Case report

**Granulicatella Causing Infective Endocarditis and Glomerulonephritis**

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**A B S T R A C T**

Granulicatella is a type of nutritionally variant Streptococcus (NVS) that requires special medium for growth. It has shown to cause infective endocarditis which is associated with higher mortality and complications. We present a case of Granulicatella causing endocarditis and glomerulonephritis. There has only been one such prior case report. An adult male with a remote history of gastric bypass presented with shortness of breath with exertion, lower extremity swelling of 1-month duration. Blood cultures 4/4 bottles grew Granulicatella albicans with infected tooth being the source. Transesophageal echocardiogram revealed a vegetation on the mitral valve. He received intravenous vancomycin. He was found to have acute kidney injury requiring hemodialysis. Kidney biopsy revealed immune complex deposits in the mesangium and along the capillary basement membrane suggestive of post infectious glomerulonephritis. It is crucial to recognize NVS as potential cause for endocarditis in cultures that are slow growing. NVS require a special medium. Though it is rare, NVS can also cause glomerulonephritis. Early recognition is important to help with determining treatment options which may include immunosuppressive therapy along with treatment of underlying infection.

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**Introduction**

Nutritionally variant Streptococcus (NVS) consists of Granulicatella and Abiotrophia.

Granulicatella (GRA) genus has three species: adiacens, elegans, balaenoptera. They are catalase-negative, oxidase- negative, facultatively anaerobic, gram-positive cocci and are part of normal oral, intestinal, and genitourinary flora (¹). Streptococci causes 60-80% cases of infective endocarditis (IE); NVS accounts for 5% of the cases (¹). Here we report a case of Granulicatella causing infective endocarditis and glomerulonephritis.

**Case Report**

A 46-year-old man with a remote gastric bypass presented with shortness of breath with exertion, bilateral lower extremity swelling, cough with pinkish expectoration for 1 month. He was afebrile and had bilateral basal rales, a 3/6 holosystolic murmur, tachycardia and normotension. He was noted to have an infected tooth that was later extracted. Labs were significant for BUN/creatinine of 65/7.3 (unknown baseline), urine microscopy showed red blood cell (RBC) casts. Other laboratory tests showed low compliment 3 and 4 (C3/C4), and negative anti-nuclear antibody (ANA), myeloperoxidase and anti-proteinase-3 (MPO/PR3 ANCA), anti-glomerular basement membrane antibody, HIV antigen/antibody, hepatitis B surface antigen and hepatitis C antibody. Blood cultures (4/4 bottles) grew *Granulicatella adiacens*. Trans-thoracic echocardiogram reduced ejection fraction of 35% with mitral valve vegetation. Trans esophageal echocardiogram revealed multiple highly mobile vegetations on the anterior and posterior leaflets, largest measuring 1.0 cm x 0.4 cm. (Figs. 1 and 2)

He was treated with intravenous vancomycin. Kidney function continued to decline. Kidney biopsy showed, non-sclerotic glomeruli with mild to moderate diffuse mesangial and endothelial cell proliferation. There were no necrotic and proliferative lesions identified. There was background of chronic glomerulosclerosis with associated tubular atrophy/intersitial fibrosis, likely preceding recurrent acute event (Fig. 3). Direct immunofluorescence study showed, immune complex deposits mainly IgA, IgM, C3, C1q (Fig. 4). On electron microscopy, immune complex dense deposits
Discussion

NVS were first described in 1961 by Frenkel and Hirsch, the genus is divided into Abiotrophia and Granulicatella on the basis of 16S rRNA sequencing (1). They require special medium for growth consisting of pyridoxine, cysteine or helper bacteria such as staphylococci for adequate growth (2). They have the ability to bind to extracellular matrix proteins and fibronectin leading to endocardial colonization and infection. The slow growth and the need for special medium for growth could be a reason for fewer reported cases. Thus, NVS are among the organisms that cause culture negative endocarditis (1). In a retrospective study of 76 cases of NVS revealed the median age for GRA infection was 50 years (interquartile range of 31.0–64.0, p = 0.06) with majority being men (3). The oral cavity was identified as the route of transfer in 26.3% of GRA cases. Pre-existing valvular disease including both congenital and bio-prosthetic valves was seen in 18.4% of cases (p = 0.04) (3). The onset of symptoms is usually insidious with sub-acute or chronic presentation. A case series showed both aortic valve (44%) and mitral valve (38%) involvement (4). Mean vegetation size of greater than 10 mm was associated with higher embolic events and death (5). Endocarditis by NVS are known to have higher rates of complications, including heart failure (30%), embolism (30%), and perivalvular abscess (11%), thus increasing morbidity and mortality (4). Apart from endocarditis, NVS can cause endophthalmitis, pancreatic abscess, and post-partum sepsis.

There has only been one previous case report of Granulicatella presenting as endocarditis and glomerulonephritis based on our literature search (6). Glomerulonephritis is seen in 20% of the patients with endocarditis and 23% of these are ascribed to...
streplococci (7). Three different forms of renal damage have been observed: post-infectious glomerulonephritis, focal glomerulonephritis and drug induced acute interstitial nephritis (AIN) presumed to be from antimicrobial treatment (8). In a retrospective study, conducted from 2002 to 2011 in 49 patients with IE associated glomerulonephritis, the mean age was 48 years with risk factors of cardio-valvular disease, intravenous drug abuse, hepatitis C, and diabetes mellitus (7). Although more than 50% of patients were not known to have prior cardiac history. Low complement levels are frequently seen (53%).

