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CASE REPORT

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Bartonella quintana endocarditis presenting with severe coombs-positive anemia: a case report

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Abstract

Background *Bartonella quintana* is a recognized cause of blood culture-negative endocarditis, often associated with predisposing social factors or pre-existing valvulopathy. Diagnosis is challenging and relies on advanced microbiological techniques.

Case presentation A 17-year-old Tibetan herdsman from a high-altitude region presented with a two-week history of fever, dyspnea, and lower limb edema. He had no history of homelessness or alcoholism but lived in poor sanitary conditions. Laboratory investigations revealed severe Coombs-positive hemolytic anemia and serological markers suggestive of systemic lupus erythematosus (SLE). Transthoracic echocardiography showed vegetations on both aortic (bicuspid) and mitral valves with severe regurgitation and rapid hemodynamic progression. All blood cultures were negative. Metagenomics Next-Generation Sequencing (mNGS) of peripheral blood identified *B. quintana* as the causative pathogen. Antibiotic therapy was adjusted to doxycycline (9 weeks) and gentamicin (3 weeks). Concurrently, immunomodulatory therapy with methylprednisolone and intravenous immunoglobulin was administered for the hemolytic anemia. Given the severe valvular insufficiency, the patient successfully underwent urgent aortic and mitral valve replacement. His clinical condition improved significantly post-operatively.

Conclusion This case highlights the diagnostic utility of mNGS in confirming *B. quintana* endocarditis in a culture-negative scenario, especially when clinical presentation is complicated by concomitant autoimmune features mimicking Libman-Sacks endocarditis. A treatment strategy combining targeted antibiotics for the infection and immunomodulation for the hematologic complication, followed by definitive surgery, led to a successful outcome. It underscores that *B. quintana* infection should be considered in patients from disadvantaged backgrounds with endocarditis, even in the absence of classic risk factors.

Keywords Bartonellosis, *Bartonella quintana*, Blood culture-negative endocarditis, Coombs-positive hemolytic anemia, Next generation sequencing, Case report

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Introduction

Bartonella spp. are fastidious, gram-negative bacteria that cause a variety of infections—many of them zoonotic—collectively referred to as bartonellosis. Clinical manifestations include, among others, unexplained fever, subacute lymphadenopathy and culture-negative endocarditis [1]. Transmission to humans occurs via hematophagous insect vectors (such as sand flies, cat fleas, and human body lice) or through animal scratches and bites. Among *Bartonella* spp. the most common causative species in humans are *B. bacilliformis*, *B. quintana*, and *B. henselae*. Humans are the only confirmed reservoir for sustained human-to-human transmission of *B. quintana.* Although *B. quintana* has been isolated from macaque species, there is no documented evidence of transmission from non-human primates to humans [2–4]. A hallmark of *Bartonella* spp. is their specific tropism for endothelial cells and erythrocytes.

B. quintana and *B. henselae* are the most frequent causes of *Bartonella* endocarditis. *B. quintana* infection is primarily associated with lice infestation, homelessness, alcoholism, poverty, and poor living conditions, particularly concerning health and hygiene, whereas *B. henselae* is the pathogen responsible for cat-scratch disease [3, 5]. The severity and type of clinical disease correlate with the host's immune status—for example, *B. quintana* typically causes trench fever and *B. henselae* causes cat scratch disease in immunocompetent individuals, whereas bacillary angiomatosis occurs mainly in immunocompromised hosts.

Metagenomics Next-Generation Sequencing (mNGS) is a powerful, high-throughput technology that enables comprehensive analysis of genetic material (DNA and/or RNA) obtained directly from clinical or environmental samples [6]. As a culture-independent and broad-range, unbiased approach, mNGS differs from traditional methods that require prior cultivation or target-specific assays. It allows for the simultaneous detection and characterization of all microorganisms—including bacteria, viruses, fungi, and parasites—in a single test.

This report presents a case of blood culture-negative *B. quintana* endocarditis affecting both the aortic and mitral valves, accompanied by severe valvular insufficiency and hemolytic anemia. The diagnosis was confirmed using mNGS. The patient's condition improved following intensive antibacterial and immunomodulatory therapy, followed by urgent surgical valve replacement.

Case presentation

A 17-year-old Tibetan herdsman was admitted to our hospital with a two-week history of fever, shortness of breath, and progressive bilateral lower limb edema. His medical history was negative for congenital heart disease, hypertension, diabetes mellitus, and dyslipidemia. Although his family lived in poverty with unsatisfactory sanitary conditions, he had no history of homelessness or alcoholism.

