CASE REPORT

Liver chemistry abnormalities and leg oedema in rheumatoid arthritis

Eva Marianne van Soest,^{1,2} Anho Liem,³ Jende van Zeben²¹Rheumatology, Erasmus MC, Rotterdam, The Netherlands²Rheumatology, Sint Franciscus Vlietland Groep, Rotterdam, The Netherlands³Cardiology, Sint Franciscus Vlietland Groep, Rotterdam, The Netherlands**Correspondence to**

Dr Eva Marianne van Soest, e.vansoest@erasmusmc.nl

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SUMMARY

A 66-year-old man with seronegative, erosive rheumatoid arthritis for 12 years presented with malaise, elevated alkaline phosphatase and gamma-glutamyl transferase, and leg oedema. He subsequently developed ascites. No liver pathology was found, but cardiac analysis including right heart catheterisation revealed constrictive pericarditis. Rheumatoid constrictive pericarditis is a rare condition, but, despite current effective treatment for rheumatoid arthritis, still occurs. Diagnostic delay is frequent. Although mortality of the intervention is high, pericardiectomy is needed for most patients.

BACKGROUND

Constrictive pericarditis is a rare extra-articular manifestation of rheumatoid arthritis and mostly occurs in patients who suffer from rheumatoid factor and/or anticitrullinated peptide antibody-positive rheumatoid arthritis, that is, seropositive patients. Despite current effective drug treatment for rheumatoid arthritis, rheumatoid constrictive pericarditis still occurs. This case illustrates that seronegative patients are not free of risk. Rheumatoid constrictive pericarditis often presents with vague symptoms and knows a mean diagnostic delay of 10 months.¹ Diagnosis depends on a high index of suspicion. Symptoms may be indistinguishable from congestive heart failure. CT/MRI of the heart and right heart catheterisation may be needed to confirm the diagnosis. Timely diagnosis and treatment are important for a favourable outcome.

CASE PRESENTATION

A 66-year-old man was regularly seen at the rheumatology outpatient clinic with erosive seronegative rheumatoid arthritis, for which he had been treated with methotrexate, prednisolone and several biological agents successively. His medical history included hypercholesterolaemia, cataract and a lumbar spine stenosis for which he had been treated surgically. Since 2 years, he was successfully treated with methotrexate, tocilizumab and low-dose prednisone. In addition, he used paracetamol, diclofenac, osteoporosis prophylaxis, pantoprazole and simvastatin. Apart from the rheumatoid arthritis and the medication he used, there were no other factors compromising his immune system. Recently, he had been thoroughly analysed for back pain and abnormalities in the lumbar spine seen on X-ray and MRI. A malignancy was feared but no signs were found. Eventually, analysis revealed the lesion to

be an enostosis or 'bone island', and the back pain to be caused by recurrence of the spinal stenosis. Despite the benign diagnosis, the patient was deteriorating and developed pitting oedema of both legs and arthritis of both knees.

INVESTIGATIONS

Laboratory results showed an unexplained leucocytosis, and an elevated gamma-glutamyl transferase (GGT) and alkaline phosphatase. Tocilizumab, methotrexate and diclofenac were stopped temporarily to exclude drug toxicity. The patient was advised to stop drinking alcohol. After that, liver chemistry abnormalities only increased (GGT 277 U/L (normal <50) and alkaline phosphatase 182 U/L (normal <125)). Other liver chemistry was normal: aspartate aminotransferase was 25 U/L, alanine aminotransferase 18 U/L, bilirubin 23 µmol/L and lactate dehydrogenase 219 U/L. Serology for autoimmune hepatitis was negative. The knee arthritis was treated with intra-articular prednisone. Culture of the synovial fluid was negative for tuberculosis. Ultrasound of the abdomen showed ascites, which had not been present on recent abdominal CT scan. There were no signs of liver cirrhosis. The ascites fluid was aspirated and showed no signs of a malignancy. The serum ascites albumin gradient was high with 14 g/L (serum albumin was 33 g/L), indicating portal hypertension or cardiac failure as cause of the ascites. Absolute neutrophil count was $0.85 \times 10^9/L$, which is suggestive of a spontaneous bacterial peritonitis. This is however unlikely in the absence of cirrhosis. The patient was nevertheless treated with antibiotics. Gastroscopy showed no signs of oesophageal varices or other abnormalities. Since no evident liver disease could be detected, the patient was sent to the cardiologist for further analysis of leg oedema and ascites. N-terminal pro-hormone of brain natriuretic peptide (NtproBNP) was elevated (140 pmol/L, normal <35). The ECG differed from the one taken before, with repolarisation changes in the left lateral leads. Cardiac ultrasound showed changes suggestive of inferoposterior infarction with decreased left ventricular function. However, left heart catheterisation revealed normal ventricular contractions and no signs of coronary disease. Right heart catheterisation showed abnormal filling of the ventricles during diastole with a plateau phase, which is suggestive of constrictive pericarditis. MRI of the heart showed a thickened pericardium of 3–7 mm with a minimal amount of pericardial fluid, confirming the diagnosis of constrictive pericarditis.

