



## Sepsis induced bacterial peritonitis caused by *Granulicatella adiacens* <sup>☆</sup>

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### 1. Introduction

*Granulicatella adiacens*, formerly classified in the genus *Abiotrophia*, was first described in 1961 as a nutritionally variant streptococcus (NVS) [1]. It is a Gram-positive coccus, facultative anaerobic bacterium that requires agar-rich supplemented media to grow, leading to the original genus naming of *Abiotrophia* [2,3]. It is part of the normal, commensal flora of the human oral cavity, gastrointestinal and genitourinary tracts, but is rarely implicated in disease in healthy hosts [1]. To date, there have been three species of *Granulicatella* described in the literature, *G. adiacens*, *G. elegans*, and *G. balaenopterae*, with only the *adiacens* and *elegans* species causing infection in humans. While most of the reports have focused on the *G. adiacens* causing bacteremia, vertebral osteomyelitis and endocarditis, few have reported sepsis or septic shock due to this genus and none in the setting bacterial peritonitis [4, 5,6]. There has been one case report describing bacterascites in a patient with portal vein thrombosis caused by *G. adiacens*; however, the patient was asymptomatic prior to initiation of antimicrobial therapy and repeat paracentesis to demonstrate eradication was not completed due to the positive clinical progress of the patient [5]. To our knowledge, this is the first case describing clinically defined sepsis caused by secondary bacterial peritonitis in a patient with malignant ascites in which *G. adiacens* was isolated from ascitic fluid.

### 2. Case

A 38-year-old, 101 kilogram male with a past medical history of colon cancer status-post palliative open sigmoid resection with metastases to the liver and peritoneum complicated by recurrent symptomatic malignant ascites requiring a chronic indwelling PleurX™ (Becton, Dickinson and Company, Franklin Lakes, NJ) ascites drain, presented to the emergency department (ED) with worsening abdominal pain for three days, decreased fluid output from drain, and new onset severe shortness of breath for the last 2 h. In the ED, the patient was afebrile and other initial vitals including blood pressure, heart rate and respiratory rate were 92/62 mm Hg, 105 beats per minute, and 35 breaths per minute, respectively. He was initially started on a non-rebreather and then trialed on Bilevel Positive Airway Pressure (BiPAP) but due to his worsening mental status as well as increased work of breathing, he was intubated and sedated.

Due to concern for sepsis, the patient received 3 L of Lactated Ringer's for fluid resuscitation. Cultures of ascitic fluid, blood and urine were obtained. Vancomycin, aztreonam and metronidazole were started in the ED, as patient had a documented reaction of urticaria and pruritis to piperacillin/tazobactam in his medical chart. Initial labs were significant for leukocytosis  $11 \times 10^9$  cells/L, lactate 2.7 mmol/L, serum creatinine 0.67 mg/dL, INR 1.38, platelets 251,000 per microliter, and total bilirubin 1.0 mg/dL.

A computed tomography (CT) scan of the abdomen/pelvis showed evidence of malignant ascites which was unchanged from prior scans; however, the CT demonstrated new peritoneal thickening suggestive of peritonitis but no evidence of bowel obstruction. Peritoneal fluid analysis revealed a nucleated cell count of 9163 with 83% polymorphonuclear leukocytes (PMNs), a total protein of 1.7 g/dL, glucose concentration less than 1 mg/dL and a lac-

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tate dehydrogenase (LDH) level of 1429 U/mL. The peritoneal catheter was removed by interventional radiology and sent for culture. The patient was later stabilized and extubated and did not require vasopressors at any point during his stay. Final cultures showed methicillin-susceptible *Staphylococcus aureus* from the catheter tip and in the ascitic fluid, as well as *Granulicatella adiacens* in the ascitic fluid. Antibiotics were deescalated to vancomycin, which the patient received for a total of 8 days before being discharged from the hospital.

### 3. Discussion

Although unlikely to cause infection, *G. adiacens* is most frequently reported in the setting of endocarditis. The incidence of NVS causing endocarditis is 5–6% of all streptococcal endocarditis [7]. *Granulicatella* has also been isolated from cultures related to infections such as otitis media, pancreatic abscesses, meningitis, and brain abscesses.

