Rheumatoid arthritis mimicking infective endocarditis with severe aortic regurgitation and aortic root abscess: a case report

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Background
Rheumatoid arthritis (RA) may involve the cardiovascular system and can cause significant structural cardiac disease. RA mimicking infective endocarditis (IE) is rarely reported.

Case summary
A 46-year-old man with a medical history of seropositive RA attended a planned outpatient visit for infliximab treatment. The pre-infusion examination revealed a pulse of 41 b.p.m. and the following electrocardiogram showed 3rd degree atrioventricular block. A temporary pacemaker was inserted, and subsequent transthoracic and transoesophageal echocardiograms showed severe aortic valve regurgitation with thickened cusps and thus raised suspicion of infective aortic endocarditis with root abscess. The patient underwent surgery with valve and root replacement the next day. What was thought to be IE, proved to be suppurative and granulomatous inflammation with sporadic necrosis and hyaline fibrosis, compatible with a rheumatoid nodule linked to the patient’s RA diagnosis.

Discussion
IE is a disease with high mortality and morbidity. In some cases of IE perivalvular cavities develop, most commonly abscesses and/or pseudoaneurysms, which necessitates surgery. Several conditions may mimic IE: for example, malignant and benign tumours, rheumatic diseases, and common age-related valve calcification. In patients with valvular vegetations that are ‘culture-negative’, alternative pathologies should be considered.

Keywords
Rheumatoid arthritis • Endocarditis • Aortic root abscess • Rheumatoid nodulosis • Cardiac surgery • Atrioventricular block • Case report

Learning points
• Acute aortic regurgitation (AR) with involvement of the root, 3rd-degree aortic valve block and signs of infection are all findings indicative of infective endocarditis (IE), but other diagnoses should be considered when patients have no registered growth in the blood cultures.
• Rheumatoid arthritis may rarely resemble a case of IE with no growth registered in the blood cultures.
• Rheumatoid nodule may cause severe AR and annular pseudoaneurysm.
Introduction

Infective endocarditis (IE) is associated with high mortality and morbidity and diagnosis may be difficult. Several diseases may mimic IE, such as malignant and benign tumors, rheumatic diseases, and especially IE with no growth registered in the blood cultures, so-called ‘blood-culture-negative’ IE, which constitute 9.3–31% of cases.\(^1\)\(^-\)\(^3\) can be challenging to diagnose. Perivalvular extensions should be suspected in a case of a new atrioventricular block in suspected IE patients.\(^1\) Here, we present a case, where a patient was suspected of having IE and underwent surgery, but where rheumatoid arthritis (RA) turned out to be the underlying cause of the structural abnormalities.

Timeline

| Day  | Event Description |
|------|-------------------|
| 1    | Patient was admitted to the Department of Cardiology. |
| 2    | Temporary pacemaker (PM) was inserted into the right ventricle through the right internal jugular vein and fastened as a Temporary Externalized System. The lead was fixated in the right ventricle at the apex using an active fixation screw. Transthoracic echocardiogram (TTE) showed dilated left ventricle, normal left ventricular ejection fraction, and severe aortic regurgitation (AR). The patient had slightly elevated inflammatory markers. There was no growth registered in any blood cultures. |
| 3    | Transoesophageal echocardiogram (TOE) confirmed severe AR and there was a suspicion of infective endocarditis and aortic root abscess. |
| 4    | Aortic valve and root replacement surgery. The root abscess did not have characteristics of being related to an infectious endocarditis. The patient was extubated later the same day. |
| 13   | Histopathological examination showed that valve material was compatible with a rheumatoid nodule and there was no evidence of fungal, bacterial, or TB infection. |
| 16   | Computed tomography and TTE showed pericardial effusion. Pericardiocentesis drained 1 L of blood stained pericardial fluid. |
| 17   | Thoracocentesis on the right side drained 1 L of pleural fluid. |
| 18   | Thoracocentesis on the left side drained an unrecorded amount of pleural fluid. |
| 19   | The patient developed peripheral oedema and furosemide treatment was started. |
| 26   | The patient was discharged to have ambulatory care. The patient continued intravenous antibiotic treatment at the hospital once daily. |
| 38   | Because the patient had a 3rd degree atrioventricular block, a dual chamber PM was implanted as an outpatient elective procedure in which the temporary PM also was removed. |
| 48   | The intravenous antibiotic treatment and the ambulatory care was concluded 6 weeks post-surgery. TOE showed a left ventricular ejection fraction of 50%, a small central AR and no vegetation on any valve. No abnormal findings were found on the X-ray of the thorax except for a slightly enlarged heart. The patient has no peripheral oedema and is in good health. |
| Month 8 | At a follow-up, the patient is described as well, but with minor dyspnoea (New York Heart Association Class 1) and with joint pains in the hip and knees. He is working as a carpenter and biking a lot. |