Laboratory investigations revealed severe anemia (hemoglobin 56 g/L) and a positive Coombs test (both IgG and C3d). Extensive serological testing was positive for anti-nuclear antibody (ANA, titer 1:320), anti-dsDNA antibody (titer 1:80), and anti-cardiolipin IgM antibody. Blood cell counts and biochemistry values are summarized in Table 1, and detailed serum immunological indicators are provided in Table 2.

Transthoracic echocardiography demonstrated a reduced left ventricular ejection fraction (LVEF, 47%), an enlarged left ventricle, and vegetations on both the aortic and mitral valves. The mitral valve was significantly compromised due to prolapse of the anterior leaflet, resulting in severe regurgitation. A congenital bicuspid aortic valve with mild regurgitation was discovered (Fig. 1; Table 3). However, a repeat echocardiogram three days later revealed rapid progression to severe aortic regurgitation with multiple reflux jets, indicating worsening valvular destruction (Fig. 2).

All multiple blood cultures returned negative. The diagnosis was ultimately confirmed by mNGS of peripheral blood, which identified *B. quintana* DNA. Antibiotic therapy was consequently adjusted from norvancomycin (a vancomycin-analog glycopeptide) to a combination of doxycycline (for a total of 9 weeks) and gentamicin (for 3 weeks). Given the presence of hemolytic anemia, intravenous methylprednisolone (80 mg/d) and human immunoglobulin (10 g/d) were administered, supplemented with iron sucrose and red blood cell transfusions. The patient's symptoms improved markedly within five days. Subsequently, he successfully underwent aortic and mitral valve replacement surgery with cardiopulmonary bypass support.

Following double valve replacement, the patient remained clinically stable with respect to heart failure, thrombotic events, and anemia during follow-up. The methylprednisolone dosage was gradually tapered, guided by close monitoring of hematological and immunological parameters (Table 4).

Discussion

We report a case of *B. quintana* endocarditis complicated by severe hemolytic anemia in a young Tibetan herdsman residing at 4,300 m above sea level, where polycythemia would normally be expected. The patient also had a congenital bicuspid aortic valve and serologic findings suggestive of systemic lupus erythematosus (SLE).

Bartonella spp. have emerged as significant pathogens in blood culture-negative endocarditis, accounting for up

Table 1 Blood cell counts and other chemistry values on admission

Variables	Values	Normal Reference	Variables	Values	Normal Reference
Leucocyte, $\times10^9$/L	4.97	4.1–11.0	SCr, μmol/L	63	52–101
Neutrophil, $\times10^9$/L	3.26	1.8–8.3	UA, μmol/L	433	208–428
Lymphocyte, $\times10^9$/L	1.40	1.2–3.8	K, mmol/L	3.66	3.5–4.9
Eosinophil, $\times10^9$/L	0.02	0.00-0.68	Na, mmol/L	134.3	135–145
Basophil, $\times10^9$/L	0.02	0.00-0.07	Cl, mmol/L	102.9	98–110
Erythrocyte, $\times10^{12}$/L	3.25	4.5–5.9	Ca, mmol/L	2.01	2.1–2.8
Hemoglobin, g/L	56	129–172	PT, s	15.60	9.0–13.0
MCV, fL	65.50	80–100	PT-INR	1.39	0.85–1.25
MCH, pg	17.20	25–34	APTT, s	27.3	20–40
MCHC, g/L	263	310–355	D-Dimer, mg/L	5.03	0-0.5
Platelet, $\times10^9$	178	150–407	Myoglobin, ng/mL	16.8	0-140.1
ALT, U/L	23	8–46	CK-MB, ng/mL	0.8	0-6.6
AST, U/L	31	12–37	hsTnI, ng/mL	0.0386	0-0.028
Albumin, g/L	30	42–56	BNP, pg/mL	2849.3	0-100
TBil, μmol/L	17.9	3.4–17.1	hsCRP, mg/L	28.08	0–10
DBil, μmol/L	10.4	0-3.4	PCT, ng/mL	0.748	0-0.05

