

## *Granulicatella adiacens* Bacteremia in an Elderly Trauma Patient

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### Abstract

**Background:** *Granulicatella adiacens* is a normal commensal of human mucosal surfaces, inhabiting the oral cavity and urogenital and gastrointestinal tracts and only rarely causing disease. These gram-positive cocci can be difficult to identify.

**Case report:** We report a first case of bacteremia caused by *Granulicatella adiacens* in an elderly female trauma victim. The infection was diagnosed accurately, and the patient was treated successfully.

**Conclusion:** *Granulicatella adiacens* may be a more important pathogen than thus far recognized because of a lack of adequate diagnostic resources. Standards for sensitivity testing are needed urgently.

**G**RANULICATELLA ADJANS is a normal commensal of human mucosal surfaces, inhabiting the oral cavity and urogenital and gastrointestinal tract and only rarely causing disease [1, 2]. Bacteria of the genus *Granulicatella* are catalase-negative, gram-positive cocci that tend to grow in pairs or chains and display satellites, but can appear pleomorphic under less-than-ideal nutritional conditions [3–5]. This bacterium often is difficult to identify because it will grow initially in blood culture broth or mixed cultures but not on sheep blood agar unless pyridoxal (vitamin B<sub>6</sub>) is added [4]. The bacterium was first described nearly 50 years ago, when it was grouped with several other fastidious, “satelliting,” gram-positive bacteria as a new type of viridians streptococci termed “nutritionally variant streptococci” (NVS) by Frenkel and Hirsch because of the necessity for pyridoxal for growth [6]. Other names throughout the years have included “nutritionally deficient,” “thiol-requiring,” “pyridoxal-requiring,” and “satelliting” streptococci [7]. This group of organisms was subdivided in 1989 into *Streptococcus defectiva* and *Streptococcus adiacens*. Using 16S rRNA sequencing, these bacteria were found actually to be unrelated to any species belonging to the genus *Streptococcus*, and Kawamura et al. proposed the new genus *Abiotrophia*, including *A. defectiva* and *A. adiacens* [8]. The fledgling genus *Abiotrophia* subsequently expanded to include four species but was found to be polyphyletic in 2000 [9], when the genus was further subdivided, finally giving

rise to the genus *Granulicatella*, as designated by Collins and Lawson [10]. The genus *Abiotrophia* was left with merely one species [10].

*Granulicatella* spp. are among the four most common genera in the normal flora of the oral cavity [11]. *Granulicatella adiacens* was found to account for 85% of the NVS in the human mouth, making it by far the most common type [12]. *Granulicatella* spp. were recently associated with malodorous breath in various indigenous populations in Japan [13]. However, the virulent potential of this organism is well established, and it has been implicated in numerous diseases far more harrowing than halitosis. Many reported infections involved immunocompromised patients, and the most common infections were sepsis and endocarditis, with more than 20 such cases reported [14–17]. The organism also has been associated with meningitis, osteomyelitis, peritonitis, various abscesses, pneumonia, and severe infections of foreign bodies such as pacemaker wires or prosthetic valves [18–27]. A common pattern of reported cases of infection with this species are high pharmacologic failure rates and a high mortality rate [14, 25]. This may be attributable to difficulties in making an accurate diagnosis, as *Granulicatella* is a slowly-growing, nutritionally-demanding organism. In addition, an increasing resistance rate to several classes of antibiotics has been observed recently. *Granulicatella adiacens* infections in the normal host are rare, and little is known about infections in trauma victims and the elderly. We herein report the first confirmed

case of bacteremia caused by *Granulicatella adiacens* in an elderly female trauma victim.

### Case Report

An 89-year-old woman was involved in a motor vehicle crash after she drove her car head on into a tree at approximately 75 miles per hour, and sustained multiple injuries. She was intubated on the scene by emergency medical services, who reported that she sustained bilateral lower extremity injuries and an injury to her right hand and had suffered widespread abrasions and lacerations. Her medical history was notable for cardiac dysrhythmias, cataract surgery, hysterectomy for uterine leiomyomas, and typhoid fever as a child. Examination in our emergency department revealed multiple traumatic injuries, including an aortic intimal tear, multiple neck fractures and cervical disk herniations, a cervical epidural hematoma compressing the spinal cord, multiple rib fractures with bilateral pneumothoraces, right-sided phalangeal fractures, a left-sided radial fracture, and widespread abrasions and lacerations leading to an exposed right tibia. After initial stabilization, she was transferred to the intensive care unit, where she remained intubated for several days. No prophylactic antibiotics were administered.

