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Brucellosis may present initially as infective endocarditis complicated with splenic and renal infarction：A Case Report

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Case Report

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Abstract

Background

Brucellosis is a zoonotic infectious disease caused by *Brucella* species, typically presenting with undulant fever, hepatosplenomegaly and arthralgia. Infective endocarditis is a rare complication of brucellosis, and concurrent splenic and renal infarction is even rarer.

Case presentation:

We report a 55-year-old man admitted with fatigue and abdominal pain, who was definitively diagnosed with brucellosis complicated by infective endocarditis, splenic and renal infarction. Clinicians should remain highly vigilant about these rare severe complications. For patients with unexplained fever accompanied by abdominal pain and embolic manifestations, timely etiological and imaging evaluations are essential for early diagnosis and individualized medication. The patient's condition improved significantly after standardized treatment.

Conclusions

Early diagnosis of brucellosis complicated by infective endocarditis and tissue infarction, timely diagnosis and standardized treatment in endemic areas are crucial to reduce embolism risk and improve prognosis.

Background

Brucellosis is a zoonotic infectious disease caused by *Brucella* species, which is predominantly prevalent in regions with developed animal husbandry and particularly common in developing countries [1]. In human infections, the primary manifestation is an acute febrile illness, accompanied by non-specific symptoms such as headache, diaphoresis, and fatigue. Additionally, 10%–20% of patients present with mild lymphadenopathy, and 20%–30% have splenomegaly or hepatomegaly. Isolated pericarditis, myocarditis, aortitis, arteriovenous thrombosis, as well as sternal and joint infections, have been reported in clinical practice [2].*Brucellar* species in fection can involve multiple systems throughout the body and induce various severe complications. Beyond the aforementioned complications, it can also trigger tissue infarction in different organs, specifically presenting as stroke, infected aneurysm, myocardial infarction, mesenteric ischemia, splenic infarction, and renal infarction [3–5]. Owing to the extremely low clinical incidence of such infarctive complications, they are liable to misdiagnosis or missed diagnosis by clinicians. Among these complications, infective endocarditis caused by *Brucella* species infection, despite its low incidence, is associated with high mortality and extremely poor prognosis, making it a severe complication that demands close clinical vigilance.As rare complications of brucellosis, splenic and renal infarction have only been documented as isolated splenic rupture cases,

and no case of concurrent splenic and renal infarction has been reported to date. Recently, our hospital admitted a patient who was diagnosed with *Brucella* infective endocarditis complicated with multiple infarctions (splenic and renal) through blood culture, agglutination test, abdominal enhanced computed tomography (CT), and cardiac color Doppler ultrasound. This case is relatively rare in clinical practice and possesses significant clinical research value. Clinicians often encounter multiple challenges in diagnosing and treating such rare complications of brucellosis, including diagnostic difficulties and complex differential diagnosis. This case is reported in detail in conjunction with literature analysis, aiming to expand our current knowledge in the field of rare complications of brucellosis and provide a reference for clinicians and researchers in the diagnosis and treatment of similar cases thereafter.

Case presentation

A 55-year-old man of Han Chinese ethnicity, a sheep herder, sought medical attention due to persistent fatigue and abdominal pain lasting two months as the initial symptoms. The specific manifestations included continuous dull pain in the upper abdomen, radiating to the lumbar region, generalized abdominal distension, chest pain and dyspnea after physical activity, followed by a week-long intermittent fever. Symptoms could be alleviated with antipyretic analgesics. Past history and genetic history were unremarkable, physical examination revealed a 4/6 diastolic murmur at the aortic valve auscultation area, abdominal muscle rigidity, and marked tenderness in the upper abdomen. The results of the laboratory examinations are summarized in Table 1.

