

Rickettsiosis and Coronary Artery Disease: Is The Association Atherosclerosis and Rickettsiosis Fortuitous?

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ABSTRACT

Rickettsial infection can affect multiple organs. Heart involvement is rare, although cases of acute myocarditis, pericarditis, advanced atrioventricular block have been reported. We report 2 cases of Rickettsia related to myocardial injury. The first case concerns a 65-year-old patient with minimal atherosclerotic risk factors, who had rickettsiosis one month before admission and who presents with silent myocardial ischemia revealed by a positive stress test, coronary angiogram showed a sub-occlusive stenosis of left anterior descending artery (LAD) with successful recanalization by implantation of one drug-eluting stent. The second one is 71-year-old patient treated for rickettsiosis. He was admitted to our department with Non-ST elevation myocardial infarction, coronary angiogram showed severe calcified triple vessel disease, he had a successful surgical revascularization. Through our observations, we will discuss the physio pathological mechanisms of coronary involvement by Rickettsiosis which would cause vasculopathy by endothelial cell damage.

Keywords: Coronary artery disease; Rickettsial infection; Endothelial cell; Coronary angiogram; Coronary artery bypass graft

INTRODUCTION

Rickettsia are gram-negative coccobacilli first described in 1906 [1]. Rickettsial infections are caused by a variety of obligate intracellular bacteria in the genus *Rickettsia* and are grouped into one of four categories: the spotted fever group (SFG) rickettsiae, typhus group rickettsiae, the ancestral group, and the transitional group. Rickettsial infection can affect multiple organs. Heart involvement is rare, although cases of acute myocarditis, pericarditis, advanced atrioventricular block [2] have been reported. We report two cases of a 65 and 71 years old men presenting with Rickettsial infection and coronary artery disease. Through our observations, we will discuss the physio-pathological mechanisms of coronary involvement by Rickettsiosis which would cause vasculopathy by endothelial cell damage.

CASE REPORTS

The first case concerns a 65-year-old patient, with minimal atherosclerotic risk factors, who had rickettsiosis one month before admission and who presents with silent myocardial ischemia revealed by a positive stress test. The patient was asymptomatic

without angina or dyspnea. Cognitive function was well preserved, the physical examination at admission revealed a normal blood pressure and regular heart rate (81 beats/min), a normal cardiac and pulmonary examination, and an eschar at the inoculation site in the lower limb, without fever, petechial, maculopapular rash, or lymphadenopathy. The ECG showed was in normal sinus rhythm, incomplete right Bundle branch block, abnormal R wave progression in inferior territory and normal T-waves (Figure 1). Transthoracic echocardiographic examination showed Ischemic sequels in anteroseptal and anterior wall and preserved ejection fraction, without valve involvement or pulmonary hypertension.

To evaluate wall motion abnormalities, we performed a coronary angiogram, it showed a sub-occlusive stenosis of left anterior descending artery (LAD) (Figure 2) with successful recanalization by implantation of one drug-eluting stent (Figure 3) without peri procedural complications. Operational suites were simple in cardiovascular intensive care. Our patient was treated with dual antiplatelet therapy with acetylsalicylic acid and clopidogrel, angiotensin converting enzyme inhibitor, a beta blocker and statins. He was discharged from the hospital 2 days later. The