Within one week, she developed fever and showed signs of sepsis with hemodynamic instability, an elevated white blood cell count, and worsening renal function. Empiric therapy with cefazolin was started. Paroxysmal atrial fibrillation was controlled with metoprolol. Cultures (sputum, urine, pleural effusion, and blood) were negative initially; however, blood drawn from the central line yielded slowly-growing organisms. The specimen was sent to a reference laboratory, and this facility described growth of *Granulicatella adiacens*. The organism was assumed to be sensitive to cefazolin, although no testing was available, as no standards have thus far been determined for this organism; cefazolin was continued, as the patient was improving slowly. No signs of endocarditis appeared, and the infection finally resolved, with hemodynamics and renal function improving and the white blood cell count normalizing. Subsequently, she underwent multi-level spinal fusion. Because of the prolonged intubation for respiratory failure in association with the rib fractures and advanced age and dysphagia, she developed aspiration pneumonia, which responded to antibiotic therapy. *Granulicatella* could not be isolated again. She underwent gastrostomy and tracheostomy. Because of the severity of her trauma and complicated course, she required a hospital stay of 63 days but was discharged ultimately to a rehabilitation center. She recovered remarkably well after discharge and regained ambulatory capacity, eventually having her tracheostomy and gastrostomy removed. She is alive and well after more than one year of follow-up.

### Discussion

When *Granulicatella* is a cause of infection, it most commonly causes endocarditis or bacteremia [16]. Brouqui and Raouff found in 2001 that, when combined with *Abiotrophia*, *Granulicatella* was implicated in 4.3–6% of all cases of endocarditis, and this number is likely substantially higher in culture-negative endocarditis [15]. Bouvet reported that cases of endocarditis caused by these bacteria exhibit much higher rates of treatment failure, relapse, and death than those at-

tributable to other viridans group streptococci [14]. This pathogen has the ability to bind to the host extracellular matrix, which may play a major role in its ability to cause endocarditis and other endovascular infections, especially in neutropenic patients [17]. *Granulicatella* also has the ability to bind to fibronectin, facilitating intravascular infections, including endocarditis [17]. Infections with *Granulicatella* have been reported in a wide variety of settings, including the central nervous system [20, 24], joints [23, 26], osteomyelitis [27], tubo-ovarian abscess [22], peritonitis [18, 19], and a breast implant [21]. Resistance to beta-lactam and macrolide antibiotics has been described [28, 29].

Ultimately, the outcome of our patient was more favorable than for many who suffer this infection. Elderly trauma victims such as our patient may be at higher risk for *Granulicatella adiacens* bacteremia, particularly if they require long hospitalization and intensive care unit treatment, or if they develop complications [30]. Critically ill patients have multiple risk factors for infection [31] such as impairment of cortisol metabolism [32], increased serum concentrations of various cytokines [33], and an unspecific depression of the immune system. Moreover, mucosal barrier function is impaired, allowing normal commensals to invade the bloodstream [34]. The microbiologic results of our patient were not available for many days after culture because the specimen had to be sent to an outside facility. The infection seems to have responded to cefazolin in the interim; however, this treatment regimen may become inadequate as resistance to beta-lactam agents develops in this pathogen.

*Granulicatella adiacens* is one of the most common bacteria that make up the normal flora of the oral cavity in the general population, but it has virulent potential and may be an emerging challenge. It is possible that infection with *G. adiacens* is missed or identified as being caused by *Streptococcus* the majority of the time [35]. It is a clear cause of endocarditis, and the spectrum of infections it can be responsible for seems to be expanding. Because of its propensity to cause endocarditis, its fastidious nature and slow rate of growth, and the increasing resistance to macrolide and cephalosporin antibiotics, special vigilance is needed. Many culture techniques fail to show growth of this organism initially, and the diagnosis is missed easily. Using 16S rRNA sequencing, this bacterium can be identified in roughly 4 h, avoiding the delays currently encountered in many clinical settings [12]. The spread of routine 16S rRNA sequencing in laboratories might prevent missed diagnoses and misdiagnoses in the future [36].

### Author Disclosure Statement

No conflicting financial interests exist.

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