Table 1
Laboratory examinations

Test Item	Result	Reference Range
Red Blood Cell (RBC)	3.45×10^12/L	4.4 0–6.60
White Blood Cell (WBC)	5.46×10^9/ L	3.50–9.50
Lymphocyte	1.37×10^9/L	1.1–3.2
polymorphonuclear	1.84×10^9/L	1.8–6.3
Platelet count(PLT)	127×10^9/L	70–300
Erythrocyte Sedimentation Rate (ESR)	15mm/h	0–20
Hemoglobin (HGB)	115g/L	138–183
Interleukin-6 (IL-6)	48. 1pg/ml	0–7
C-Reactive Protein (CRP)	8.399mg/L	0–5
Procalcitonin (PCT)	1.88ng/ml	0.0–0.046
Lactate Dehydrogenase (LDH)	603U/L	135–225
Gamma-Glutamyl Transferase (γ-GT)	518.6U/L	10–47
Aspartate Aminotransferase (AST)	57 U/ L	15–45
Prothrombin Time(PT)	13.7s	10–14
International Normalized Ratio(INR)	1.19	0.84–1.40
Activated Partial Thromboplastin Time(APTT)	28.9s	23.3–32.5
Urea	5.84mmol/L	2.8–7.6
Creatinine(Cr)	97umol/l	72–127
alanine aminotransferase(ALT)	40U/L	9–60

Enhanced abdominal CT (Fig. 1) revealed hepatosplenomegaly, portal hypertension, and low-density lesions in the spleen and right kidney, suggesting infarctions. Echocardiography (Fig. 2) revealed aortic valve thickening with enhanced echogenicity and adhesion,

presenting as a mass-like hyperechoic mass with cotton-like echoes above. The valve appeared bilobed with a restricted opening and eccentric regurgitation bundle, indicating valvular heart disease with aortic valve bicuspid malformation and valvular vegetation. Upon admission, empirical treatment with cefoperazone sodium/sulbactam sodium (1.5 g every 12 hours) was initiated. Despite persistent recurrent high fever, blood cultures from both aerobic and anaerobic bottles after three days revealed

Brucella melitensis, with no other abnormalities. Concurrent RBT test result is positive, and the titer of serum agglutination test (SAT) is 1:400, indicating active brucellosis. Imaging findings confirmed or indicated involvement of multiple organs. Therefore, the patient was diagnosed with brucellosis, infective endocarditis, cardiac insufficiency, valvular heart disease, aortic insufficiency,

bicuspid aortic valve, splenic infarction, and right renal infarction. The treatment regimen was adjusted to doxycycline (100 mg every 12 hours, po), rifampicin (600 mg once daily, po), and levofloxacin (0.5 g once daily, ivgtt). After the patient's body temperature gradually returned to normal, the patient was transferred to the Department of Cardiac Surgery for aortic valve replacement. Postoperatively, the same antimicrobial regimen was continued for 1 month. During follow-up, the patient had no recurrent fever, and the function of the prosthetic valve was normal.

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(Fig. 1. Infarction of the spleen and kidney)

(Fig. 2: Thickened aortic valve with clustered strong echoes, showing flocculent echo shadows.)

Discussion and Conclusions

Brucellosis is relatively common in countries and regions with livestock farming as the main industry; it is prevalent mainly in the Middle East, Mediterranean, Central America, and South America and has a global distribution [6]. The latest studies indicate that there are 16,000 to 2.1 million new infection cases annually [7,8], causing significant impacts and losses in terms of public health and livestock development. Since 2000, annual reports on human brucellosis in China have shown a rapid increase in cases, primarily in northern pastoral areas such as Inner Mongolia, Gansu, and Xinjiang, whereas the incidence in nonpastoral areas such as southern China has also been increasing [9]. *Brucella* species include six types: *B. melitensis*, *B. abortus*, *B. suis*, *B. canis*, *B. neotomae*, and *B. ovis*. In China, *B. melitensis* is the predominant causative species, followed by *B. abortus, B. suis* is only found in a few regions. There are three transmission routes from livestock to humans: via the digestive tract, via direct contact with the skin, and via aerosols through the respiratory tract [10].Consumption of unpasteurized milk and dairy products is a major transmission route of brucellosis in the general population. In China, direct contact with sheep, goats and cattle may be a more important mode of infection. According to World Health Organization (WHO) reports, there are 500,000 new brucellosis infections globally each year [11], Human brucellosis is a systemic infectious disease caused primarily by bacteria, with *B. melitensis* being the most virulent and invasive. Widespread human infection with *B. melitensis* typically results from consumption of contaminated dairy products. The symptoms of human brucellosis include fever, night sweats, fatigue, and lymphadenopathy, with typical manifestations of fluctuating fever. It can also involve multiple body organs, such as musculoskeletal, genitourinary, digestive, respiratory, and central nervous.

