Unusual electrocardiographic changes in a patient with pericardial effusion caused by rheumatoid arthritis: a case report

Giuseppe Cocco[1*]

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ABSTRACT

Background: Rheumatoid arthritis (RA) is an immune-related inflammatory disease which affects almost 1% of the general population and which is ranked among the top 15% of diseases causing major disability worldwide. RA shares some pathologic features, genetic predisposition, and risk factors with atherosclerosis, and inflammation plays a central pathophysiologic role in both diseases. RA is associated with an increased risk of cardiovascular mortality. In RA, pericardial involvement is a frequent complication but rarely occurs as the first manifestation.

Case Presentation: A 63-year-old male patient with RA presented with an acute chest pain and in the Electrocardiography (ECG) ischemic ST-down-sloping in multiple leads. Echocardiography showed an abnormal "bounce" of the interventricular septum and a small-medium size pericardial effusion. The laboratory values showed high inflammatory parameters and confirmed the presence of active RA. Troponin T was normal and NT-proBNP was at level 2. There were no signs for vasculitis. Coronarography found only small non-stenotic changes in the coronary arteries. A rheumatologic consultant recommended prednisone and later on, tocilizumab. He was also treated with colchicine. The clinical condition improved within 2 weeks and the ECG changes normalized within a month. Three months later, an echocardiographic follow-up showed that the pericardial effusion and the left ventricular bounce had disappeared.

Conclusion: Small-medium size pericardial effusion manifesting as an acute coronary syndrome and with ischemic ECG changes is the most unusual finding. Indeed, the proper diagnosis of a pericardial effusion was made retrospectively

Keywords: Pericardial effusion, rheumatoid arthritis, acute chest pain, atypical ECG changes.

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Correspondence Author: Giuseppe Cocco
*Cardio-Rheumatology Office, Rheinfelden, Switzerland.
Email: praxis@cocco.ch
Full list of author information is available at the end of the article.

Background

Rheumatoid arthritis (RA) is an immune-related inflammatory disease which affects almost 1% of the general population and which is ranked among the top 15% of diseases causing major disability worldwide [1]. RA shares some pathologic features, genetic predisposition, and risk factors with atherosclerosis, and inflammation plays a central pathophysiologic role in both diseases.

RA is associated with an increased risk of cardiovascular mortality [1–5]. Post-mortem data [6] have shown that asymptomatic cardiac pathology can be detected in most patients with an early stage of RA. In these patients, the prevalence of vulnerable coronary plaques is much higher than in controls without RA. These data have been confirmed by computed tomography angiography [7]. Altogether, as compared with the general population, in RA, the prevalence of cardiovascular events is increased to an extent comparable to that of type 2 diabetes mellitus [1–7]. RA-patients have a higher incidence of myocardial ischemia and infarction, cardiac failure, valvular heart disease, pericarditis, myocarditis and, to a lesser extent, venous complications. The occurrence of sudden cardiac death is two-fold increased and that of major adverse cardiovascular events is almost 50% augmented. Seven years following the symptoms onset of RA cardiovascular deaths increase. A Swedish cohort study using national registries [7] found that an increased severity of disease at presentation is associated with the occurrence of the acute coronary syndrome (ACS) and worse short-term all-cause mortality in patients with active RA compared with matched controls. Interestingly, the worse outcome in patients with RA compared with matched controls persisted after adjustment for clinical covariates, including the type of ACS. Moreover, among deaths, the majority of cases had a cardiac cause (89.9% *vs*. 90.8%). Of note, all-cause mortality during the first 30 days after an ACS was quite high in patients with RA (15.7%) compared with matched controls (10.7%) [4]. RA and atherosclerosis share several features in pathophysiology, genetic predisposition, and risk factors, assigning a central role to inflammation [1–10]. Dynamic changes in arteries culminate in plaque rupture or erosion, followed by thrombus formation [9,10]. However, in RA, the occurrence of

ACS as the first cardiac manifestation is very rare. Lastly, pericardial involvement is a frequent complication in RA but rarely occurs as the first manifestation [1–3]. It may be asymptomatic and generally reflects the activity of RA [1–5].

