**Lactococcus garvieae** Endocarditis with Initial Presentation of Acute Cerebral Infarction in a Healthy Immunocompetent Man

Wei-Kai Li, Yao-Shen Chen, Shue-Ren Wann, Yung-Ching Liu and Hung-Chin Tsai

**Abstract**

*Lactococcus garvieae* is considered a rare, opportunistic pathogen with low virulence in human infection. There are only scattered case reports of *L. garvieae*-related infection in humans in the past 20 years. The majority of them were reported to be infective endocarditis. We present a case study of a 41-year-old man with infective endocarditis caused by *L. garvieae* which is the first reported case with initial presentation as acute cerebral infarction.

**Key words:** cerebral infarction, endocarditis, *Lactococcus garvieae*

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**Introduction**

*Lactococcus* is a lactic acid bacterial genus, which contains eight species and subspecies (1) and is characterized by catalase-negative, facultatively anaerobic, serogroup N Gram-positive cocci (2). *Lactococcus garvieae* is considered as an unusual pathogen with low virulence in humans and is reported to rarely cause human infection. A review of associated literature (3-9) showed eleven cases of *L. garvieae* infection in humans. However, the various clinical manifestations lead to difficulties in diagnosis. Herein, we report a case of native-valve endocarditis caused by *L. garvieae* in a healthy man who did not exhibit any symptoms of underlying cardiovascular disease. We analyzed the possible risk factors and clinical course by reviewing the relevant associated literature.

**Case Report**

A 41-year-old man was brought to the Kaohsiung Veterans General Hospital with sudden onset of right side hemiplegia and slurred speech upon waking up from a nap. The man, a cooker by profession, was healthy in the past and did not have any systemic disease before. At presentation, his temperature was 36.7°C, pulse rate 72 beats per minute, the respiratory rate was 28 beats per minutes and his blood pressure was 92/49 mmHg. On physical examination, there was slurred speech, his tongue deviated to the right side, impairment of the right visual field was observed, and there was a loss of right side body sensation and poor coordination. In addition he was disorientated to time with a positive right Babinski’s sign. A grade 3 systolic murmur over the left lower sternal border was also observed. Upon examination, the abdomen was soft without tenderness or bruit. His brain computed tomography (CT) scan performed with and without contrast enhancement revealed no abnormal mass in the brain (Fig. 1).

The neurologist was consulted to evaluate the National Institute of Health Stroke Scale (NIHSS) score. The NIHSS score was 21 and tissue plasminogen activator (rt-PA) thrombolytic therapy with 50 mg (5 mg bolus for one minute and 45 mg infusion for 60 minutes) was given. The NIHSS score 2 hours after rt-PA infusion follow-up was 18.
However, he developed a fever of 38.8°C about 6 hours after admission. Laboratory tests were performed in the presence of leukocytosis (white blood cell count 12,570 per mm³ with 87% of segment and no band); elevated C-reactive protein (CRP): 4.6 mg/dl. Two sets of blood cultures were collected. An electrocardiography revealed a normal sinus rhythm. Physical examination revealed no peripheral embolic signs. Antibiotics were not prescribed due to lack of evidence of infection and the vital signs were stable.

On the second hospital day, the 24-hour follow-up NIHSS score was 23. Repeat brain CT scan (Fig. 2) was arranged, which revealed a slightly lower density with brain sulcus effacement involving the left side fronto-temporo-parietal and left side basal ganglion region. Laboratory tests to survey the etiologies of young age stroke were performed. The serologic titer including anti-nuclear antibody (ANA), serum rheumatoid arthritis factor test (RF test), serum C3/C4 level, anti-cardiolipin antibody, antithrombin III, antiplatelet antibody and the lipid profile (cholesterol, high-density lipoprotein, low-density lipoprotein and triglycerides) were all unremarkable. The serum tests for VDRL and enzyme-linked immunoassay (ELISA) for human immunodeficiency virus antibody were non-reactive. However, fever up to 38.4°C and productive cough persisted. On the third day at the hospital, the blood culture showed gram positive cocci (GPC) in chains. Infective endocarditis with septic embolic cerebral infarction was suspected. Crystal penicillin 3 M.U intravenously per 4 hours and gentamicin 80 mg intravenously per 8 hours were prescribed. The cardiologist was consulted and a transthoracic echocardiography (TTE) was performed on the seventh hospital day. It presented severe anterior mitral leaflet prolapse with moderate eccentric MR (Fig. 3). The 4 sets of blood cultures yielded *Lactococcus garvieae* on the 7th hospital day, which was intermediate resistance to penicillin. The minimum inhibition concentration (MIC) was 0.75 mcg/ml. The isolate was phenotypically identified as *Lactococcus garvieae* with the automated Phoenix system (Becton Dickinson Diagnostic Systems, Franklin Lakes, NJ) and Vitek2 (BioMérieux Vitek System, Durham, NC). These discrepant results prompted us to identify this isolate by the dideoxynucleotide chain termination method with the Microseq 500 16S ribosomal rRNA bacterial sequencing kit (PE Applied Biosystems, Foster City, CA, USA) and analyze it on a ABI PRISM 310 Genetic Analyzer (PE applied Biosystems). Follow-up transesophageal echocardiography (TEE) on the twelfth day of admission disclosed small chordae tendinae rupture of anterior mitral leaflet with severe eccentric MR and presence of vegetations. The left ventricular (LV) systolic function was essentially preserved.