Damage to the circulatory system is less common, but once involved, has a high mortality rate. *Brucella*-related infectious endocarditis is the most common cause of death in adult patients with brucellosis, whereas it is a rare complication in children. Neurobrucellosis should also be mentioned as a significant cause of mortality. This article reports a middle-aged male patient with no underlying disease who was a sheep keeper. He developed fatigue and abdominal pain, followed by fever, which was consistent with the general manifestations of the disease reported in the literature. Brucellosis carries a certain risk of recurrence, which may be attributed to the ability of *Brucella* to survive in host macrophages and persist long-term in the acidic intracellular environment by inhibiting phagolysosome fusion[12]. Additionally, in patients with chronic brucellosis, the level of interferon-γ(IFN-γ) is significantly higher during the recurrence phase than during the remission phase, suggesting that the immune response status is closely associated with disease activity[13].

Infectious endocarditis is the most common cause of death in patients with brucellosis [14], with pathological changes primarily characterized by fibrosis, calcification, and hyaline degeneration. Various valve types may be affected, predominantly involving the aortic valve, whereas the involvement of right heart system valves is rare [15]. Echocardiography serves as a crucial diagnostic tool for infectious endocarditis. *Brucella* can also cause infected aneurysms or ulcerative lesions in the aorta and its branches (such as the iliac arteries). Although these lesions are rare, they carry a fatal risk [16]. Blood culture remains the gold standard for brucellosis diagnosis, but the tiger red agar agglutination test (TRAT) has higher positivity rates than blood culture. In this case report, both the blood culture and TRAT results were positive. Physical examination findings, including cardiac murmurs and echocardiographic evidence of valvular damage, collectively support the diagnosis of infectious endocarditis.

Splenic infarction caused by brucellosis is uncommon and usually occurs in the following situations: thromboembolism, cardiovascular etiologies or hypercoagulable states, acute infections leading to rapid splenomegaly, hematological diseases, triggers of pulmonary embolism, and vasculitis[17]. Sevgi Ozan Kose et al. reported a case of brucellosis with splenic infarction presenting only with local abdominal pain without fever. Geetanjali Puvvada et al. reported a middle-aged woman with long-term fever and left-side abdominal pain.There were also some cases with fever,large liver, spleen, and lymph nodes,muscle and joint pain[18,19]. The patient reported persistent upper abdominal pain during the disease course, which, combined with imaging findings, was considered to be related to splenic infarction. Splenic infarction is an extremely rare complication of brucellosis, primarily attributed to the following factors[20]:

Concurrent infective endocarditis may cause valve vegetation to dislodge and travel disseminate the splenic vessels, leading to splenic embolism,severe aortic regurgitation detected by echocardiography which may predispose patients to thrombus formation due to significant hemodynamic changes,severe brucellosis-induced sepsis can result in bacterial emboli forming in the splenic vessels. Treatment for splenic infarction focuses on addressing the underlying cause. Some cases may resolve spontaneously after eliminating the causative agent, so surgical intervention with splenectomy is only considered when severe complications such as splenic rupture or abscess occur [18,21]. Although the patient experienced

abdominal pain, the infarcted area was small. Therefore, standardized anti-infective therapy targeting the cause was administered without surgical or anticoagulant treatment, and no further deterioration of the splenic infarction was observed [22,23]. Although no reported cases of brucellosis-associated renal infarction have been documented, studies have indicated that infective endocarditis may induce renal pathological changes and subsequent infarction, which is consistent with findings reported by Zakaria et al. [24].

