

First known case of *Eperythrozoon* endocarditis in China

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Abstract

Eperythrozoonosis is a zoonosis transmitted from animals to humans. It is caused by bacteria in the genus *Eperythrozoon*. These bacteria have a high infection rate and can cause varying degrees of damage. This is the first case report of infective endocarditis caused by *Eperythrozoon*. The patient had a 30-day history of remittent fever accompanied by chills and progressive weakness and gradually recovered after 6 weeks of minocycline treatment.

Keywords

Eperythrozoonosis, *Eperythrozoon*, infective endocarditis, blood smear, zoonosis, fever

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Introduction

Eperythrozoonosis is a zoonosis transmitted from animals to humans. It is caused by bacteria in the genus *Eperythrozoon*; these species are now considered to be part of the genus *Mycoplasma* according to 16sRNA sequencing.^{1–3} *Eperythrozoon* species are parasitic bacteria that invade erythrocytes, plasma, and bone marrow. These bacteria have a high infection rate and can cause varying degrees of damage.⁴ This is the

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first case report of infective endocarditis caused by *Eperythrozoon*. The diagnosis relies mainly on blood smear findings. Eperythrozoonosis should be considered in patients with a fever of unknown origin that does not improve with empirical antibiotic therapy and in patients with endocarditis who have negative blood cultures.

Case report

A 37-year-old woman with no significant medical history presented to an outside hospital with a 30-day history of remittent fever that gradually worsened during the first week. The fever fluctuated daily, rising as high as 41°C and decreasing to afebrile levels with no medical intervention. She also reported chills and progressive weakness. She had no history of heart disease. Six months before presentation, she had eaten roasted lamb. Thirty days before presentation, she had spent 1 week in Hainan, China's only tropical province, where she had eaten raw seafood.

Laboratory investigations revealed an initial hemoglobin concentration of 14 g/dL, which decreased to 10.7 g/dL (reference range, 11–15 g/dL) after 1 month. Her white blood cell count ranged from 3.3 to $4.9 \times 10^9/L$ (reference range, 3.5 to $10 \times 10^9/L$) with normal neutrophil and lymphocyte counts. Her erythrocyte sedimentation rate and C-reactive protein level were mildly elevated at 46 to 51 mm/h (reference range, 1–15 mm/h) and 8.7 to 18.4 mg/L (reference range, 0–5 mg/L), respectively. The T-SPOT.TB test (Oxford Immunotec, Oxfordshire, UK), antinuclear antibody test, viral antibody panel (coxsackievirus, Epstein–Barr virus, *Cytomegalovirus*, and herpesvirus), Widal reaction, blood smear for malarial parasites, and agglutination test for brucellosis were all negative. The results of thyroid function tests, a urine dipstick, electrocardiography, and chest radiographs were unremarkable.

At the outside hospital, the patient completed 4 days of treatment with amoxicillin/clavulanic acid, 5 days of treatment with levofloxacin, 3 days of treatment with ceftriaxone, and 3 days of treatment with artemisinin. Despite this wide variety of antibiotics, the patient's symptoms did not improve; she was then transferred to our hospital. All antibiotic treatment was discontinued for 7 days to rule out drug-induced fever. Three sets of blood cultures post-antibiotic therapy were negative,¹ but the patient's fever continued. A transthoracic echocardiogram performed about 20 days after onset of symptoms revealed a 0.97- × 0.65-cm vegetation on the non-coronary aortic cusp (Figure 1). The patient then completed 6 days of treatment with amoxicillin/clavulanic acid with no improvement in her fever.^{1,2}

The final results from two separate blood smears sent to the Hangzhou Centers for Disease Control and Prevention (CDC) were positive for *Eperythrozoon* (Figure 2). The patient was diagnosed with *Eperythrozoon* endocarditis according to the Duke criteria.³ For combined treatment of endocarditis and eperythrozoonosis, she was started on oral minocycline at 200 mg daily for 6 weeks.^{1,2,4} Her fever and weakness rapidly resolved within the first 3 days of treatment, and blood smears were negative for *Eperythrozoon* after antibiotic therapy. A follow-up transthoracic echocardiogram at 6 months revealed that the vegetation had become smaller and more stable. The patient remained afebrile, and her hemoglobin concentration normalized.

The patient provided written informed consent, and the report was approved by the ethics committee of our institution.

Discussion

Eperythrozoonosis is a zoonosis transmitted from animals to humans.⁵ More than 30 countries worldwide, mainly China,