Case presentation

The case concerned a 46-year-old man, with a medical history of seropositive RA with no previous extra-articular manifestations, but who was otherwise healthy. The patient was physically active, married and working as an architect. The patient had mainly been treated for moderate doses of prednisolone—10 mg/day for 2 years, 7.5 mg/day for 5 months, and 5 mg/day for 5 months but, 1 year prior to admittance, Infliximab treatment was commenced to achieve better disease control and in order to decrease the dose of prednisolone, which earlier had caused muscle spasms.

A regular bradycardia of 41 b.p.m. was detected at a planned visit due to infliximab infusion. A 12-lead electrocardiogram was recorded showing a 3rd degree atrioventricular block (see Figure 1).

The patient had no overt cardiovascular symptoms and only reported low-level joint pain. However, he did report a subtle decrease in physical ability over the course of the last 6 months, having mild dyspnoea when walking on stairs [New York Heart Association (NYHA) 2]. He had a blood pressure of 114/48 mmHg, a temperature of 36.3°C, and a body mass index of 26.7 kg/m². Lung auscultation was normal, but there was a diastolic murmur heard loudest over the second intercostal space on both sides of the sternum. There was no peripheral oedema. The patient was admitted to a cardiology ward the same day.

A temporary pacemaker (PM) was implanted in the right ventricle through the right internal jugular vein and fastened as a Temporary Externalized System. The lead was fixated in the right ventricle at the apex using an active fixation screw. Transthoracic echocardiography showed left ventricular dilatation, with an end-diastolic diameter of 6.3 cm, a left ventricular ejection fraction of 55% and severe aortic regurgitation (AR). Blood biochemistry analysis showed near-normal leucocyte count of 11.6 × 10⁹ L (ref 3.5–8.8 × 10⁹ L), and a...
A creatinine level of 76 μmol/L (ref 60–105 μmol/L). A total of 18 pairs of blood culture analyses were performed. Transoesophageal echocardiography (TOE) confirmed severe central AR (see Figure 2). The aortic valve was tricuspid, and all cusps were thickened. Hyperechogenic and heterogeneous masses were observed in the interventricular septum, raising the suspicion of a solid aortic root abscess. There was mild functional mitral regurgitation, but no vegetations could be identified on the valve. The tricuspid and pulmonary valves appeared normal.

Based on the above history and echocardiographic findings the patient was suspected of having IE with an annular abscess. He was started on empiric antibiotic treatment (vancomycin 1 g two times a day, meropenem 2 g three times a day, and gentamycin 240 mg once daily) and was subsequently transferred to a tertiary centre for surgical assessment by the multidisciplinary endocarditis team. Coronary angiography showed normal coronary arteries. Although echocardiographic findings were not considered typical for IE, the patient was found to have an indication for surgery, which is why a whole body 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) scan was not performed at this time. Surgery including aortic valve and root replacement with a biological composite graft was performed.
performed the following day. The pericardial cavity contained no fluid, and there were no signs of inflammation in the pericardial tissues or around the aortic root. At the bottom of both the right and left coronary sinuses, the surgeon found openings of 6–8 mm, which led to large underlying cavities measuring 2 × 2 × 3 mm and extended into the interventricular septum and the left ventricular free wall, respectively. On macroscopic examination, the cavities showed no evidence of infection. The non-coronary cusp base was substantially thickened and consisted of material undergoing degradation and with destruction of the periannular tissues. The tissues were considered too friable to allow for standard suturing of a rigid aortic mechanical composite root, and thus a flexible Medtronic Freestyle
canine bio-root was implanted. The patient was in a stable condition after the surgery. He was extubated and discharged to a low-dependency unit on the first postoperative day.

The postoperative period was complicated by pleural and pericardial effusions. The patient underwent thoracocentesis from both pleural cavities as well as pericardiocentesis. In order to prevent recurrence of effusion colchicine treatment was initiated to reduce pericardial and pleural inflammation. Intravenous antibiotic treatment was continued until 6 weeks post-surgery, the last 22 days in ambulatory care. Because the patient had a 3rd degree atriointricular block the temporary PM was replaced by a permanent PM, which was installed successfully. A week later, a TOE showed a left ventricular ejection fraction of 50% and a well-functioning aortic prosthetic valve. A week after discharge, the patient was physically well and had no signs of infection.

