocarditis [8].

Nutritionally variant streptococci should be suspected upon detection of Gram positive cocci through stained films together with negative culture results, due to required fastidious culture conditions, therefore, appropriate supplemented media and a reliable detection system is required for identification [9]. Commercial blood culture media contain pyridoxal, thus, support growth of NVS, also, Satellitism around *Staphylococcus aureus* colonies can enhance growth. Using the API Strep or the advanced laboratory systems as Matrix-assisted laser desorption ionization time-of-flight mass spectrometry or the VITEK 2 system, NVS can be identified to the species level with good sensitivity and specificity [2].

*Granulicatella* isolates were mainly isolated from immunocompromised patients, perhaps due to the weakened immune mechanism and the disrupted mucosal barrier immune function, which enhance the patient own normal flora to cross these barriers reaching different body sites

as blood, endocardium, bones or body fluids as ascitic or pleural fluid where, they can exert a virulent pathogenic effect [10].

Kawai and Shiojiri [11] reported a case of a 58 years old adult Japanese male with Bipolar disorder, treated with Lithium and presented to the emergency department with fever and loss of consciousness, pan-CT (Computed Tomography) scan with contrast was done to identify the infected focus, revealing left cervical vein thrombosis, intramuscular abscesses around the left femur and pulmonary embolism, the patient was diagnosed with Jugular vein thrombophlebitis, lithium intoxication and uremia, for which he underwent hemodialysis, also blood culture was withdrawn which showed positive signal within 20 hours of incubation, *G. adiacens* was found to be the implicated organism. Ampicillin (AMP) was started and subsequent blood cultures were negative. On day 16, AMP was changed to cefotaxime (CTX) as drug fever was suspected to be caused by AMP. CT scan was done on day 40, pulmonary embolism disappeared, but, the left cervical vein thrombus did not get smaller in size, and the femur abscesses got larger, which necessitated drainage. After drainage, edoxaban was added. Repeated CT scan on day 56, showed complete resolution of the left cervical vein thrombus and gluteal abscesses, however, femur abscesses did not disappear completely. Intravenous (IV) CTX was changed to oral amoxicillin. On day 98, He was transferred to a healthcare facility that provide psychiatric care with oral amoxicillin for another two weeks and long-term edoxaban

administration. In this patient, poor dental hygiene with periodontitis, was incriminated as the risk factor for left cervical vein thrombus, since, *G. adiacens* is a part of the normal oral flora and can cause endodontic infections with subsequent spread to surrounding tissues.

Also, Cho et al. [12] reported a case of a 45-year-old male presented to the outpatient clinic after accidental discovery of a left sided abdominal mass. Endoscopic ultrasound-guided fine needle aspiration or biopsy (EUS-FNA or FNB) was done as a part of the patient investigations which was complicated after ten days by septic shock and splenic abscess. Piperacillin/tazobactam (TZP) was started with the onset of septic shock, and blood culture was withdrawn, which showed positive growth of *G. adiacens*, TZP was changed to ampicillin/sulbactam (SAM). The patient condition improved and was discharged. Pathological examination of the resected splenic mass revealed diffuse large B-cell lymphoma. After recovery from septic shock, he got vaccination against encapsulated organisms and splenectomy was performed four weeks after vaccination. Then, the patient received chemotherapy and underwent complete remission. This case highlighted that EUS-FNA or FNB in rare cases may precipitate infection with subsequent septicemia.

## CONCLUSION

*Granulicatella* species are nutritionally deficient fastidious organisms, part of the human normal flora, which usually affect immunocompromised patients. *Granulicatella* should be suspected in patients where slowly-growing mucoid alpha-haemolytic gram positive cocci are isolated. In case of absent or poor growth on culture plates, we recommend to perform satellitism to enhance recovery of the organism together with further incubation of the culture plates.

**Funding:** None

**Ethical consideration:** All the information gathered from the patients was handled confidentially, and it was used only for research purpose.