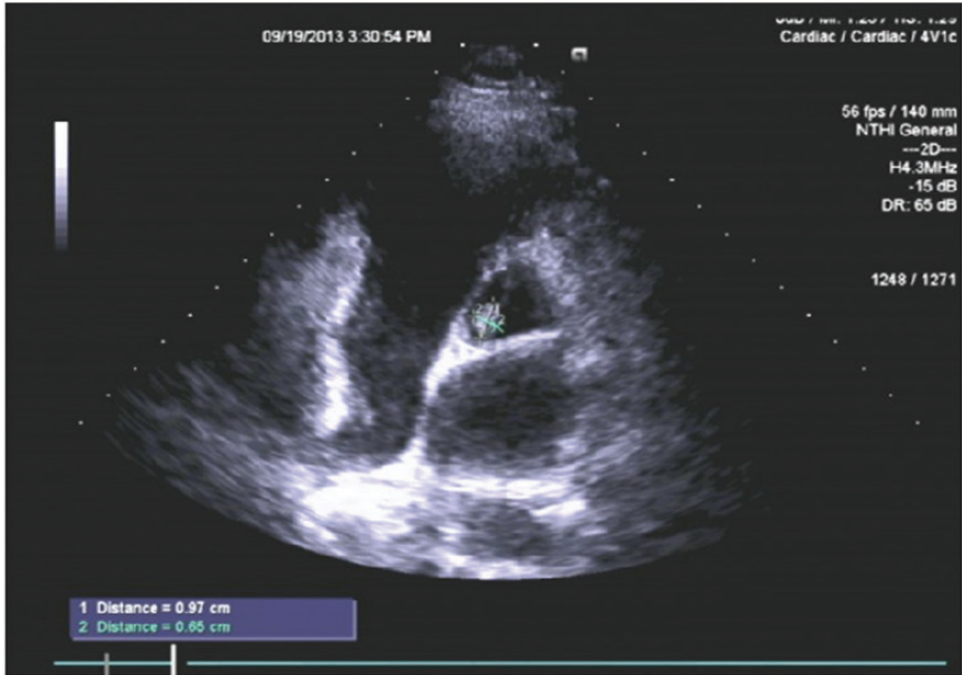


Figure 1. A 0.97- × 0.65-cm vegetation on the non-coronary aortic cusp.

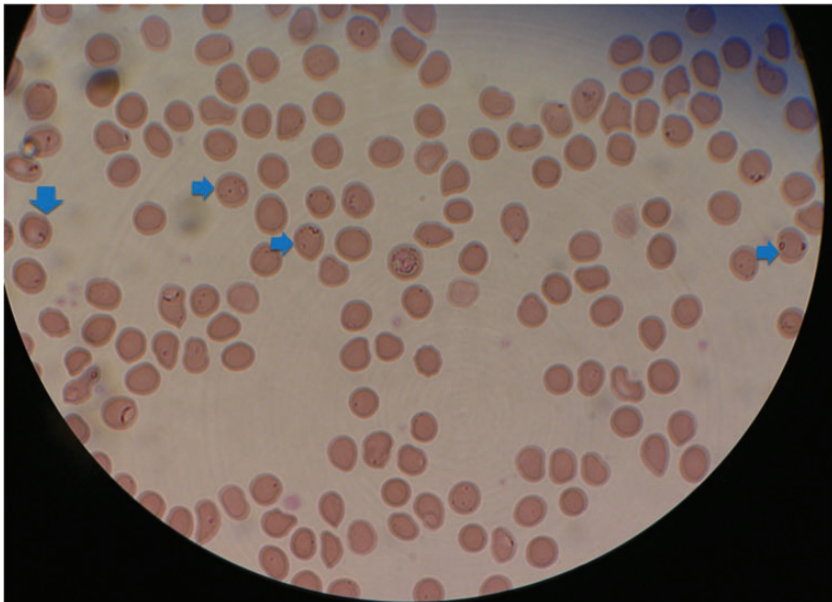


Figure 2. Erythrocytes infected by *Eperythrozoon* as shown in the microscopic examination.

have reported this disease in sheep, cattle, pigs, and humans. Patients with eperythrozoonosis and animal carriers of *Eperythrozoon* are the sources of this infectious disease. The infection rate varies from 0% to 97% in China, and the incidence rate is significantly higher in the summer and autumn than in the winter and spring.⁵ Survey data from the Hangzhou CDC showed that the average infection rate in Hangzhou was 9.31% of 580 people, including controls, meat processing workers, slaughter operators, veterinarians, and farm workers. The data also showed that the infection rates were significantly different between individuals who did and did not wash their hands after contact with animal fur, feces, and raw meat as well as between those who did and did not use antibacterial soap to wash their hands. Eperythrozoonosis is caused by *Eperythrozoon* species, which are considered to be part of the genus *Mycoplasma* according to 16sRNA sequencing.^{6–8} *Eperythrozoon* species are parasitic bacteria that invade erythrocytes, plasma, and bone marrow. They are diversiform and mostly spherical, fusiform, and short rods. The clinical manifestations of eperythrozoonosis vary from asymptomatic subclinical infection to fever, weakness, scleral icterus, and anemia depending on the proportion of infected erythrocytes. More serious symptoms appear when more than a certain percentage of erythrocytes are infected. Similar to malaria, eperythrozoonosis typically manifests as a remittent fever. It can be difficult to identify because its nonspecific clinical signs may be consistent with a wide variety of diseases including influenza, malaria, and anemia. Diagnosis relies mainly on blood smears; DNA testing continues to be imprecise because of incomplete knowledge of the gene sequence for *Eperythrozoon*.⁹ Therefore, a blood smear should be considered in patients with a fever of unknown

origin that does not improve with empirical antibiotic therapy and in patients with endocarditis who have negative blood cultures.¹⁰ *Eperythrozoon* species have a high infection rate and can cause varying degrees of damage. To the best of our knowledge, this is the first report of eperythrozoonosis involving the endocardium in China.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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