Brucellosis rarely presents with renal involvement. Reported renal manifestations mainly include edema, proteinuria, and hematuria, and even glomerulonephritis progressing to end-stage renal disease[25]. Brucellosis may be one of the etiologies of glomerulonephritis in endemic areas, and serological testing is helpful for early diagnosis[26]. Renal abscess (brucelloma) is extremely rare, with only a few cases reported in the literature. Patients usually present with fever and low back pain. Imaging studies (such as CT) show thick-walled abscesses or low-density lesions[27]. There are also reports that *Brucella* can cause acute and chronic interstitial nephritis, and some patients develop acute kidney injury due to acute tubular necrosis, manifested by elevated urea and creatinine[28]. The patient we reported presented with renal infarction without manifestations such as renal function impairment.

Although case reports of brucellosis complicated with splenic infarction and renal infarction are rare, Brucella, as an intracellular parasitic bacterium, can disseminate widely to multiple organs such as the liver, spleen, kidneys, and bone marrow, and survive and replicate in immune cells including macrophages 29–31. Brucellar infection can induce a strong inflammatory response and immune regulation imbalance, meanwhile, it may promote chronic infection and tissue damage by affecting host cell functions (such as regulating S100A4 expression) to influence macrophage proliferation and bacterial survival,or interfering with host glycosylation pathways (such as effector protein Rhg1 reprogramming the host N-glycome). This extensive systemic inflammation,vascular endothelial dysfunction,and potential microthrombosis mechanism provide a pathophysiological basis for multiple organ infarctions32-34 (including mesentery,spleen,kedney,etc).

The standard first-line treatment regimens recommended by the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) include a six-week course of doxycycline (100 mg daily, administered in two divided doses) combined with rifampicin (600–900 mg daily, administered as a single dose) for 6 weeks[35].According to the Brucellosis Diagnosis and Treatment Protocol (2023 Edition) formulated by the National Health Commission of China, the recommended antibiotic regimen for *Brucella* endocarditis is doxycycline+ rifampicin + levofloxacin or thecompound sulfamethoxazole[1]. In this case, the patient was treated with doxycycline (100 mg, q12h,ivgtt) + rifampicin (600 mg, qd,po) + levofloxacin (0.5 g, qd,ivgtt) for three days. The patient's temperature gradually decreased, and no fever was observed after one week. Three months later, the outpatient follow-up described complete remission of fever and abdominal pain, and the disappearance of cardiac valve vegetations.

In summary, during the medical history collection, history taking clinicians should detailedly inquire about occupational exposure to avoid missed diagnosis. the clinical manifestations of brucellosis are

typically nonspecific, and blood cultures along with agglutination tests are crucial for diagnosis. Among its complications, infectious endocarditis and splenorenal infarction are relatively rare.

Abbreviations

CT
computed tomography
WHO
World Health Organization
IFN
γ-interferon-γ
TRAT
tiger red agar agglutination test
CDC
Centers for Disease Control and Prevention

Declarations

Ethics approval and consent to participate

According to national regulations and institutional policies, formal ethics committee approval was not required for this case report, as it describes a single patient without experimental intervention. Consent to publish.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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Author Contribution

Ling Yuan,Conceptualization,Writing-original draft,Data curationXueqing Zhang,Formal analysis,Writing-review&editingHui Zhang,Investigation,ResourcesLingling Qiao,Supervison,ValidationZhilan Liu,Visualization,Writing-review&editing

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Availability of data and materials

The datasets supporting the conclusions of this article are available from the author upon reasonable request.

Competing interests

The author declares no financial or institutional conflict of interest.