**Conflict of interest:** There is no conflict of interest.

## HIGHLIGHTS:

- *Granulicatella* species (spp) is an opportunistic infection in immunocompromised patients especially neutropenic, particularly if they required long hospitalization and intensive care unit admission.
- Infection rate of *Granulicatella* spp may be underestimated since the organism necessitates automated identification.
- Resistance among *Granulicatella* spp to penicillin, macrolide and cephalosporins has been described and should be taken into account when considering empirical therapy.

## REFERENCES

- 1- Cho S, Cho E, Park CH, Kim H, Koo J. Septic shock due to *Granulicatella adiacens* after endoscopic ultrasound-guided biopsy of a splenic mass: A case report. *World J Gastroenterol* 2021; 27(8): 751-759. DOI: <https://dx.doi.org/10.3748/wjg.v27.i8.751>
- 2- Geetarani P, Baijayantimala M, Satyajeet S, Ashoka M. *Granulicatella adiacens* as an Unusual Cause of Empyema: A Case Report and Review of Literature. *J Lab Physicians* 2022; 14(03): 343-347. DOI: 10.1055/s-0042-1744236
- 3- Goswami A, Chandra S, Adhikari S, Mandal P. Understanding the Impact of the Microbiome on Lung Cancer. In: Gupta G, Oliver B, Dua K, Singh A, MacLoughlin R. (eds) *Microbiome in Inflammatory Lung Diseases*; 2022. Springer, Singapore. [https://doi.org/10.1007/978-981-16-8957-4\\_10](https://doi.org/10.1007/978-981-16-8957-4_10)
- 4- Siafaka P, Bulbul E, Miliotou A, Karantas I, Okur M, Okur N. Delivering active molecules to the eye; the concept of electrospinning as potent tool for drug delivery systems. *J Drug Deliv Sci Technol* 2023; 84: 104565. <https://doi.org/10.1016/j.jddst.2023.104565>
- 5- Clinical & Laboratory Standards Institute (CLSI) 2015. Methods for antimicrobial dilution and disk susceptibility testing of infrequently isolated or fastidious bacteria, 3rd ed, CLSI guideline M45. Clinical and Laboratory Standards Institute, Wayne, PA.
- 6- Gupta S, Garg M, Misra S, Singhal S. *Granulicatella adiacens* abscess: Two rare cases and review. *J Lab Physicians* 2018; 10:121-3. DOI: 10.4103/JLP.JLP\_58\_17

- 7- Palen E, Zuijdewijn C, Castelijjn D, Wattel-Louis G, Kalpoe J. A Rare Case of *Granulicatella adiacens* Vertebral Osteomyelitis. *Case Rep in Infect Dis* 2021; Article ID 1483846, 1-3. doi: 10.1155/2021/1483846. <https://doi.org/10.1155/2021/1483846>
- 8- Molly C, Coffey K, Shannon N, Dushant U, Molly A. Case Report of *Granulicatella adiacens* as a Cause of Bacterascites. *Case Rep in Infect Dis* 2015; Article ID 132317. <http://dx.doi.org/10.1155/2015/132317>
- 9- Alberti M, Hindler J, Humphries R. Antimicrobial susceptibilities of *Abiotrophia defectiva*, *Granulicatella adiacens*, and *Granulicatella elegans*. *Antimicrob Agents Chemother* 2016; 60:1411–1420. doi:10.1128/AAC.02645-15.
- 10- Acharya A, Sattar Z, Ahmad A, Sattar F, Fiksman A. Case Report: Complex parapneumonic effusion and bacteremia secondary to *Granulicatella adiacens* in immunocompetent host. *F1000Res* 2020; 9:977. <https://doi.org/10.12688/f1000research.25044.1>
- 11- Kawai H and Shiojiri T. Internal jugular vein thrombosis associated with *Granulicatella adiacens*. *BMJ Case Rep* 2021; 14: e238404. doi:10.1136/bcr-2020-238404
- 12- Cho S, Cho E, Park C, Kim H, Koo J. Septic shock due to *Granulicatella adiacens* after endoscopic ultrasound-guided biopsy of a splenic mass: A case report. *World J Gastroenterol* 2021; 27(8): 751-759. DOI: 10.3748/wjg.v27.i8.751.