MCV mean corpuscular volume, *MCH* mean corpuscular hemoglobin, *MCHC* mean corpusular hemoglobin concerntration, *ALT* alanine aminotransferase, *AST* Aspartate aminotransferase, *TBil* total bilirubin, *DBil* direct bilirubin, *SCr* serum creatinine, *UA* uremic acid, *PT* prothrombin time, *PT-INR* prothrombin time-international normalized ratio, *APTT* activated partial thromboplastin time, *CK* creatine kinase, *hsTnI* high-sensitivity troponin I, *hsCRP* hypersensitive C-reactive protein, *PCT* procalcitonin

Table 2 Serum immunological indicators on admission

Variables	Values	Normal Reference	Variables	Values	Normal Reference
ESR, mm/h	42	0–15	Anti-SSB antibody	(-)	(-)
P-ANCA	(-)	(-)	Anti-centromerin B antibody	(-)	(-)
C-ANCA	(-)	(-)	Anti-histone antibody	(-)	(-)
ANA (IFA)	(+, 1:320)	(-, 1:80)	Anti-mitochondrion-M2 antibody	(-)	(-)
Anti-dsDNA IgG antibody (CLFT)	(+, 1:80)	(-, 1:10)	Anti-cardiolipin IgG antibody (ELISA), GPL	≤ 9.4	< 15
Anti-RNP antibody	(-)	(-)	Anti-cardiolipin IgM antibody (ELISA), MPL	43.5	< 12.5
Anti-Sm antibody	(-)	(-)	Anti-cyclic citrullinated peptide IgG antibody (CLIA), CU	< 4.6	< 20
Anti-SSA antibody	(-)	(-)	Erythrocyte G6PD activity, U/gHb*min	4.80	2.8–7.3
Anti-Ro-52 antibody	(-)	(-)	Coombs test	(++)	(-)
Anti-SSB antibody	(-)	(-)	Coombs-IgG	(++)	(-)
Anti-SCL-70 antibody	(-)	(-)	Coombs-IgC3d	(++)	(-)
Anti-PM-Scl antibody	(-)	(-)	Isopropanol test	(-)	(-)
Anti-Jo-1 antibody	(-)	(-)	Hams test	(-)	(-)

ESR erythrocyte sedimentation rate, *ANCA* anti-neutrophil cytoplasmic antibodies, *ANA* antinuclear antibodies, *RNP* ribonucleoprotein

to 28% of such cases [1]. *B. quintana* and *B. henselae* are the most commonly identified species, within the *Bartonella* genus, responsible for approximately 3% of all infective endocarditis cases [7]. Traditional diagnosis of *Bartonella* endocarditis has largely relied on serological testing and specific serological criteria are included in the recently revised Duke criteria [8]. In the appropriate clinical setting, an anti-*Bartonella* sp. IgG titer ≥ 1:800 has a 95% positive predictive value for infective endocarditis. In our patient, mNGS provided definitive confirmation of *B. quintana* infection. Compared to conventional methods, mNGS offers high efficiency and accuracy, presenting a distinct advantage for diagnosing culture-negative endocarditis [9]. However, the clinical utility of untargeted mNGS can be limited by its susceptibility to technical contamination and detection of irrelevant commensals. Key challenges include false-negative results, potentially from misclassification of microbial sequences as host-derived, and false positives from erroneous inclusion of host sequences into microbial genomes. Thus, while mNGS has a high positive predictive value, its limited analytical sensitivity means that a negative result does not rule out endocarditis [6].

B. quintana can cause prolonged intraerythrocytic bacteremia in humans. Clinical manifestations vary from asymptomatic infection to life-threatening disease,