Case Presentation

In a 63-year-old Caucasian, a seropositive RA was diagnosed at the age of 56. The patient had refused a treatment. Since 30 years he was an active smoker, with a total of 35 packs-years. The patient came to the clinic with a history of crushing retrosternal pain. The pain had begun 16 hours earlier, was persisting, and had changing intensity. He also mentioned that since a week he was suffering from myalgia and malaise. He had taken ibuprofen but the pain did not change.

On physical examination, the patient appeared to be in mild discomfort, was afebrile, with asymmetrical blood pressure (130/82 mm Hg), a regular heart rate (70 per minute), a respiratory rate of 14 breaths per minute, and an oxygen saturation of 98% while he was breathing ambient air. There was no evidence of a jugular venous pulse with the bed elevated to 30°. His chest was clear to auscultation. The heart sounds were regular, with no murmur, rub, or gallop. His abdomen was tender. The skin examination did not reveal jaundice, erythema, or telangiectasias. His legs were warm, without edema. The rest of the examination was normal.

A chest radiographic examination showed a slightly enlarged left ventricle and a possible pericardial effusion. There was a small basal bilateral pericardial effusion. The lungs showed no abnormalities.

A conventional radiographic examination showed erosion of the fourth and fifth metacarpal and phalangeal bones of the hands and feet.

His laboratory values are shown in Table 1. I will focus on the normal value of troponin, the slightly increased value of B-type natriuretic peptide (BNP), the highly elevated signs of inflammation [C-reactive protein (CRP), erythrocyte sedimentation rate], and the typical laboratory changes for RA. There were no changes indicating vasculitis.

An Electrocardiography (ECG) (Figure 1) showed a normal sinus rhythm and a normal conduction, there were ischemic ST-down-sloping in I, II, III, aVL, and $V_{4–6}$ with mirror mild ST-up-sloping in aVR and V_1, and large negative T-waves in I, II, aVL, and $V_{2–6}$.

Transthoracic echocardiography showed the left ventricle with normal size, normal regional wall movement, and systolic function (LVEF 62%). There was a moderate relaxation dysfunction [pulsed wave (PW) Doppler mitral valve E/A 0.5 and fusion of the E–A waves]. An abnormal "bounce" of the interventricular septum was noted and a medium size pericardial effusion was detected (Figure 2). There was no evidence of pericardial thickening and no valvular disease.

In the hospital, an MRI showed a dilated inferior vena cava and hepatic vein, a ventricular septal bounce without pericardial thickening. There was no evidence of aortitis. Coronarography found only small non-stenotic changes in the coronary arteries.

The patient was strongly advised to stop smoking. A rheumatology consultant prescribed prednisone (1 mg/kg for 6 months) and tocilizumab (4 mg/kg i.v. over 60 minutes every 4 weeks). He was also treated with oral colchicine.

The clinical condition improved within 2 weeks. The ECG changes normalized within a month. Three months later, an echocardiographic follow-up showed that the pericardial effusion and the left ventricular bounce had disappeared. The left ventricular relaxation dysfunction remained unchanged.

The 2015 Guidelines for the Diagnosis and Management of Pericardial Diseases [12] discuss extensively modern diagnostic tools but there is not a specific chapter on the ECG changes. Most papers on this pathology were published many years ago.

In acute pericarditis, the most typical ECG changes are ST-up-sloping with concave morphology and positive T waves in I, II, aVL, and $V_{4–6}$ and, when typically distributed among limb and precordial ECG tracings, these findings are virtually diagnostic of acute pericarditis [13–15].

As little as 150 ml of pericardial effusion is capable of compressing the heart [16]. Published ECG changes associated with pericardial include low QRS voltage, electrical alternans, *P* wave changes, and *T* wave inversion [13–15]. Repolarization may also be normal [15]. Atypical ECG responses in acute pericarditis include the absence of ST deviations, which conceals the diagnosis, and restricted distribution of ST deviations, which suggests myocardial injury [17]. Of note, published ECG changes associated with pericardial effusion are based on data from animals and only on small series of human cases [13].

In pericardial disorders, the ECG changes are usually transient. In the subacute phase, there may be the appearance of negative *T*-waves and this abnormality may persist for months [11–17].

