Case report on right ventricular mural endocarditis, not diagnosed clinically, but histopathologically after cardiac surgery

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Background
Right ventricular mural endocarditis (RVME) is an extremely rare type of infective endocarditis that can occur even in the absence of predisposing factors. The diagnosis is a challenge when no causative pathogen can be detected.

Case summary
A previously healthy young man was admitted to a local hospital with a diagnosis of prolonged febrile syndrome and treated for acute sinusitis. As complaints returned, he was hospitalized 3 weeks later, where an echocardiogram demonstrated multiple mobile masses in the right ventricle, and a computed tomography scan revealed extensive pulmonary thromboembolism. During surgery, the endocardial masses were excised, and the pathologist considered an inflammatory myofibroblastic tumour. Despite appropriate medication and initial improvements, the complaints persisted, and 2 weeks after the surgery, the patient returned to the hospital. Imaging studies documented reappearance to the previous findings, whereas blood cultures remained negative. During the second surgery, the new masses resembling vegetations were excised, and histologic analysis indicated infective endocarditis. Adjusted medication was given for 30 days. Just before discharge, no vegetations were seen. At follow-up, 5 years later, he was in a healthy condition.

Discussion
Despite careful examinations, initial treatments according to standard protocols were unsuccessful. At final discharge, the patient reported that a tattoo complication prior to the first hospitalization was treated by antibiotics but that he did not complete the course. This omission in the communication further complicated the diagnostic and management processes, leading to surgical interventions that could have been prevented if the neglected antibiotic course was properly disclosed.

Keywords
Infective endocarditis • Tattooing • Case report • Right ventricle

ESC Curriculum
2.1 Imaging modalities • 2.2 Echocardiography • 4.11 Endocarditis • 6.8 Cardiac tumours • 9.5 Pulmonary thromboembolism

Learning points
- Right ventricular (RV) mural endocarditis is an extremely rare type of infective endocarditis and forms a diagnostic challenge which often depends on predisposing factors. The diagnosis of RV mural endocarditis requires a high degree of clinical suspicion in patients with prolonged fever and RV endocardial masses, even when blood cultures are persistently negative and established risk factors are absent or not communicated by the patient.
- Without a detailed and complete medical history and physical examination in patients with prolonged febrile syndrome, the diagnosis of infective endocarditis can be delayed and may be associated with a poor prognosis.
Introduction
Infective endocarditis (IE) has an annual incidence of 3–10/100 000 in the global population with a mortality of up to 30% at 30 days. IE traditionally involves the heart valves, both native and prosthetic.

Timeline

Survey of major events, diagnoses, and medication. Each of the red bars indicates cardiac surgery. IE = infective endocarditis; FU = follow-up; IMT = inflammatory myofibroblastic tumour; PA = patho-anatomical diagnosis; PTE = pulmonary thromboembolism; RV = right ventricle; RVME = right ventricular mural endocarditis

Hospital admission 1: C-reactive protein 25 mg/L [upper normal limit (UNL) 5 mg/L]; total white blood cell (WBC) count 13 000/mm³ (neutrophils 84.7%); haematocrit (Hct) 38.9%; haemoglobin (HGB): 13.7 g/dL; erythrocyte sedimentation rate: 86 mm/h (UNL 20 mm/h). Urinary and two sets of blood cultures were negative. Cerebrospinal fluid was normal. Anti-nuclear antibodies, hepatitis B virus surface antigen, hepatitis C antibodies, and HIV were negative. Electrocardiograms and chest X-rays were normal.

Hospital admission 2: showed a WBC of 14 300/mm³ (neutrophils 85.5%); Hct 31%; HGB 11.1 g/dL; procalcitonin 4.6 ng/mL (UNL 0.15 ng/mL), D-dimer 3958 ng/mL (UNL 500 ng/mL). Polymerase chain reaction (PCR) amplification for Bartonella henselae and Coxiella, blood cultures, and testing for galactomannans, as well as universal PCR were negative.