Secondary bacterial peritonitis is defined as an infection in the ascitic fluid due to an underlying intraabdominal source which may or may not be associated with perforation. Secondary bacterial peritonitis and spontaneous bacterial peritonitis (SBP) are often non-distinguishable upon initial clinical presentation. Secondary bacterial peritonitis is similar in nature to SBP with the same PMN cell count criteria of at least 250/mm<sup>3</sup>; however, there are several characteristics that may help distinguish SBP from secondary bacterial peritonitis. Secondary bacterial peritonitis can occur in any form of ascites whereas SBP is predominately seen in patient with cirrhotic ascites. Additional features which support a diagnosis of secondary bacterial peritonitis include polymicrobial infection by gram stain or culture, presence of a higher PMN count, imaging studies consistent with perforation or loculated infection, and poor response to initial antimicrobial therapy [8,9].

During initial evaluation of SBP, red flags could raise clinical suspicion of an alternate diagnosis, including secondary bacterial peritonitis. Some of these symptoms include abdominal pain, abdominal tenderness or rebound tenderness as these were found to occur significantly more often in a recent series report [10]. Ultrasound can be useful in helping differentiate secondary bacterial peritonitis from SBP. Free-air on bedside ultrasound may be indicative of secondary bacterial peritonitis as sensitivity is 85–90% and specificity nears 100% [11]. Sterile ascitic fluid should be anechoic and free of septations. While septations do not differentiate between spontaneous and secondary peritonitis and can also indicate malignancy, the presence of these on ultrasound suggests a more severe infection such as secondary bacterial peritonitis.

The Runyon criteria, which can support the diagnosis of secondary bacterial peritonitis, was first described in a study from Runyon et al. [8]. The utility of an algorithm and the sequential information from repeat paracentesis was evaluated to differentiate spontaneous from secondary bacterial peritonitis. Authors detail that the ascitic fluid in secondary peritonitis will likely reveal at least 2 of 3 specific lab abnormalities: a total protein content greater than 1 g/dL, a glucose concentration less than 50 mg/dL, and a lactate dehydrogenase (LDH) level greater 225 U/mL. Perforation should be ruled out with appropriate radiologic studies in all patients which meet this criteria and secondary bacterial peritonitis without perforation is most likely if the criteria are fulfilled, but there is no evidence of free air or extravasation on imaging. In addition, they also report that the optimal timing for repeat paracentesis is 48 h after initiation of treatment. Secondary bacterial

peritonitis, without intestinal perforation, may also be differentiated from spontaneous peritonitis if there is a lack of response of the ascitic fluid neutrophil cell count to antibiotics. While the sensitivity of the algorithm in detecting actual gut perforation was 100%, the specificity was only 45% [8].

Given that mortality during hospitalization is higher in patients with secondary bacterial peritonitis compared to SBP, 66.6% vs 26.4% respectively, it is imperative to correctly differentiate the two entities. Improved prognosis has been demonstrated in patients with secondary bacterial peritonitis when an aggressive approach to therapy is utilized which includes prompt diagnosis and imaging in addition to early surgical evaluation [12].

Our laboratory could not complete susceptibility testing on *G. adiacens*, therefore in-vitro testing of *Granulicatella* spp. isolates from previous literature was used to guide antimicrobial therapy. Alberti et al. tested the antimicrobial susceptibilities of 90 isolates of *G. adiacens* to several different antibiotics. Results showed that 38.9% of the isolates were susceptible to penicillin but were resistant to ceftriaxone and cefotaxime 34.5% and 50% of the time, respectively. Interestingly, out of all the species tested, *G. adiacens* showed the highest resistance to levofloxacin and clindamycin. None of the isolates showed resistance to vancomycin [13]. Our patient had an adverse reaction to piperacillin/tazobactam listed in his chart and the choice was made to use vancomycin as the sole agent to complete the patient's antimicrobial therapy. He completed an 8-day course of vancomycin therapy and was discharged home. Repeat paracentesis, while recommended but not necessary in those who present with characteristics of secondary bacterial peritonitis [14], did not reveal growth of bacteria in the ascitic fluid during the rest of the patient's stay.

This first-of-its-kind case presents the findings of sepsis from polymicrobial bacterial peritonitis with *G. adiacens* isolated in the ascitic fluid. While normal flora, *G. adiacens* may be thought of as a differential bacterium causing infection in patients with secondary bacterial peritonitis. Due to resistance patterns of *G. adiacens*, clinical suspicion of this bacterium should be heightened in patients who are not responding to customary empiric antibiotics of choice for bacterial peritonitis.

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