CASE REPORT

A Rare Case of Relapse Infective Endocarditis Caused by *Granulicatella adiacens* in Pregnancy.

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Abstract

This is a case of a 33-year-old woman at her 12 weeks of pregnancy with underlying rheumatic heart disease presented with chest pain and diagnosed as infective endocarditis with *Granulicatella adiacens* bacteremia. She had a relapse of infective endocarditis complicated with splenic infarction, 6 weeks after the completion of intravenous ceftriaxone. She was put on another course of antibiotic regimen which consisted of intravenous ceftriaxone and gentamicin. She underwent elective lower segment caesarian section at 30 weeks of pregnancy and was discharged well. She had a valve surgery 3 months after the delivery.

Keywords: *Infective endocarditis, Granulicatella adiacens, pregnancy, bacteremia, relapse*.

Introduction

Infective endocarditis is a life-threatening infection of the endocardium of the heart, including large intrathoracic vessels, native or prosthetic heart valves, or even cardiac chambers. The occurrence in pregnancy is extremely rare with the estimated prevalence of 0.006% worldwide. However, it carries a significant maternal mortality risk of about 22%. It has a large number of causative organism, predominantly of *Streptococci, Staphylococci* and *Enterococci*, but less commonly by fungi [1]. Thus, *Granulicatella* species are an unlikely cause of the infection. Here, we describe a patient with infective endocarditis caused by *G. adiacens* at the first trimester and the therapeutic challenges in the management of the patient.

Case Report

A 33-year-old Malay woman, gravida 3, para 2, was presented to our facility at 12 weeks of pregnancy. Her previous pregnancies were all uneventful. At 17 years old, she was diagnosed with rheumatic heart disease with severe mitral regurgitation and completed monthly intramuscular benzylpenicillin until the age of 21. She was offered surgical intervention previously but refused. She complained of having central chest pain which she described as sharp pricking in nature, non-radiating for the past one week. She denied any recent indwelling catheter procedure or tooth extraction.

On admission, she was afebrile, with vital signs recorded were; pulse rate = 107 beats per min, respiratory rate = 24 breaths per min and blood pressure = 110/60 mmHg. Apex beat was displaced with grade IV pansystolic murmur heard over the apex radiating to axilla. Electrocardiogram was performed and interpreted as normal. Examination revealed a normal white blood cell count with predominant neutrophilia and mild anemia (hemoglobin = 9.9 g/dL). The C-reactive protein and erythrocyte sedimentation rate was elevated (46 mg/L and 110 mm/hr, respectively).

The diagnosis of infective endocarditis was confirmed after transthoracic echocardiography detected vegetation (0.5 to 0.6 cm^2) at the anterior mitral leaflet with severe mitral regurgitation (Figure 1). Ejection fraction was good with 72%. Ultrasound abdomen showed an appropriate for gestational age foetus in vertex presentation. The patient was started on intravenous ceftriaxone after blood cultures grew *Granulicatella adiacens* (Figure 2). After 6 weeks of antibiotic treatment, echocardiography showed a reduction of vegetation to 0.2 cm^2. Blood cultures also came back as negative.

The patient was seen in the clinic every fortnightly and she was stable until 6 weeks post-discharge. She then complained of having fever for almost 2 weeks associated with mild shortness of breath and cough. This time, echocardiography revealed an increase in size of vegetation to 0.4 cm^2. She was hospitalized and once again, blood culture grew *G. adiacens*. She also developed acute left loin pain which radiated to the back. Ultrasound abdomen discovered a splenic infarction.

She was put on another course of antibiotic regimen which consisted of intravenous ceftriaxone and gentamicin for 6 weeks. To prevent any complications, she underwent elective lower segment caesarian section at 30 weeks of pregnancy. She was discharged well after repeat blood culture showed no growth and the C-reactive protein test was negative. She had a valve surgery 3 months after the delivery. The delay of surgery was due to financial restriction.

Discussion

Infective endocarditis in pregnancy normally has a sub-acute course and usually appears around the third trimester of pregnancy. Nevertheless, in our case, it can still occur in the first trimester of pregnancy due to a complication of a pre-existing cardiac lesion such as rheumatic heart disease [2]. The usual organism causing infective endocarditis in pregnancy is *Streptococcus* [1].

However, blood cultures from our patient repeatedly grew *G. adiacens*. The organism, along with *G. elegans* and *G. balaenopt*erae are the three species of *Granulicatella* described which belong to *Carnobacteriaceae*. A normal component of the oral flora, they are catalase-negative and oxidase-negative, facultatively anaerobic, Gram-positive cocci [3].

Granulicatella species are nutritionally variant streptococci (NVS) as they require thiol or pyridoxal to be incorporated into standard media for successful laboratory isolation and may fail to grow on conventional blood culture media [4,5]. The isolates can be identified using either biochemical testing and / or molecular confirmation [3]. As for the samples from our patient, they were inoculated in the blood culture broth, BD BACTEC^{TM} Plus Aerobic/F which contained pyridoxal, and incubated at 37°C in 5% CO_2 for 48 hours [5,6]. The isolate was then confirmed as *G. adiacens* using the automated bacterial identification system, Vitek® [4,5,7].

