A 61-year-old man presented to the emergency department with acute anterior ST-segment myocardial infarction. A 12-lead ECG showed normofrequent sinus rhythm, a right bundle-branch block, significant ST-segment elevations in precordial leads V1 through V4 (Figure 1), and increased troponin I of 5.219 μg/L (normal range, 0–0.045 μg/L). Typical angina pectoris worsened during exercise to Canadian Cardiovascular Society grade II to III for almost 3 days and finally sustained at rest for the last 2 hours (Canadian Cardiovascular Society grade IV). Physical activity was markedly limited over the past weeks to New York Heart Association grade III. The patient’s cardiovascular risk profile consisted of active smoking status and arterial hypertension, whereas comorbidity was characterized by chronic obstructive pulmonary disease, and seropositive rheumatoid arthritis, as well (Figure 2). Daily medication consisted of methotrexate 15 mg (1 time/wk), folic acid (1 time/wk), torsemide (5 mg/d), and tiotropiumbromid and formoterol aerosol sprays.

Primary coronary angiography revealed 3-vessel coronary artery disease with concomitant severe ectatic malformation of coronary vessels. The culprit lesion was a subtotal stenosis of the proximal left anterior descending artery with reduced thrombolysis in myocardial infarction flow (Figure 3A). The proximal part of the circumflex artery had a 90% stenosis, and the proximal left obtuse marginal artery did as well (Figure 3A). In addition, a chronic total occlusion (CTO) was verified at the proximal right coronary artery (RCA; thrombolysis in myocardial infarction flow 0; Movie I in the online-only Data Supplement) with retrograde filling from the left posterior interventricular artery through epimyocardial collaterals to the right coronary vessels. The patient reported worsening signs and symptoms of rheumatoid arthritis disease activity, and, therefore, disease-modifying antirheumatic drug therapy was also optimized by additional antirheumatic drug therapy was also optimized by additional antiplatelet therapy with the tumor necrosis factor (TNF) inhibitor adalimumab 40 mg subcutaneously (1 time/wk).

Furthermore, 4 months later, the patient was readmitted to our hospital in a persistent New York Heart Association grade III heart failure condition despite optimized pharmacological heart failure treatment still without any typical angina pectoris (Canadian Cardiovascular Society grade 0). Recurrent noninvasive exercise testing by spiroergometry revealed an insufficient increase of heart rate and blood pressure, and T-wave inversions were seen in leads V1/2 and aVL at a maximum stress level of 100 W. Peak oxygen uptake (V\textsubscript{O\text{2max}}) was 12.9 mL·kg\textsuperscript{-1}·min\textsuperscript{-1} as assessed by spiroergometry corresponding to Weber heart failure class C. Accordingly, pharmacological heart failure treatment was optimized by increasing the dosages of β-blocker and angiotensin-converting enzyme inhibitor. However, around that time the patient reported worsening signs and symptoms of rheumatoid arthritis disease activity, and, therefore, disease-modifying antirheumatic drug therapy was also optimized by additional treatment with the tumor necrosis factor (TNF) inhibitor adalimumab 40 mg subcutaneously (1 time/wk).

Two months later, routine outpatient follow-up revealed a stable cardiopulmonary health status (New York Heart Association grade III, Canadian Cardiovascular Society grade 0). The left ventricular ejection fraction was improved and calculated to be slightly reduced (ejection fraction, 54%) with inferior hypokinesia and anteroseptal to apical akinesia as assessed by transthoracic echocardiography. Consequently, noninvasive treadmill testing demonstrated an insufficient increase of heart rate and blood pressure, and T-wave inversions were seen in leads V1/2 and aVL at a maximum stress level of 100 W. Peak oxygen uptake (V\textsubscript{O\text{2max}}) was 12.9 mL·kg\textsuperscript{-1}·min\textsuperscript{-1} as assessed by spiroergometry corresponding to Weber heart failure class C. Accordingly, pharmacological heart failure treatment was optimized by increasing the dosages of β-blocker and angiotensin-converting enzyme inhibitor. However, around that time the patient reported worsening signs and symptoms of rheumatoid arthritis disease activity, and, therefore, disease-modifying antirheumatic drug therapy was also optimized by additional treatment with the tumor necrosis factor (TNF) inhibitor adalimumab 40 mg subcutaneously (1 time/wk).

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Specifically addressing the prognostic benefit of a complete revascularization of 3-vessel coronary artery disease, elective percutaneous coronary intervention of RCA-CTO was planned. Dual-injection angiography using a 2 guide catheter strategy with a 6F extra backup 4.0 catheter with sideholes being placed at the left coronary artery via right radial access and a 7F Amplatz left 1 catheter with sideholes being placed at the RCA via right femoral access (ie, dual femoral–radial access), as well, proved good intermediate results after percutaneous coronary intervention with DES implantation into the proximal left anterior descending and circumflex arteries. Most notably, however, the former RCA-CTO lesion revealed spontaneous and complete antegrade revascularization with a resting 90% tandem stenosis at the proximal RCA (Figure 3E; Movie IV in the online-only Data Supplement). Final percutaneous coronary intervention with DES implantation was performed without any further complications (2 bare metal stents, Prokinesis 5.0/26 mm and 5.0/15 mm, Biotronik SE & Co.KG, Berlin Germany; Figure 3F).

