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# Infective Endocarditis and Meningitis Caused by *Granulicatella elegans*

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**Abstract** *Granullicatella elegans* is a nutritionally variant streptococci (NVS) known to cause a board spectrum of infections including infective endocarditis(IE), pneumonitis, peritonitis, meningitis, urinary tract, genital tract and other infections. NVS does not grow on routine laboratory media and requires specific biochemical tests for identification. We report a case of *Granullicatella elegans* causing infective endocarditis and a rare complication of septic emboli to brain manifested as meningitis in a previously healthy patient with mild dental manipulation. The patient was managed with empiric antibiotics until final identification was made. The patient made a full recovery after 6 to 8 weeks of treatment with no complications. NVS including Granullicatella species is a well known cause of IE which could be missed and should be considered in the differential of culture negative IE. Molecular testing is very helpful in the definite diagnosis and identification of of NVS.

***Keywords:*** *infective endocarditis, nutritionaly variant streptococci, granullicatella*

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## 1. Introduction

Infective endocarditis (IE) is a life threatening disease of the endocardium. Nutritionally variant streptococci (NVS) were first described in 1961 by Frenkel and Hirsch as fastidious organisms that showed satellitism around colonies of other bacteria [1]. NVS are commonly found in the oral cavity, genitourinary and intestinal tract accounting for up to 6% of all streptococcal endocarditis [2,3]. The two genera of NVS include *Granulicatella* and *Abiotrophia*. The genus *Granulicatell*a includes four species: *Granulicatella adiacens*, *baleaenopterae*, *elegans* and *para adiacens* [4,5]. We report a case of IE and meningitis due to *Granulicatella elegans* in a previously healthy patient.

## 2. Case Report

A 38-year-old man was admitted through the accident and emergency department of a tertiary care hospital with complaints of headaches and intermittent fever of 3 week duration. The patient described the headaches as frontal/compression without history of chills, rigors, photosensitivity, neurological signs or neck rigidity. The patient reported loss of appetite and weight loss. There was no history of co morbid conditions, allergies or excessive sweating reported. On physical examination, the patient was haemodynamically stable. He had decayed teeth but no previous invasive dental procedures were done. His abdomen was soft. On cardiovascular examination, grade 4 systolic murmur was heard at the mitral valve area. His lungs were clear. No neurological deficit was seen and Kernig's and Brudzinki's signs were negative. No lymphadenopathy was observed. Clinical impression was that of infective endocarditis.

Three sets of blood cultures from different sites were submitted along with a septic work up. All blood culture bottles flagged positive and the direct Gram stain showed pleomorphic Gram positive organism (gram positive cocci in chains, bacilli and bacilli with swollen centres). Subcultures were done on blood agar and chocolate agar in 7-10% $CO_2$ incubator at 37°C for 18 to 24 hours, Mac-conkey's agar in Oxygen at 37°C for 18-24 hrs and blood agar anaerobically with metronidazole disc for 48 hrs. All the above subcultures were negative for bacterial growth. Accordingly NVS was suspected and reported hence satellitism test was set up directly from blood culture broth. This is a test specific for identification of NVS where these colonies used to grow around staphylococcus aereus colonies. This test was positive and few tiny colonies were seen the next day around staphylococcus streak. Biochemical analysis revealed that the isolate was catalase, oxidase and PYR test negative. Identification for the organism could not be ascertained using Phoenix (Becton-Dickinson) or Vitek/API (bioMerieux) automatic identification systems. MALDITOF analysis could not be performed. Sensitivity testing was not performed due to lack of selective media. Analysis at the Central Public Health Laboratory in Muscat of 16s RNA identified *Granulicatella elegans*.

Laboratory investigations revealed normal haemoglobin, bone profile and liver function tests throughout his stay in hospital. Laboratory tests for HIV, hepatitis, Q fever and

Brucella were negative. Malaria parasite screen was negative. Urine analysis and culture examination was normal. Laboratory tests revealed a white blood cell count of 10.4 x $10^9$/L (neutrophils 57.7%, lymphocytes 20.2%), platelets 305,000/$mm^3$, CRP 170mg/L, Creatinine/eGFR 90/87.

A head CT showed no evidence of acute intracranial insult. Transthoracic echocardiograms showed no vegetation, thrombus or pericardial effusion but there was evidence of mitral valve regurgitation, thickening and prolapse due to chordal rupture suggestive of IE. A brain MRI showed mild tentorial and dural enhancement and meningitis was considered. The patient refused lumbar puncture. The dental team observed decayed teeth and an extraction was performed.

The patient was started on intravenous ceftriaxone 2gm and vancomycin 1gm twice daily for 2 weeks, after which he was discharged and managed with outpatient parenteral antibiotic therapy (OPAT) and blood work in a day care unit. The patient was readmitted on 12th March. There were no new findings except for a mild increase in inflammatory markers. The antibiotic regimen was switched to intravenous ceftriaxone 2gm and gentamicin 60 mg twice daily. The patient refused trans oesophageal echocardiogram and was discharged as OPAT to complete 4-6 weeks of intravenous antibiotics.

The patient was seen by the cardiothoracic team as a follow up and offered surgery for valve transplant however he refused as he feels that his condition is totally stable.

## 3. Discussion

The incidence of IE caused by NVS is probably underestimated due to the fastidious nature of these organisms and the challenge of recovering isolates from clinical specimens [2,6,7,8,9]. *Granulicatella* species are an uncommon cause of infection [10]. Although a susceptibility profile was not performed in the present case study, it is known that *Granulicatella* strains are sensitive to clindamycin, erythromycin, rifampicin and vancomycin. Previous studies have shown that NVS strains are susceptible to penicillin however their susceptibility to aminoglycosides is variable [11].

Previous reports have shown that the rate of oral colonization by Granulicatella is more than that of Abiotrophia spp. *G elegans* accounts for about 10% of colonization of adult dental plaque [12]. The tooth-tissue interface is a common portal for entry of bacteria into body. Bacteremia can occur following dental manipulations however in our patient, transient bacteremia following tooth brushing could have occurred or poor dental hygiene [13,14]. Our patient did not have any history of dental treatment or invasive procedures. It has been reported that bacteraemia is one of the most common predisposing factors for meningitis [15]. In our patient, *G. elegans* bacteraemia caused meningitis, however CSF examination was not possible as the patient refused lumbar puncture.

Although part of normal human oral, genital, and intestinal flora, organisms in the genera Abiotrophia and Granulicatella have been implicated in the development of endocarditis, vertebral osteomyelitis, endovascular infections, and central nervous system (CNS) infections after instrumentation. There were no predisposing factors for meningitis in our patient. However, a case study of a brain abscess in an immunocompetent adult due to *Abiotrophia/Granulicatella* without preceding neurosurgical intervention was reported [16]. Furthermore, *Granulicatella elegans* bacteraemia and meningitis in a child without neurosurgical interventions was also recently reported [17].

Endocarditis and meningitis due to *Granulicatella spp* is a rare and severe condition. Due to the difficulty in isolation of the bacteria in blood cultures and the clinical significance, it is of paramount importance that microbiologists should consider this bacterium in culture negative cases of infectious endocarditis.

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