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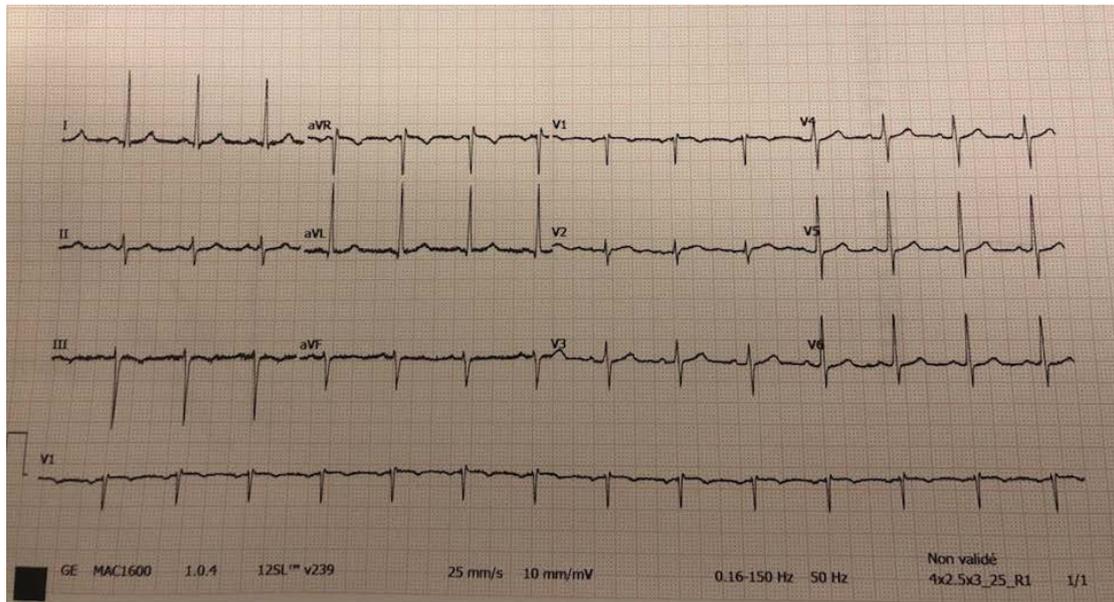


Figure 1: 12 lead ECG showing normal sinus rhythm, incomplete right Bundle branch block, abnormal R wave progression in inferior territory and normal T-waves.

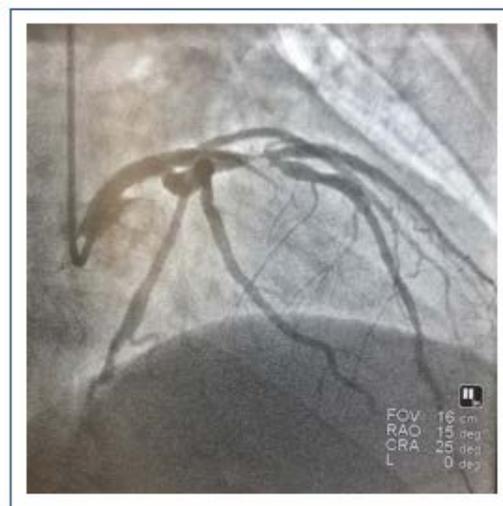


Figure 2: Coronary angiography demonstrating a sub-occlusive stenosis of Left Anterior Descending artery (LAD).

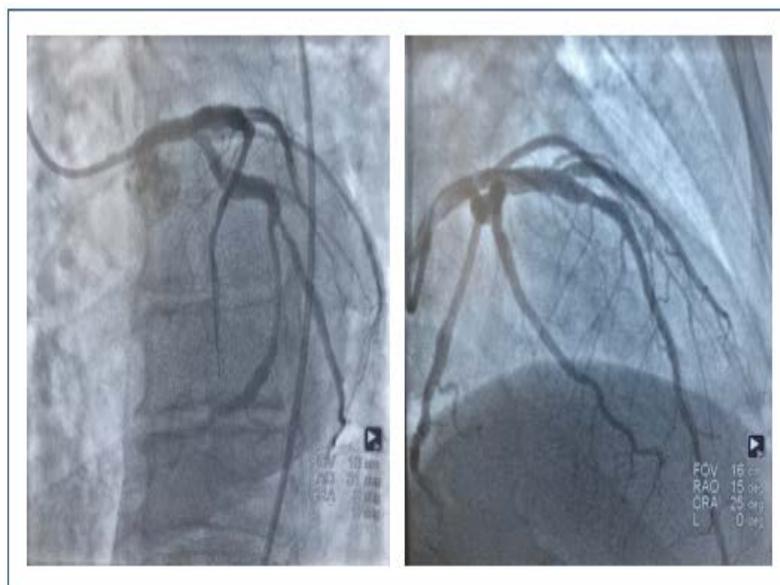


Figure 3: Coronary angiography demonstrating a successful recanalization by implantation of one drug-eluting stent on the Left Anterior Descending artery (LAD).



Figure 4: Coronary angiography demonstrating severe calcified triple vessel disease.

second case is 71-year-old patient treated for rickettsiosis one month before admission and having a low cardio-vascular risk profile. He presented to our department of cardiology with chest pain related to Non-ST elevation myocardial infarction. He had chest pain at rest and dyspnea 3 days before admission.