Medication doses and route of administration are as follows:
- amoxicillin 1500 mg/day orally
- paracetamol 500 mg orally every 6 h

low-molecular-weight heparin enoxaparin 30 mg subcutaneously twice daily
- warfarin orally to keep INR at 2–3
- vancomycin 30 mg/kg intravenously daily
- moxifloxacin 400 mg intravenously daily
- amoxicillin/sulbactam 3 g intravenously every 6 h
- ceftriaxone 2 g intravenously daily
- ciprofloxacin 400 mg intravenously every 8 h
- amphotericin B 1 mg/kg/day intravenously
- caspofungin 50 mg intravenously daily
- fluconazole 400 mg orally

Primary non-valvular mural endocarditis is uncommon, particularly in the absence of predisposing factors such as valvular vegetations, myocardial abscesses, cardiac structural abnormalities, or prosthetic materials. Right ventricular mural endocarditis (RVME) is extremely rare, its
origin mainly fungal, and the diagnosis usually documented by biopsy or autopsy. The first case as diagnosed by echocardiography was reported in 1986.

Cardiac thrombi and tumours must be considered in the differential diagnosis. In this scenario, the precise diagnosis of RVME remains clinically challenging. Especially when blood cultures are persistently negative and cardiac examination is normal, a clinical diagnosis is nearly impossible.

We describe an unusual case of isolated RVME in a patient without reported risk factors whose diagnosis was determined after two heart surgeries following clinical misdiagnosis.

Case presentation

A 20-year-old man without any medical history of alcohol or drug abuse was hospitalized at a local hospital with a 3-week history of fever, chills, weakness, night sweats, and vomiting. He denied respiratory and urinary symptoms. On physical examination, his temperature was 38.4°C, pulse rate 101 bpm, respiratory rate 21 breaths/min, and blood pressure 105/60 mmHg. Cardiac and pulmonary examinations were unrewarding. No skin or oral cavity lesions were observed, nor inflamed cervical or inguinal lymph nodes.

Laboratory investigations are summarized in the legend of the Timeline. Brain computed tomography (CT) showed signs of acute sinusitis, treated with amoxicillin 1500 mg/day orally and paracetamol 500 mg every 6 h. He was discharged after 1 week and advised to maintain prescribed treatment for another week.

Three weeks later, he was readmitted at this institution with fever, chills, fatigue, headache, and significant weight loss (11 kg). Laboratory tests are summarized in the Timeline. A chest CT scan revealed extensive PTE with signs of RV overload. During cardiac surgery, the tricuspid and pulmonary valves appeared normal, whereas RV masses resembling vegetations were removed. Despite the macroscopic appearance of the excised tissue suggesting vegetations, the pathologist considered that it could correspond to an inflammatory myofibroblastic tumour (Figure 3A). Based on a suspicious diagnosis of methicillin-resistant Staphylococcus aureus IE, empirical intravenous antibiotic (AB) therapy with vancomycin, amoxicillin/sublactam, and moxifloxacin was started. Soon the patient felt better, the fever disappeared and TTE showed only a small RV mass.

Two weeks after surgery, the patient’s fever, chills, and vomiting reappeared. A TTE showed new large RV vegetations and a chest CT scan revealed signs of recurrent septic pulmonary emboli. Bacterial and fungal blood cultures remained negative. The patient underwent a second cardiac surgery, due to uncontrolled infection with recurrence of PTE, new large mobile RV vegetations, and suspected fungal IE. The vegetations were removed, and the pathologist’s histology report was consistent with IE (Figure 3B). Treatment concerned a combination of ceftriaxone, ciprofloxacin, and amphotericin B because fungal endocarditis was considered likely in view of the negative blood cultures and poor response to previous AB therapy. After 1 week, amphotericin B was replaced by caspofungin as fever persisted. Subsequent recovery was satisfactory and treatment was maintained for 30 days. TTE before discharge showed a normal RV without vegetations. At this moment, the patient reported that 1 month before his first hospitalization he received a tattoo on his right arm (Figure 3C). Because of presumed infection, he was prescribed AB treatment but he did not complete the course. Bacteraemia related to this event was probably the reason for the initial development of non-valvular RVME. He was discharged as asymptomatic and prescribed oral fluconazole for 4 weeks. At a 5-year follow-up (FU), he was asymptomatic and living a completely normal life.
Figure 2 (A) Transthoracic echocardiogram. (Left) Right ventricular inflow tract view showing various mobile masses in the right ventricle (RV) (left arrow). The tricuspid valve appears morphologically normal (leaning arrow). (Right) Apical modified four-chamber view shows the RV masses arising from the moderator band indicated by the arrow. Cardiac magnetic resonance imaging. Full short axis stack of slices covering from the base of both ventricles to the cardiac apex. (B) cine perfusion images and (C) late gadolinium enhancement images. Side by side evaluation of the images revealed various highly mobile hypointense masses in the right ventricle in cuts 4 and 5 (B, circles), some of them having discrete heterogeneous enhancement (C, circles).
Discussion