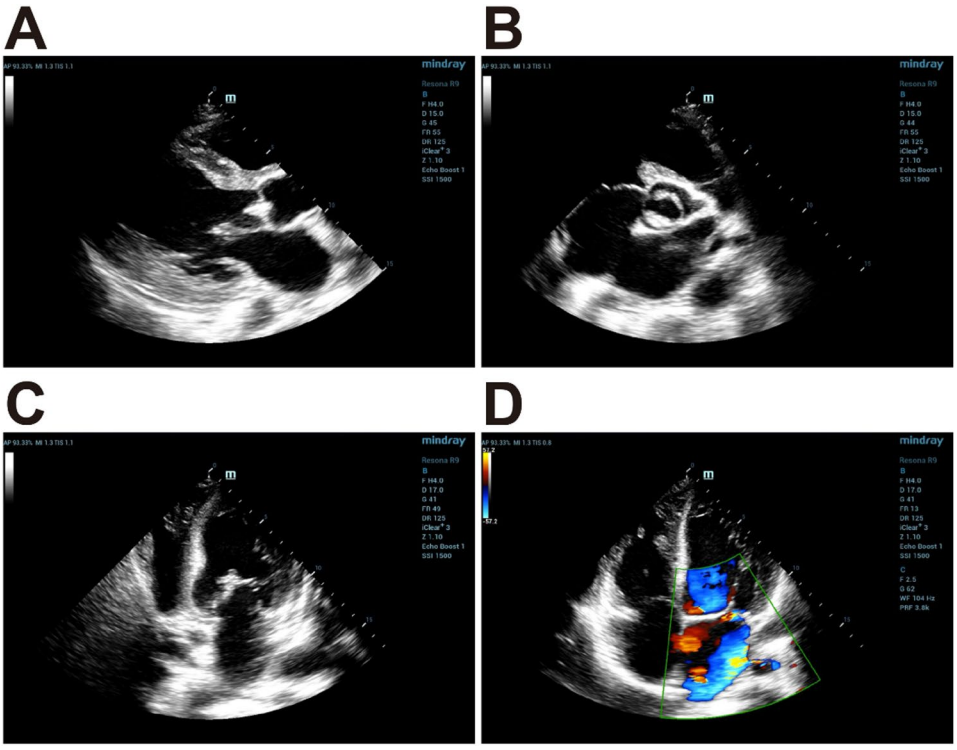

Fig. 1 The results of transthoracic echocardiography at admission. **A** Aortic vegetation. **B** Bicuspid aortic valve malformation. **C** Mitral valve vegetation with prolapsed anterior mitral valve. **D** Severe mitral regurgitation

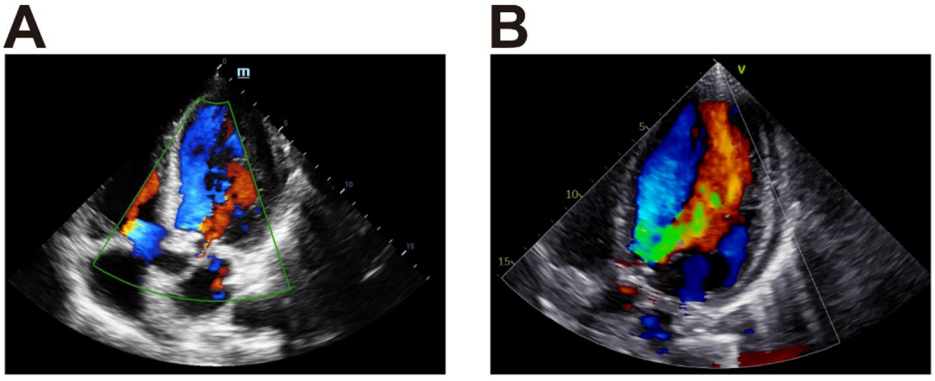

Fig. 2 Progression of aortic valve regurgitation. **A** Mild aortic regurgitation at admission. **B** Severe aortic regurgitation with multiple reflux beams 3 days later

Table 3 Characteristics of echocardiography on admission

Variables	Values	Variables	Values
EF, %	47	Aortic Root Diameter, mm	23
FS, %	24	PA Diameter, mm	20
LVEDD, mm	60	RVEDD, mm	35
LA Dimension, mm	44	RA Dimension, mm	37
LVPWd Thickness, mm	13	RVPW, mm	4
IVSd Thickness, mm	13		

EF ejection fraction, *FS* fractional shortening, *LVEDD* left ventricular end-diastolic diameter, *LA* left atrium, *LVPWd* left ventricular posterior wall diastole, *IVSd* interventricular septum diastole, *PA* pulmonary artery, *RVEDD* right ventricular end-diastolic diameter, *RA* right atrium, *RVPW* right ventricular posterior wall

Table 4 Laboratory indicators three months after valve replacement

Variables	Values	Normal Reference	Variables	Values	Normal Reference
Leucocyte, $\times 10^9$/L	8.88	4.1–11.0	ANA (IFA)	(+, 1:320)	(-, 1:80)
Erythrocyte, $\times 10^{12}$/L	5.01	4.5–5.9	Anti-dsDNA	(-)	(-)
Hemoglobin, g/L	157	129–172	Anti-RNP antibody	(-)	(-)
Platelet, $\times 10^9$/L	190	150–407	Anti-Sm antibody	(-)	(-)