The physical examination at admission revealed a normal blood pressure and regular heart rate (98 beats/min), a normal cardiac and pulmonary examination, without eschar, or fever, or petechial, or maculopapular rash, or lymphadenopathy. The 12 lead ECG showed a normal sinus and regular rhythm, negative T-waves in anterior territory. A complete echocardiographic evaluation showed significant wall motion abnormalities and normal systolic function, thickening of mitral and aortic valve leaflets without significant stenosis or insufficiency and without pulmonary hypertension. Biology tests showed significant elevation of high sensitive troponin (≥ 10 times the upper normal limit). Coronary angiogram showed severe calcified triple vessel disease without coronary occlusion (Figure 4), if it was the case, we should dilate the artery causing the acute event first. The fact that the lesions were severely calcified without acute occlusion led us to opt for the CABG instead of PCI, especially because of elevated syntax score at 30. After five days of discontinuation the Clopidogrel and attending a preoperative assessment, our patient had a successful surgical revascularization without peri procedural complications. Operational suites were simple in cardiovascular intensive care, dual antiplatelet therapy has been resumed. The return to the sector was made on the third post-operative day. Patient was discharged with dual antiplatelet therapy with acetylsalicylic acid and clopidogrel, angiotensin converting enzyme inhibitor, a beta blocker and statins. He was discharged from the hospital 7 days later. Our two patients benefited from cardiac rehabilitation.

DISCUSSION

Rickettsia are obligate intracellular organisms that have a predilection for vascular endothelial cells. Its incidence on the Mediterranean rim is 50/100000 inhabitants/year. The frequency in Morocco is still poorly known, however, it seems to be frequent

in our climates. They attach to the host's vascular endothelium via surface cell antigens (SCA) including ompA, ompB, SCA1 and SCA2 that bind to the host cell's surface specific receptors (Ku70 receptors) and lead to engulfment into the cytoplasm of non-phagocytic endothelial cells [3]. The pathological effect is then exerted via release of reactive oxygen species and proinflammatory cytokines including IL-1 α , IL-6, IL-8, IFN γ and IFN β causing widespread endothelial inflammation and dysfunction of small and medium-sized vessels and increased vascular permeability [4]. Additionally, endothelial release of von Willebrand multimers, enhancement of thromboxane A2 synthesis and platelet activation induce a hypercoagulable state [5].

This constitutes the Rickettsial vasculitis which is the hallmark of the disease. Indeed, thrombosis is a known complication of Rickettsial infections ranging from small vessel microthrombi to limb gangrene and life-threatening thrombotic thrombocytopenic purpura. Prior to this case, there have been one reported cases of acute myocardial infarction in a patient with angiographically normal coronary arteries secondary to Rickettsial infection [6], although reports of large vessel thrombosis secondary to Rickettsiae do exist. A case of Rickettsia conorii infection causing internal carotid artery thrombosis and stroke was reported. The acute coronary syndrome can be secondary to this infectious disease when the coronary arteries are normal, the physiopathogenesis is very variable the predominant mechanism is vasculitis by inflammation of the arterial wall in response to the presence of the microorganism, with a local immune reaction inducing lesions of the endothelium and the formation of local vascular thrombosis, or even rupture of the walls, explaining the infarcts. This is a special case, given the onset of ACS a few days after the diagnosis of rickettsiosis, a rickettsiosis / atherosclerosis association is suggested and that rickettsiosis may be the cause of the complication of atheromatous plaque. We certainly cannot be definitive, but given the pathophysiological mechanisms of rickettsiosis, this disease may be the cause of the acute atherosclerosis outbreak. Our 2nd case illustrates this hypothesis as well as the possibility of thrombotic complications related to this infectious disease.

On the other hand, for the first case there was no acute event, it was a stable coronary disease (silent ischemia) diagnosed following the fortuitous discovery of signs of ischemic heart disease on the ECG, echocardiography and stress test. It is difficult to find a link between these atherosclerotic lesions and rickettsiosis, we are convinced that it is a fortuitous association. It is not clear whether the usual treatment for ACS will have the same impact on outcome. In our patients, we opted for a treatment of rickettsial infection, a long-term treatment of coronary artery disease and cardiac rehabilitation.

CONCLUSION

Rickettsial infection may be an important pathogen in the pathogenesis of coronary artery disease. It may be the cause of thrombotic complications of atheromatous plaque. Studies need to be done, in order to better understand this association and define the optimal management.

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