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DIFFERENTIAL DIAGNOSIS

The combination of abnormal liver chemistry and ascites may be mistaken for liver failure due to liver cirrhosis or metastasis of an unknown malignancy.

Clinical symptoms may be similar to those of congestive heart failure due to several causes.

Constrictive pericarditis can be seen after viral or bacterial pericarditis, cardiac surgery, radiation therapy of the chest and can be associated with malignancy, or with connective tissue disorders such as rheumatoid arthritis.^{2 3} Our patient had no history of cardiac surgery or chest radiation. Serology for enteroviruses was negative. Tests for tuberculosis were negative. A malignancy was unlikely since the patient had been thoroughly screened because of the recent spine abnormality. The patient was not uraemic and the drugs that he used are, to our knowledge, not associated with constrictive pericarditis. In absence of suggestions of other aetiologies, we feel in this case the most likely cause is rheumatoid constrictive pericarditis.

TREATMENT

Initial treatment was with loop diuretics and ACE inhibitors. Constriction of the pericardium is transient in a minority of patients; therefore, a course of conservative treatment is advisable in stable patients. Most often surgical pericardiectomy is necessary, as was in this patient.

OUTCOME AND FOLLOW-UP

The patient underwent surgical pericardiectomy and is doing well. Pathology of the pericardial specimen showed thickened and fibrotic pericardial tissue with signs of chronic inflammation, with lymphocytes and plasma cells. No micro-organisms were found. One month after pericardiectomy, alkaline phosphatase and GGT decreased to 104 U/L (normal <125) and 164 U/L (normal <50), respectively. One year after pericardiectomy, alkaline phosphatase was 55 U/L and GGT was 54 U/L.

DISCUSSION

Despite current effective treatment options for rheumatoid arthritis, we found six case reports on rheumatoid constrictive pericarditis published in the last two decades.^{4–9} There were three women and three men, in the age of 36–69 years. One patient had seronegative rheumatoid arthritis, two were seropositive and the remainder of the reports did not include this information. Three patients had erosive disease; three reports did not state. Time from diagnosis of rheumatoid arthritis to presentation of the first signs of constrictive pericarditis was 4–22 years. At time of pericarditis diagnosis, one patient was treated with sulfasalazine and prednisone, three with prednisone monotherapy and for two patients information on treatment of rheumatoid arthritis was missing. To treat the constrictive pericarditis, one patient was successfully put on a combination of etanercept and steroids. One patient was treated with loop

diuretics and ACE inhibitors but needed subsequent pericardiectomy. One patient was treated with diuretics and steroids and also needed subsequent pericardiectomy, but refused surgical intervention and died. Two patients underwent pericardiectomy straight away and for one patient treatment was not reported.

Learning points

- Cholestatic liver chemistry abnormalities and ascites in patients with rheumatoid arthritis may point at cardiac involvement.
- Despite current effective treatment modalities for rheumatoid arthritis, rheumatoid constrictive pericarditis still occurs. A high index of suspicion is key to timely recognition and treatment.
- Rheumatoid constrictive pericarditis may occur in seronegative rheumatoid arthritis.
- Right heart catheterisation and/or CT/MRI of the heart are often required to confirm the diagnosis.

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