Granulicatella species are often found in dental plaque, endodontic infection and dental abscess, but can also cause a variety of serious infections [3]. Nowadays, reports of native vertebral osteomyelitis or spondylodiscitis, prosthetic-related infections and septic arthritis are increasingly recognized [3,6].

In a literature review, only a few cases of infective endocarditis caused by *G. adiacens* were reported and none of them were among pregnant patients [8]. A total of 17 cases of *Granulicatella* endocarditis were identified over a course of 25 years which include infections of prosthetic valves and of pacemaker leads [3]. The prevalence is rare and *Granulicatella* species account for 5 to 16% of all streptococcal infective endocarditis cases [6].

G. adiacens appears to have a high degree of infectivity and this has been attributed to its capacity to bind to the cardiac valvular tissue [5]. The endovascular infectivity of *G. adiacens* is related to its fibronectin-binding capacity, an essential process for bacterial adherence, initiation and sustaining endovascular bacterial adhesion in infective endocarditis and dissemination of infection [8]. The infection caused by this species of organism has high pharmacological failure and has high resistance to macrolides and beta lactam [9].

This patient was afebrile and presented with atypical chest pain which led to a low index of suspicion of infective endocarditis in the first place. She did not fulfil any Duke Criteria based on the symptoms and physical examination [1]. The diagnosis was difficult to establish and could only be confirmed by microbiological and echocardiography [2].

Antibiotic choice in an infective endocarditis patient plays a main role in his/her treatment. It is recommended that for infection caused by *G. adiacens*, a combination therapy of penicillin with aminoglycosides is needed. This was based on the largest study of the susceptibility pattern of NVS, whereby it was found that *G. adiacens* isolates were susceptible to penicillin and did not display high-level resistance to aminoglycosides. Susceptibility to other antibiotics noted were meropenem, vancomycin, cefotaxime, ceftriaxone, erythromycin, clindamycin and levofloxacin [4].

In our case, the organism was susceptible to ceftriaxone which deemed that the reasonable alternative treatment option was ceftriaxone combined with gentamicin [10]. However, in view of aminoglycosides could cause ototoxicity and nephrotoxicity to the foetus, it was not prescribed during the first admission [11]. Unfortunately, a relapse meant that the patient required a stronger combination of antibiotics [12]. Furthermore, it was complicated with splenic infarction. Aminoglycosides was added in view of the benefit outweighed the risk. Indications for valve surgery in infective endocarditis are heart failure, uncontrolled infection and embolization, which prompted the intervention after the delivery [13].

This case report demonstrated the dilemmas in managing infective endocarditis in pregnancy. A pregnant patient is unique as each decision made needs to consider the well-being of the mother

and the foetus. Often time, the first choice of treatment should be medical instead of surgical to minimize the maternal and foetal risks. Also, pregnancy has higher risk for embolic events which may lead to catastrophic consequences [14].

Conclusion

In order to rule out the diagnosis of infective endocarditis, close attention should be paid to any pregnant woman with an unexplained fever and a cardiac murmur. Patients with history of cardiac lesions are at high risk of acquiring such infection. Rapid detection and appropriate treatment with suitable antibiotics are important in reducing the risk of both maternal and foetal mortality.

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Ethics
A written informed consent was obtained from the patient to publish this case report anonymously.

Conflict of Interest
The authors declare that they do not have any personal conflict of interest that may arise from the case report publication.

Author Contributions
WNAAWJ, VRNM and WYHWI drafted the design and medical practices. WNAAWJ collected the data while NLA was involved in the literature search and writing. All authors read and approved the manuscript for publication.