CTOs represent the most challenging coronary lesions to treat, frequently left unvascularized because of perceptions of high failure rates and technical complexity even in patients experiencing symptoms of coronary ischemia. However, in experienced centers, the success rates of interventional revascularization of >85% are reported (http://www.ercto.org/). A CTO lesion is defined by standard characteristics, which were also evident in the case reported here: (1) a large vessel diameter (in this case, proximal RCA, segment 1) before the proximal cap of the CTO lesion with minimal residual antegrade filling corresponding to an incompetent target coronary vessel at the distal cap; (2) an estimated lesion length >20 mm; (3) retrograde epicardial collateral circulation from the repaired donor vessel circumflex artery-posterolateral artery despite the large vessel diameter of the proximal RCA; and (4) persistent inferior hypokinesia in comparison with anteroseptal to apical akinesia 6 months after the initial ST-segment myocardial infarction.

To our knowledge, our case is the first description of spontaneous revascularization of a CTO lesion in a patient with concomitant TNF inhibitor treatment because of rheumatoid arthritis.

Several reports point out an increased incidence of coronary artery disease and increased cardiovascular mortality risk in rheumatoid arthritis. Increased plaques burden and severity is variably characterized by noncalcified, mixed, or fully calcified plaques and may result in obstructive or nonobstructive multivessel disease and in silent coronary ischemia, as well. However, evaluations of different diagnostic techniques to most reliably prove coronary artery disease involvement in rheumatoid arthritis (eg, coronary calcium score by computed tomography scan, invasive coronary flow reserve, etc) deliver controversial results. Accordingly, available data regarding the outcomes of acute coronary syndrome in rheumatoid arthritis are conflicting.

Treating rheumatoid arthritis with TNF inhibitors, such as adalimumab, is recommended in patients with a high disease activity (ie, Clinical Disease Activity Index >22 or Simplified Disease Activity Index >26) and refractory treatment response to combined methotrexate and prednisone at 3 months. TNF is a key cytokine-mediating effector pathway in both inflammatory disease target tissues and in atherosclerotic vessels. Treatment of inflammatory arthritis with TNF inhibitors additionally modulates vascular risk factors and has beneficial effects on vascular outcomes. These beneficial effects of TNF inhibitors toward artherosclerotic lesions have been attributed to the modulation of endothelial cell function, the reduction of vascular stiffness, and the reduction of fibrinogen, homocysteine, and lipoprotein (a), as well.

Therefore, it is conceivable to assume that these anti-inflammatory effects of the TNF inhibitor adalimumab might be the reason for the effects seen in our case. Accordingly, the patient reported about an improvement of typical clinical features of rheumatoid arthritis such as joint swelling and morning stiffness of hands and feet since the time of adalimumab treatment, and further improvement of cardiac exercise level being assessed by noninvasive spiroergometry was documented.

Highlighting the association of systemic inflammation in rheumatoid arthritis with an increased cardiovascular event and mortality risk, this case exemplarily represents severe extra-articular manifestation of coronary vasculitis. Treating relevant coronary lesions with DES in patients with systemic inflammatory arthritis or vasculitis has been described even with good long-term results. Accompanying prednisolone medication after stent implantation was shown to possibly lower the recurrence of angina pectoris. Whether or not the development of new coatings of DES with TNF inhibitors might lead to an improvement for this specific patient group remains unclear.

In conclusion, systemic inflammation leading to severe coronary vasculitis leading to ST-segment myocardial infarction can occur in patients with rheumatoid arthritis and should be included in the differential diagnosis. The use of TNF inhibitors could be considered as another pharmacological treatment option for an optimal treatment strategy in this subset of patients.

Disclosures
None.

References
Figure 1. Initial 12-lead ECG demonstrated normofrequent sinus rhythm, a right bundle-branch block, and significant ST-segment elevations in precordial leads V1 through V4.

Figure 2. Patient’s hands are affected by rheumatoid arthritis, as indicated by swollen joints, rheumatoid nodules, and palmar erythema.

Figure 3. Primary coronary angiogram shows 3-vessel coronary artery disease with concomitant severe coronary vasculitis. The culprit lesion was a subtotal stenosis of LAD (TIMI I flow). The proximal part of CX shown had a 90% stenosis, and the proximal left OM had a 90% stenosis, as well (A). A CTO was verified at the proximal RCA (TIMI flow 0; B; Movies I and II in the online-only Data Supplement) with retrograde filling from the left posterolateral artery through epimyocardial collaterals to the right posterior interventricular artery (C). Results after immediate PCI with implantation of DES in proximal LAD (Xience Pro 3.5/23 mm, Abbott, Chicago, IL) and CX (Xience Pro 4.0/28 mm, Abbott), and plain old balloon angioplasty of proximal OM, as well (Trek 2.0/20 mm Trek balloon, Abbott; D). Six months after the initial ST-segment myocardial infarction, reangiogram proved good intermediate results after PCI at proximal LAD and CX. Notably, former RCA-CTO lesion (B) revealed spontaneous and complete antegrade revascularization with a resting 90% tandem stenosis at the proximal RCA (E) after treatment with the TNF inhibitor adalimumab. F. Final results after PCI with DES implantation of the RCA (2 bare metal stents, Prokinesis 5.0/26 mm und 5.0/15 mm, Biotronik SE & Co.KG, Berlin Germany). CTO indicates chronic total occlusion; CX, circumflex artery; DES, drug-eluting stent; LAD, left anterior descending artery; OM, obtuse marginal artery; PCI, percutaneous coronary intervention; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction; and TNF, tumor necrosis factor.
Effect of Tumor Necrosis Factor Inhibitor Treatment on Proximal Right Coronary Chronic Total Occlusion in a Patient With Rheumatoid Arthritis
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