In constrictive pericarditis, the typical ECG changes are low-voltage, mild ST-down-sloping, and possibly, negative *T*-waves in multiple leads [13–18].

On the other hand, a concave ST-up-sloping is usually seen in myocardial ischemia and is atypical in pericardial disorders [13–17].

Discussion

The ECG changes seen in our case suggest myocardial ischemia and are most unusual for a small-medium size pericardial effusion. However, troponin was normal and coronarography ruled out a significant coronary artery disease. Actually, as in our case, in patients with the described atypical ECG changes, in general, the diagnosis of pericardial effusion is made retrospectively.

Table 1. Laboratory data.

VARIABLE	REFERENCE RANGE (MEN)	DAY 1	3 MONTHS LATER
Blood			
Hemoglobin (g/dl)	13.5–17.5	12.3	13.2
Hematocrit (%)	41–53	44	43
Red-cell count (cm^3)	4.2–5.4	3.9	4.0
White-cell count (cm^3)	4.5–10	10,4	8.8
Platelets-cell Count (cm^3)	130–400	183	220
Erythrocyte sedimentation rate (mm/h)	<10	56	23
C reactive protein (mg/l)	<12	26	16
Chemistry			
Sodium (mmol/l)	135–145	140	141
Potassium (mmol/l)	3.5–5.5	4.3	4.1
Chloride (mmol/l)	96–106	102	103
Urea nitrogen	6–23	7.5	8.0
Creatinine (mg/dl)	0.5–1.4	0.9	0.8
Glucose (mg/dl)	65–99	98	79
Calcium (mg/dl)	8.2–10.1	8.9	8.8
Total protein (g/dl)	6.4–8.2	7.2	7.0
Uric acid (mg/dl)	3.6–7.0	5.2	4.8
Calcium (mg/dl)	8.2–10.1	8.6	8.9
Total bilirubin (mg/dl)	0–1.3	2.1	1.3
Prothrombin time (second)	14	13	12
Partial-thromboplastin time (sec)	25–35	29	31
International normalization ratio	1	1.2	1.1
Aspartate aminotransferase (U/l)	10–40	23	27
Alanine aminotransferase (U/l)	20–60	62	55
Alakaline phosphatase (U/l)	10–150	124	112
Lipase (U/dl)	<160	15	35
Lactate dehydrogenase	85–227	94	89
γ-Glutamyltransferase	<60	48	50
Rheumatologic parameters			
Rheumatoid factor (U/l)	<20	415	198
Antibodies against cyclic citrullinated peptide (U/l)	<20	180	178
ANA antibodies	Negative	1:100	1:100
ANCA antibodies	Negative	Negative	Negative
Cardiac parameters			
Troponin T (µg/l)	<0.4	0.05	<0.08
NT-proBNP (pg/ml)	<300	782	245

Vasculitis is frequent in RA and affects the small and medium-size vessels [1–3]. The patient was a smoker and tobacco consumption is associated with the occurrence of vasculitis [18]. However, we could not find a vasculitis in this patient.

Elevated natriuretic peptide levels are a common finding in symptomatic pericardial disease. As in our case, natriuretic peptide levels are less elevated in heart failure with preserved ejection fraction than in patients with heart failure with reduced ejection fraction [19].

The marked elevation of CRP and erythrocyte sedimentation rate confirms the presence of an active inflammation. It is thinkable that the high inflammation has induced endothelial activation and dysfunction, perhaps a micro-coronary dysfunction and resulted in ischemia with corresponding ECG changes.

Conclusion

In the described patients, the chest pain and the ECG changes suggested an ACS. The diagnosis of a