ANA antinuclear antibodies, *RNP* ribonucleoprotein

depending on the host's immune status and the type of infection [10]. Endocarditis typically occurs in individuals with pre-existing valvular abnormalities, however, *B. quintana* endocarditis has also been reported in patients without underlying valvulopathy. Echocardiography plays a crucial role in differentiating infectious endocarditis from non-infectious causes, such as Libman-Sacks endocarditis (nonbacterial thrombotic endocarditis). Unlike the large, mobile, shaggy, and destructive vegetations seen in infective endocarditis, Libman-Sacks vegetations are typically small, sessile, wart-like, and less destructive [11]. In our patient, transthoracic echocardiography revealed a prominent, oscillating, pedunculated vegetation on the bicuspid aortic valve. The rapid progression from mild to severe aortic insufficiency, with multiple reflux jets suggesting valvular perforation, underscored the destructive nature and severity of the infection [12]. These features are characteristic of infective endocarditis and less consistent with Libman-Sacks endocarditis. While a pre-existing congenital mitral valve prolapse could not be ruled out due to lack of prior echocardiographic studies, *Bartonella* infection itself is known to cause mitral valve vegetation and insufficiency. Surgical indications were unequivocal in this case, consistent with reports that over 90% of such patients ultimately require valve replacement [13].

Although most antibiotics, including β-lactams, aminoglycosides, macrolides, tetracyclines, and rifampin, demonstrate in vitro efficacy against *Bartonella*, the intracellular location of the bacterium must be considered [14]. There is no standardized antibiotic regimen for *B. quintana* endocarditis [15]. The combination of gentamicin reported to be bactericidal against *Bartonella* spp. and doxycycline (which penetrates erythrocytes) is supported by retrospective data [13, 16]. We employed this regimen. Given the concurrent glucocorticoid therapy, the antibiotic course was extended (gentamicin for 3 weeks and doxycycline for 9 weeks), resulting in a favorable outcome.

The laboratory findings of Coombs-positive hemolytic anemia, along with positive ANA, anti-dsDNA, and anti-cardiolipin IgM antibodies, suggested underlying SLE. In the absence of definitive mNGS results, a diagnosis of Libman-Sacks endocarditis—strongly associated with SLE or antiphospholipid syndrome (APS)—would have been a plausible and reasonable conclusion. The pathogenesis of Libman-Sacks endocarditis, believed to involve immune complex deposition and valvular endothelial inflammation leading to sterile platelet-fibrin vegetations, differs from the infectious process of *Bartonella* endocarditis, which is reflected in their distinct echocardiographic appearances.

A clinical dilemma arose regarding the management of a patient with suspected autoimmune disease, where immunosuppressive therapy could potentially exacerbate an occult infection [17]. While surgery was the definitive and urgent treatment, the increased erythrocyte fragility posed a risk for severe hemolysis and acute renal failure during extracorporeal circulation [18]. Therefore, the perioperative management strategy combined targeted antibiotic therapy with immunomodulation to concurrently address the infection and the immune-mediated hemolytic anemia. However, this approach remains controversial, as several reports have demonstrated recovery of *Bartonella* endocarditis-associated immune-mediated manifestations, including Coombs-positive hemolytic anemia, with antibiotics therapy alone, without the need for immunosuppressive therapy [19–21]. Immunosuppressive therapy (e.g., corticosteroids) for hemolytic anemia should generally be avoided unless hemolysis is severe, as illustrated in our patient.

In conclusion, the diagnosis and management of *Bartonella* infective endocarditis remain significant clinical challenges. mNGS represents a valuable diagnostic tool for culture-negative endocarditis. Coombs-positive hemolytic anemia is a serious complication that warrants close clinical attention, and a combined therapeutic approach addressing both infection and immune dysregulation should be considered.

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Authors' contributions
Yanjun Zhang and Pingcuo Wangjia participated in data collection, writing, and revision of the manuscript. Suo Yang, Panjing Liu and Xinliang Xu participated in treatment of the patient and data collection. Hui Han participated in writing and revision of the manuscript. All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The study followed the principles of the Declaration of Helsinki as revised in 2013. The publication of the individual case report was exempt from ethical approval according to the guidelines of the People's Hospital of Shigatse City and Ruijin Hospital.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Competing interests
The authors declare no competing interests.

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