Eight months post-surgery, the patient feels well and reports mild dyspnoea (NYHA 1) and with joint pains in the hip and knees. TOE showed a left ventricular ejection fraction of 45% and a small central AR. He is working as a carpenter and biking a lot.

Histological examination of the excised material showed aortic valve tissue with suppurative and granulomatous inflammation including sporadic necrosis and hyaline fibrosis, compatible with a rheumatoid nodule. Fungi or bacteria were not detected. Blood cultures remained negative throughout the postoperative period with the last set taken on Day 10. Serological tests for Coxella burnetii, Bartonella species, Legionella pneumophila, Mycoplasma pneumonia, and Aspergillus were also negative. Polymerase chain reaction (PCR) for Mycobacterium tuberculosis was performed on the surgical specimen and was negative. A broad IE PCR panel analysis was also performed, and results were negative.

Discussion

This case displayed a rare extra-articular manifestation of RA on the heart, but also illustrated the difficulty of differential diagnosis. While cases of acute AR due to severe RA have been described a few times in the literature, to our knowledge, this case represents the first description of an aortic root pseudoaneurysm with the histopathological distinction of a rheumatoid nodule. A meta-analysis of the case-control studies conducted from 1975 to 2010, which examined the valvular and pericardial involvement in RA patients without symptoms of cardiovascular disease, identified a significantly increased odds ratio of 12.5 for patients with RA to have valvar nodules. Aziz et al. described a 62-year-old woman with RA in 2012 who developed severe AR. Like in our case, the pathology showed areas of necrosis and inflammatory cells typical for rheumatoid nodules with no evidence of IE. However, in the case of the 62-year-old, no root abscess or pseudoaneurysm was described.

In 2016, Choi et al. described a 72-year-old patient with RA with a rare case of non-bacterial thrombotic endocarditis (NBTE), which resulted in an embolic stroke. They found a hyperechoic mass-like nodular lesion on the mitral valve and suggested that in the absence of infection, valvar vegetations found on the echocardiography provided strong evidence of NBTE. They initiated Disease-Modifying Anti-Rheumatic Drugs and anti-coagulation therapy. On a 4-week follow-up echocardiography, there was no residual vegetation. Unlike Choi et al., the case discussed in this report had pathological findings verifying a rheumatoid nodule.

The patient had what was believed to be imaging that was consistent with a diagnosis of IE according to the multidisciplinary IE team but did not meet any of the minor Duke criteria or any other major Duke criteria, as defined by the 2015 European Society of Cardiology (ESC) Guidelines. Ten days after the surgery, we received the pathology results, but we continued the IE therapy for 6 weeks in total. ‘Culture-negative’ IE can occur in 9.3–12.2% of IE cases and can pose serious diagnostic and therapeutic challenges. Rheumatological diseases and malignancies are relevant differential diagnoses in cases of suspected IE where no causative microorganisms can be found. The differential diagnosis can rarely be confirmed without histology, which is why acute, severely ill patients without need of surgery are treated as having IE until the identification of the pathogen. Serological tests can be an important diagnostic tool when dealing with ‘culture-negative’ IE, and the negative results were essential in the process of reaching the final diagnosis. In hindsight, the IE therapy was not needed to treat the patient and could have been discontinued after the results of the pathology. Since IE in many cases can be ‘culture-negative’, we decided to continue the therapy for the full 6 weeks. An acute 18F-FDG PET/CT scan pre-surgery may have influenced our decision to treat for a full 6-week period with antibiotics, depending on the results, but this was not performed. The postoperative period was characterized by multiple fluid drainages, a long observation period, and eventually PM implantation.

RA can mimic aortic root abscesses, but it is a rare condition. Currently, it is unknown whether screening patients with RA for cardiac involvement may have a clinical yield. Aortic valve endocarditis with perianimal abscess formation is a life-threatening condition which, under normal conditions, necessitates surgery within 48–72 h according to guidelines. In this case, the clinical presentation taken together with the echocardiographic findings was suggestive of IE. Given the potential dire spontaneous course of conservative treatment of aortic root abscesses, we felt the decision to go for surgery was justified. It remains unknown whether an alternative strategy could have altered the course of the treatment, for example postponing the surgical treatment to allow for a course of anti-inflammatory agents.
Lead author biography

Frederik Kyhl, MB graduated from the University of Copenhagen in 2015 with a bachelor degree in Physical Education. In 2018, he completed the bachelor degree of Medicine at the University of Southern Denmark and is currently doing his master degree at the University of Copenhagen.

Supplementary material

Supplementary material is available at European Heart Journal - Case Reports online.

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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