This patient was given penicillin and gentamicin for a total of 30 days. He was discharged after a total of 46 days of hospitalization. The follow-up TTE disclosed flail of the anterior mitral leaflet and the prominent left atrial (LA) systolic expansive motion, resulting from severe eccentric mitral regurgitation (MR) with jet to posterior wall of LA His heart failure persisted, and he was admitted for mitral valve replacement 16 days after the previous discharge. The culture from the vegetated mitral valve revealed no bacterial growth. He was discharged in stable condition and under long-term anticoagulatory therapy with warfarin. The patient was well after 1 year of follow-up.

**Discussion**

Prior to 1985, the bacteria of the *Lactococcus* genus, which had characteristics of catalase-negative, facultatively anaerobic, serogroup N gram-positive cocci that primarily
produced lactic acid from the fermentation of carbohydrates were included in the Streptococcus genus (2). Studies using genetic analysis of DNA-DNA relatedness and 16S rRNA sequencing data, recognized fecal streptococci in the Enterococcus genus and the lactic acid streptococci in the genus Lactococcus respectively (10, 11).

There are eight recognized Lactococcus species and subspecies (1). L. lactis subsp. lactis and L. garvieae are the two Lactococcus spp. that are most frequently found in human infections. Nevertheless, they are difficult to distinguish from each other (12). Elliott et al (13) discriminated them according to their antimicrobial susceptibilities because unlike L. lactis, L. garvieae was resistant to clindamycin. Additionally, MICs of penicillin and possibly cephalothin for L. garvieae were higher than for L. lactis. Although L. garvieae is considered a rare pathogen with low virulence in humans recently there has been an increasing number of case reports of L. garvieae infection in humans (3-9). One possible reason could be because of better diagnosis via improved identification techniques or due to the fact that clinicians are more alert whenever Enterococcus or a Streptococcus-like pathogen which does not fit all characteristics is isolated.

Analysis of the published case reports over the last 20 years, revealed eleven cases of L. garvieae related infection in humans. The most common is infective endocarditis (7/11, 64%) (3-9), followed by bacteremia without definite infectious focus (2/11, 18%) (12), osteomyelitis (1/11, 9%) (8), liver abscess (1/11, 9%) (9), and peritonitis (1/11, 9%) (7), respectively. The case reported here is the eighth case of L. garvieae-related endocarditis and, among them, the third case of endocarditis in a native-valve. The diagnosis of infective endocarditis is quite obvious because this case meets the Duke criteria (14) at least one major criterion (evidence of vegetation on mitral valve by echocardiography) and three minor criteria (fever, vascular phenomena and microbiological evidence). The brain infarction is considered as the septic embolic infarction, one of the clinical manifestations of infective endocarditis. Catheter-related infection which is not suspected due to L. garvieae has never been the nosocomial pathogen of our hospital. There also has been no patient proven to have L. garvieae infection during that time period.

In fact, this is the first case report of endocarditis in a patient with no prior history of cardiovascular disease. It is also the first case where the infection initially presented as acute cerebral infarction. There are five cases reported with prosthetic valves, one with previous coronary artery disease and one with hypertrophic cardiomyopathy and complete heart block that required a dual chamber pacemaker.

In addition, the patient is a healthy man without any systemic disease, such as diabetes mellitus, autoimmune disease or malignancy. He did not take any immunosuppressant agents. He was not an alcohol or IV drug abuser. By tracing his past medical history, he had never suffered from recurrent infection, unexplained body weight loss, fever of unknown origin or lymphadenopathy.

During the hospitalization, the laboratory examinations including serum rheumatoid arthritis factor test (RF test) and serum C3/C4 level all showed within normal limit. The anti-nuclear antibody (ANA) was negative. The serum tests for VDRL and human immunodeficiency virus were non-reactive. The only exception was the complete blood count, which revealed white blood cell count 12,570 per mm$^3$ with 87% segment, which is because the patient had an infection.

Due to the rarity of published cases reports, the source of infection caused by L. garvieae has not been identified thoroughly in many cases. In some cases, ingestion of raw fish (sashimi), cheese, and grilled fish seemed to be the cause of subsequent L. garvieae infection. Although the possible source and infectious pathway of Lactococcus garvieae in humans remains uncertain, we still could make the hypothesis that the ingestion of contaminated food, especially the fish, may be one of the possible routes of infection. There are two strong evidences to support the hypothesis. First, L. garvieae has been recognized as an important cause of bacterial disease in many fish species, resulting in significant economic losses in aquaculture (15-17). Increasing rates of infection with rising water temperatures (>16°C) typically during summer months has also been reported (15). By ingesting the contaminated food, therefore, is the possible pathway of L. garvieae infection.

Second, the history of ingestion of even raw fish or grilled fish could be traced in the published case reports. Al-
though the case we presented is the only one without underlying cardiovascular disease or immunocompromised status, frequent contact of fish during his working time may render him susceptible to the high risk of ingestion of *L. garvieae*. Therefore, the possible source in the present patient could be traced to be ingestion of *L. garvieae* from his hands, which could have been contaminated with *L. garvieae*.

In conclusion, infective endocarditis is the most common presentation of *L. garvieae* infection. Our study highlights the fact *L. garvieae* infection can also present itself initially as cerebral infarction followed by endocarditis in seemingly healthy patients with no prior history of heart disease.

References