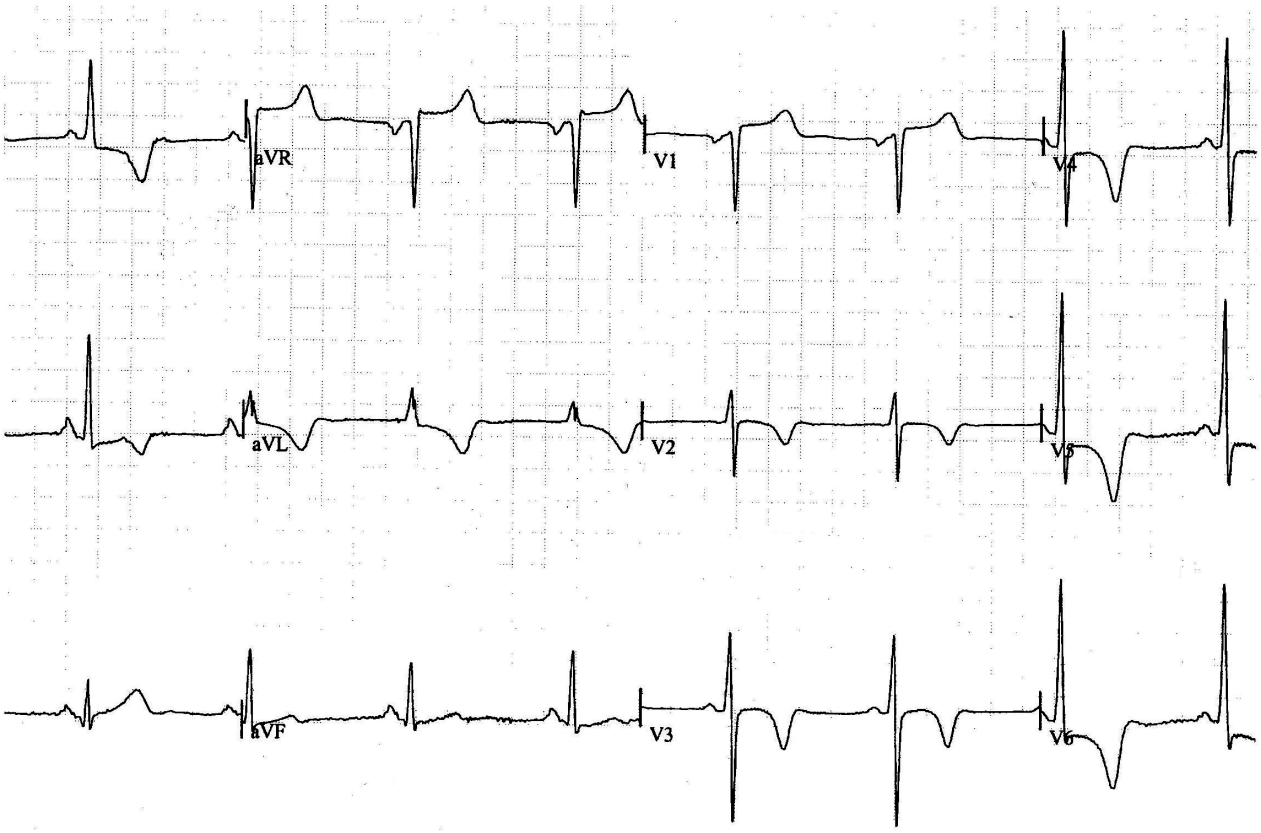


Figure 1. *ECG at presentation. The ECG shows a normal sinus rhythm with a normal conduction, ischemic ST-down-sloping in I, II, III, aVL, and V_{4-6} with mild mirror ST-upsloping in aVR and V_1, and a large negative T-waves in I, II, AVL, and V_{2-6}.*