Isolated RVME is an unusual type of IE, occurring in association with predisposing factors but also in previously healthy individuals as this patient. A hypothetical mechanism refers to the RV moderator band where trabeculations could act as a nidus for infection, similar as the location for vegetations in this case. Endocarditis was not considered in the absence of risk factors and unremarkable cardiac examination.

After a diagnosis of acute sinusitis in another hospital, he was readmitted with fever, chills and severe weight loss, signs of thromboembolism, pulmonary infarction, and RV masses, interpreted as thrombi. Anti-coagulation was started. Intermittent fever continued with blood cultures persistently negative for bacteria and fungi. He underwent cardiac surgery in view of the RV masses and extensive PTE, and specific AB therapy was started with suspected diagnosis of methicillin-resistant Staphylococcus aureus IE. Soon he felt better, without fever and only a small RV apical mass. However, fever and chills reappeared together with new RV vegetations and signs of recurrent PTE. During a second heart operation, vegetations were removed and confirmed histologically. Treatment included amphotericin B because fungal endocarditis was considered probable and organisms causing RVME are mainly fungi. With caspofungin, the evolution was satisfactory. He was discharged and prescribed fluconazole. We postulated that a favourable clinical response after vegetectomy and antifungal treatment somehow would confirm the fungal origin of endocarditis. At final discharge, the patient reported that a tattoo complication prior to the first hospitalization was treated by AB but that he did not complete the course. This omission in the communication further complicated the diagnostic and management processes as bacteraemia probably caused RVME, a key that could have led to an earlier diagnosis. A significant proportion of IE is blood culture negative. The most common cause concerns initiation of AB prior to culture (as in this patient), or presence of organisms such as Coxiella and Bartonella (with negative serological tests in this case), or fungi (fungal blood cultures remained negative in this case). Unfortunately, the surgically removed tissue in this patient did not undergo universal bacterial 16S ribosomal RNA-based PCR, which could have eventually confirmed the diagnosis. For IE, the most frequent portal of entry is cutaneous, also as complication after tattooing. Symptoms begin within 1–8 weeks, as in this patient. RVME as a definitive diagnosis was determined after two open-heart surgeries that confirmed anchored vegetations. At 5-year FU, he was asymptomatic and enjoyed a normal life.

Conclusion

RVME in the absence of predisposing factors and persistently negative blood cultures is a clinical challenge requiring a high degree of clinical suspicion. In this scenario, a complete and confirmed medical history with physical examination are crucial to avoid misdiagnosis that may worsen the prognosis.

Lead author biography

Rienzi Díaz-Navarro is a Full Professor of Cardiology at Universidad de Valparaíso, Chile. He graduated as Cardiologist at Catholic University in 1983. He then spent 3 years as a researcher at Hammersmith Hospital, RPMS, University of London. In 2014, he completed a Master’s Degree in Medical Sciences and was elected Director of the Department of Internal Medicine. He is one of the pioneers of the use of echocardiography in Chile, has published many full papers in peer review journals, book chapters, and two books on Echocardiography and Cardiac Doppler. He is a visiting professor at several universities around the world.
Supplementary material

Supplementary material is available at European Heart Journal – Case Reports.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

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