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Figures

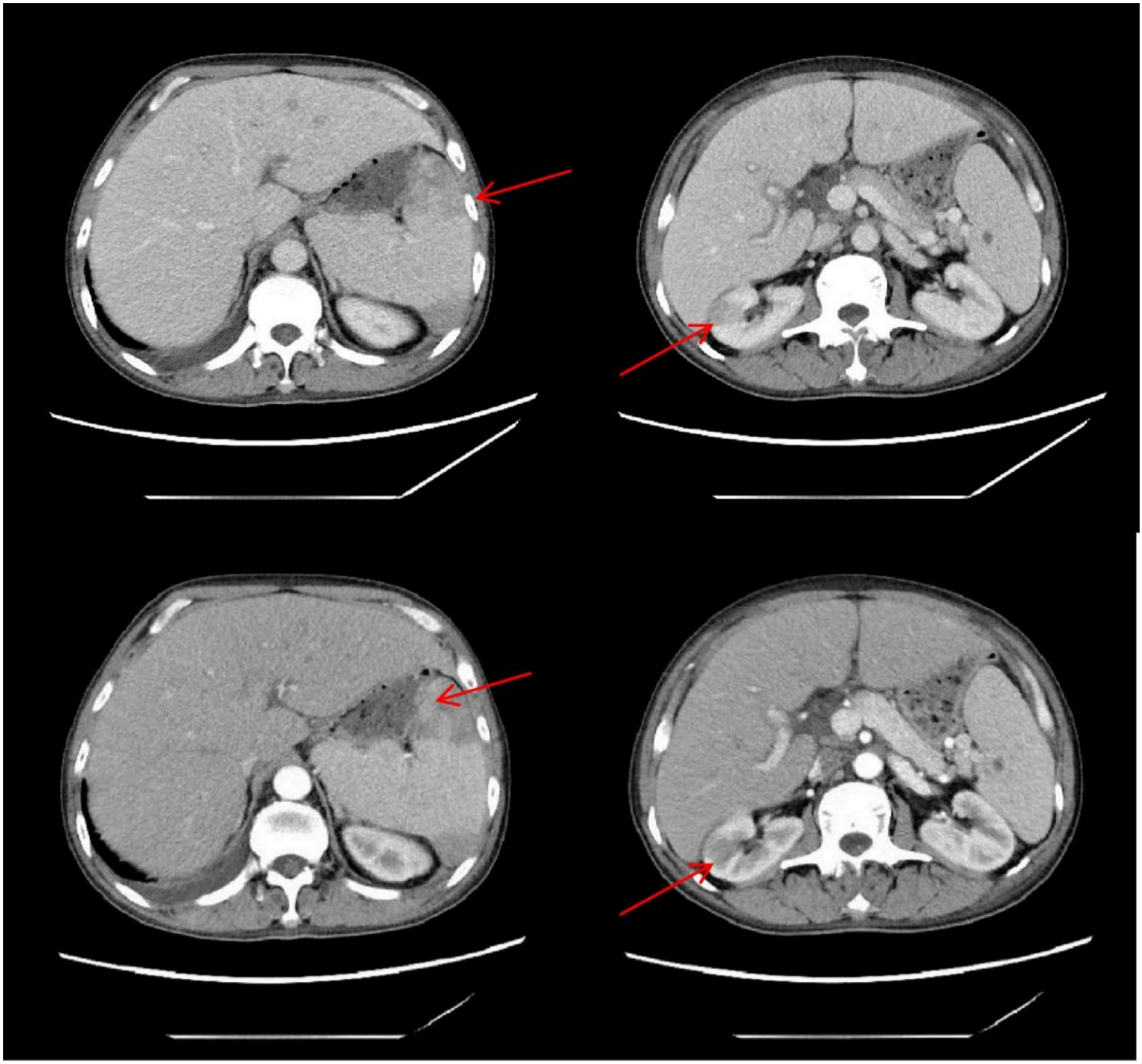


Figure 1

Infarction of the spleen and kidney