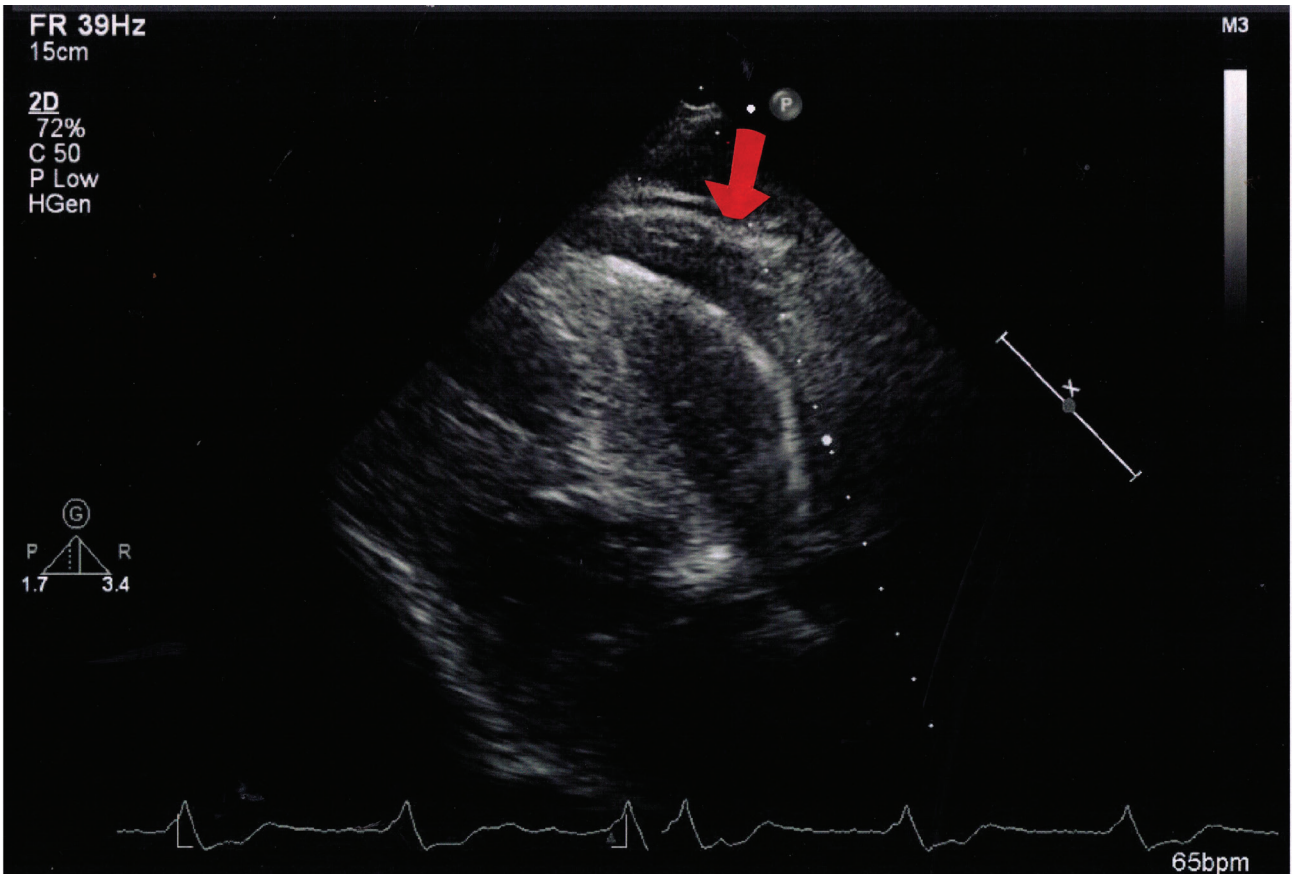


Figure 2. *Pericardial effusion. The red arrow shows the small-medium size pericardial effusion.*

small-medium size pericardial effusion without a significant coronary occlusion was obtained by exclusion. The patient had signs of high inflammation due to RA. It may be speculated that inflammation induced a micro-coronary dysfunction with myocardial ischemia. This case confirms that RA and coronary atherosclerosis share several features in pathophysiology and assigns a central role to inflammation.

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List of abbreviations

ACS	Acute coronary syndrome
BNP	B-type natriuretic peptide
CRP	C-reactive protein
ECG	Electrocardiography
PW	Pulsed wave
RA	Rheumatoid arthritis

Consent for publication

The patient has given his written consent to publish his medical data.

Ethical approval

Ethical approval is not required at our institution for publishing a case report in a medical journal.

Author details

Giuseppe Cocco[1]

1. Cardio-Rheumatology Office, Rheinfelden, Switzerland

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Summary of the case

Patient (gender, age)	1	Male, 63-year-old
Final diagnosis	2	Pericardial effusion. No coronary artery disease. Possible micro-coronary dysfunction
Symptoms	3	Chest pain
Medications	4	Prednisone, tocilizumab, colchicine
Clinical procedure	5	Getting the correct diagnosis with atypical ECG changes for medium size pericardial effusion
Specialty	6	Cardiology and Rheumatology