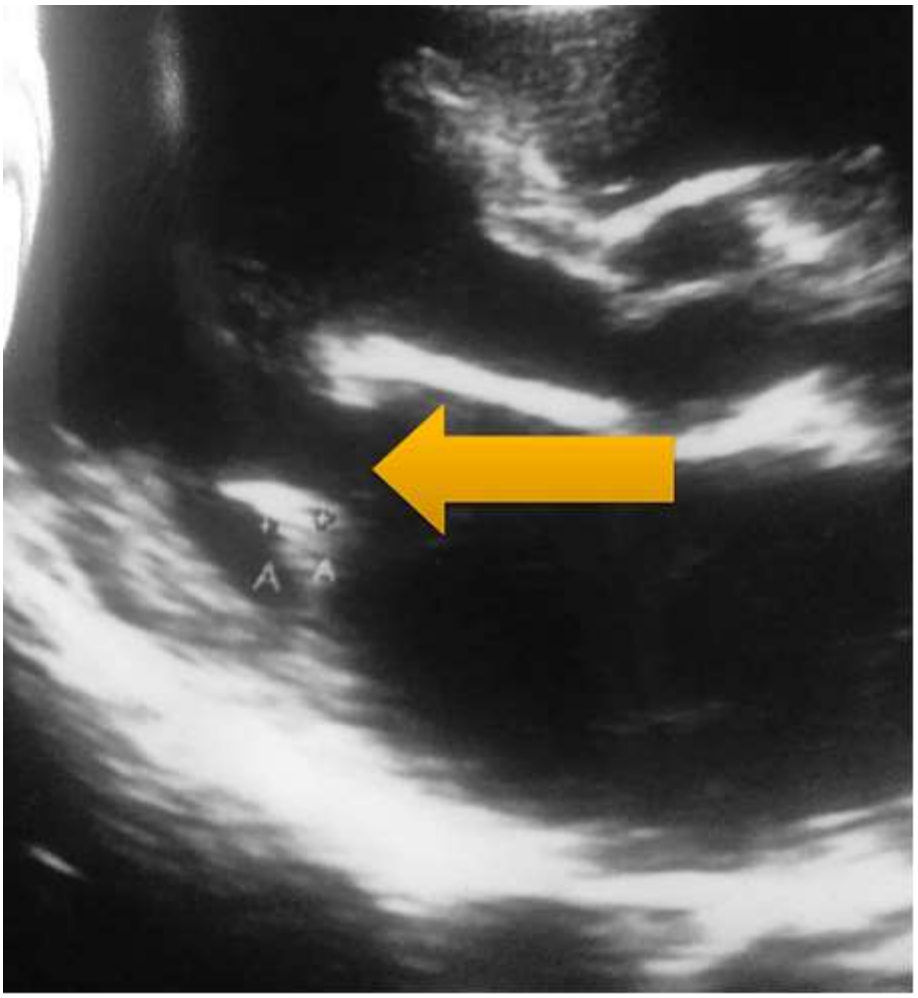

Figure 1. Echocardiography showing vegetation at mitral valve

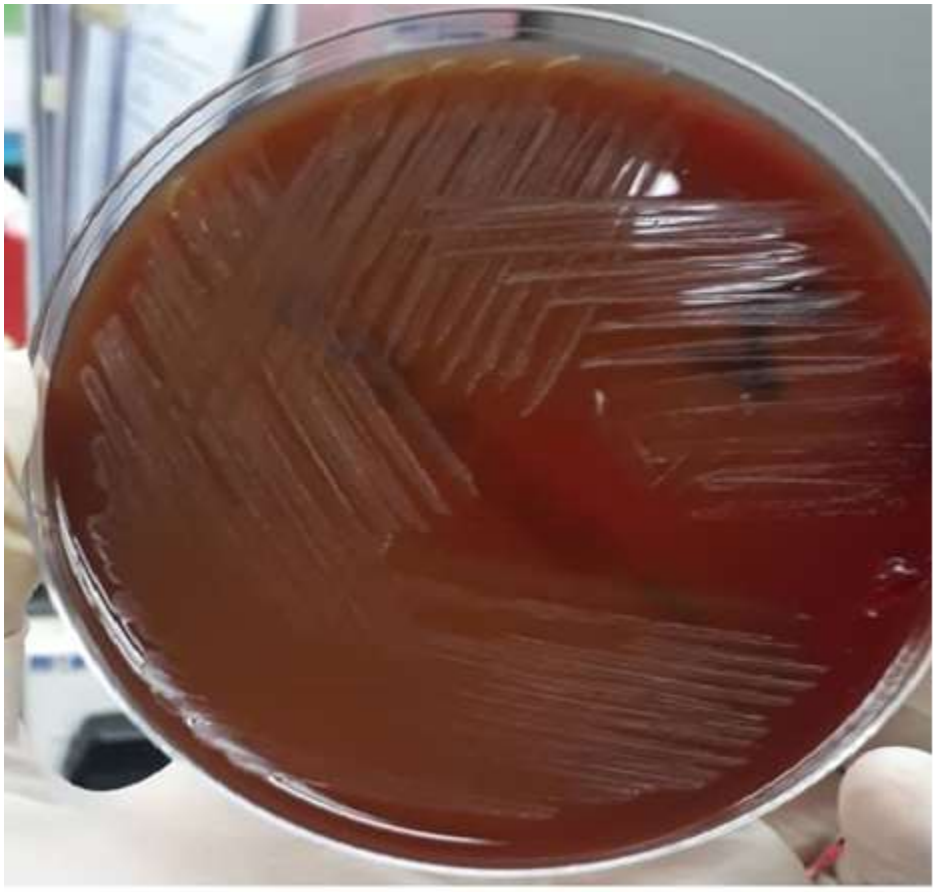

Figure 2. *Granulicatella adiacens* on blood agar after 48 hours incubation at 37°C in 5% CO_2

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