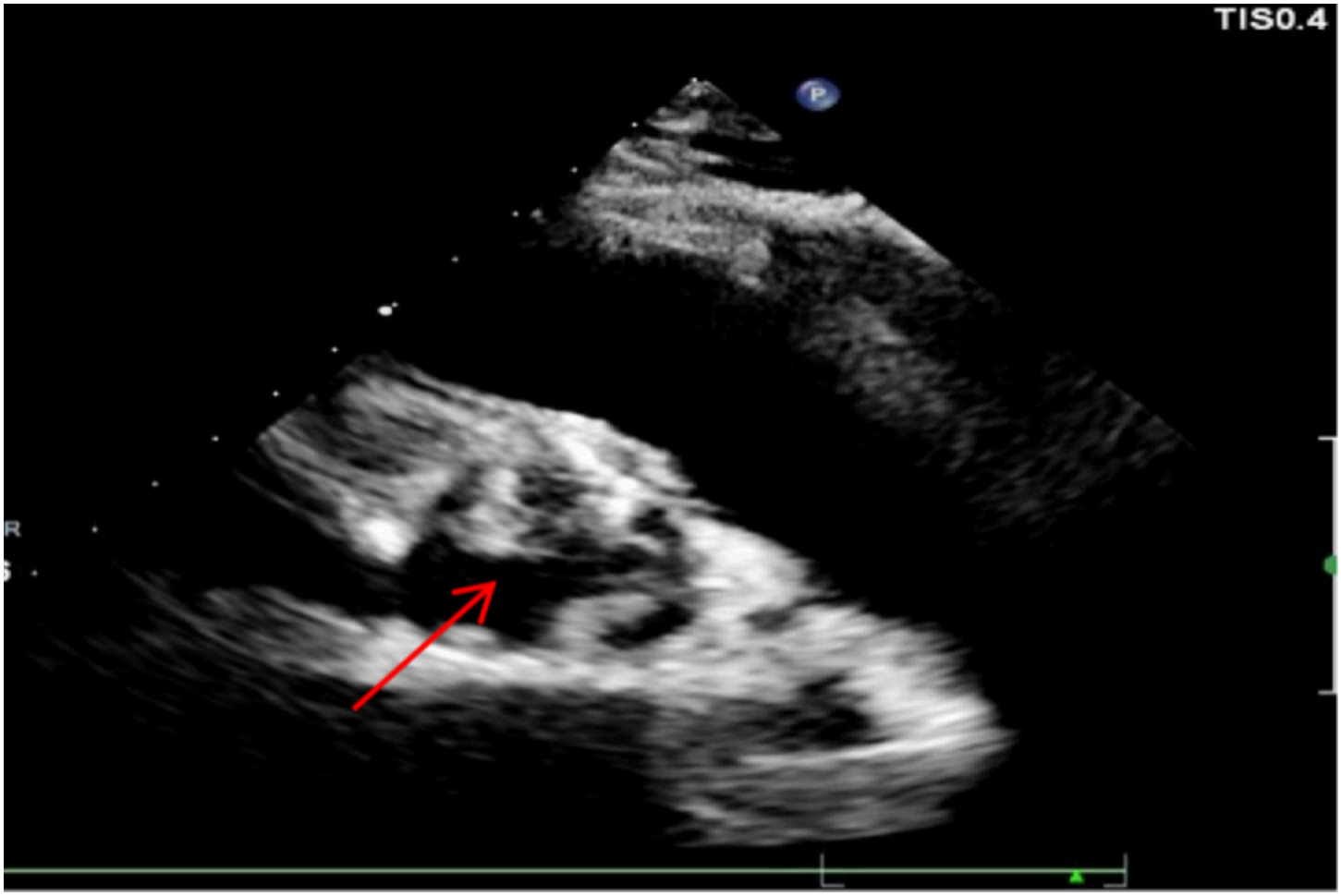


Figure 2

Thickened aortic valve with clustered strong echoes, showing flocculent echo shadows.

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