On light microscopy, crescentic GN was seen in 53% of the cases with diffuse inflammatory changes and focal necrotizing lesions. On immunofluorescence up to 94% had C3 deposits, IgM 37%, IgA 29% and IgG 27%. Interstitial nephritis was seen in 88% of the cases. Of these cases with interstitial nephritis, 63% were focal and only 14% had neutrophilic infiltrates with no eosinophils reported. Mesangial immune complex deposits, as seen in our case were most common, 84%. Only 14% had the classic hump-like deposits (7). In our patient, the biopsy findings of chronic glomerular sclerosis likely existed prior to the current event. The mesangial proliferation and immune complex deposition within the glomerular compartment were related to endocarditis. Tubulo-intestinal nephritis with neutrophilic and eosinophilic infiltration was also seen. C3 and IgM deposits were present.

The American Heart Association (AHA) 2015 treatment guidelines recommends penicillin G or ceftriaxone and gentamicin for 4 weeks. Vancomycin for 4 weeks is used in patients in whom penicillin or ceftriaxone is contraindicated or based on sensitivities (9). The European Society of Cardiology (ESC) 2015 guidelines recommends penicillin G, ceftriaxone or vancomycin for 6 weeks, combined with an aminoglycoside for at least the first 2 weeks (10). In previous studies about 27% required valve replacements for worsening heart failure and septic emboli.

Glomerulonephritis secondary to endocarditis does not always resolve with treatment of the underlying infection. A kidney biopsy is warranted to consider the role of steroids, intravenous immunoglobulin, and cytotoxic agents (8,11). Immunosuppression in endocarditis is a concern. However, previous case reports have shown improvement in renal function in these patients. It might be worthwhile to consider immunosuppressive therapy in patients if renal function does not improve despite appropriate treatment of endocarditis. This field certainly needs more evidence and data.

Conflicts of interest: none declared

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References

[1] Cargill JS, Scott KS, Gascoyne-Binzi D, Sandoe JAT. Granulicatella infection: Diagnosis and management. J Med Microbiol. 2012;61(6):755–61, doi:http://dx.doi.org/10.1099/jmm.0.039693-0.

[2] Caribyan V, Shaw D. Bioaorticular endocarditis due to Granulicatella adiacens. Am J Case Rep. 2013;14:435–8, doi:http://dx.doi.org/10.12659/AJCR.889206.

[3] Téllez A, Ambrosioni J, Llopis J, et al. Epidemiology, clinical Features, and outcome of infective endocarditis due to Abiotrophia species and Granulicatella species: Report of 76 Cases, 2000–2015. Clin Infect Dis. 2018;66 (1):104–11, doi:http://dx.doi.org/10.1093/cid/cix752.

[4] Adam EL, Siciliano RF, Gualandro DM, et al. Case series of infective endocarditis caused by Granulicatella species. Int J Infect Dis. 2015;31:56–8, doi:http://dx.doi.org/10.1016/j.ijid.2014.10.023.

[5] Thuny F, Disalvo G, Belliard O, et al. Risk of embolism and death in infective endocarditis: Prognostic value of echocardiography - A prospective multicenter study. Circulation. 2005;112(1):69–75, doi:http://dx.doi.org/10.1161/CIRCULATIONAHA.104.491355.

[6] Dang Hong T, Jordan Stanley. 98 Granulicatella adiacens endocarditis-induced ANCA-negative pauci-immune necrotizing and crescentic glomerulonephritis Successfully Treated with Aortic Valve Replacement. Am J Kidney Dis. 2019;73 (5):667, doi:http://dx.doi.org/10.1053/j.jkd.2019.03.100.

[7] Boils CL, Nasr SH, Walker PD, Couser WG, Larsen CP. Update on endocarditis-associated glomerulonephritis. Kidney Int. 2015;87(6):1241–9, doi:http://dx.doi.org/10.1038/ki.2014.424.

[8] Mantan M, Sethi G, Batra V. Post-infectious glomerulonephritis following infective endocarditis: Amenable to immunosuppression. Indian J Nephrol. 2013;23(5):368, doi:http://dx.doi.org/10.4103/0971-4065.116521.

[9] Baddour L, Wilson W, Bayer A. Complications: A statement for healthcare professionals from the committee on rheumatic fever, endocarditis, and Kawasaki disease, council on cardiovascular. Circulation. 2005;111(23):e394–434, doi:http://dx.doi.org/10.1161/CIRCULATIONAHA.105.165564.

[10] Horstkotte D, Follath F, Gutschik E, et al. Guidelines on prevention, diagnosis and treatment of infective endocarditis executive summary: The Task Force on Infective Endocarditis of the European Society of Cardiology. Eur Heart J. 2004;25(3):267–76, doi:http://dx.doi.org/10.1016/j.ejehj.2003.11.008.

[11] Le Moing V, Lacassin F, Delahousse M, et al. Use of corticosteroids in glomerulonephritis related to infective endocarditis: Three cases and review. Clin Infect Dis. 1999;28(5):1057–61, doi:http://dx.doi.org/10.1086/514734.