

Somatostatin analogue scintigraphy in a patient with viral myocarditis

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Abstract

Myocarditis may present clinically with a wide range of manifestations and often remains unrecognized. The diagnosis of myocarditis traditionally has been based on histological findings, but endomyocardial biopsy has a low sensitivity and clinicians are reluctant to proceed with an invasive diagnostic technique. Among newer diagnostic approaches, cardiac magnetic resonance imaging has gained acceptance as an efficient noninvasive tool to determine myocardial inflammation. In this context, imaging with radiolabeled somatostatin analogues could also be relevant because of their ability to delineate inflammatory sites. *In conclusion*, a case is presented in which somatostatin receptor imaging of the myocardium with ^{99m}Tc-depreotide tomography was used in the assessment of viral myocarditis.

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Introduction

The clinical presentation of myocarditis may vary widely and the disease may remain undetected or without an established diagnosis [1-3]. The diagnosis of myocarditis traditionally has been based on histological findings according to the Dallas criteria, but endomyocardial biopsy is insensitive in clinical use [4]. Clinical, laboratory and echocardiographic evaluation together with cardiac magnetic resonance imaging may lead to a diagnosis noninvasively, and biopsy may be reserved for few cases [5]. In this context, scintigraphy with somatostatin analogues could be helpful in the assessment of myocardial inflammation because of the increased density of somatostatin receptors in activated lymphocytes and macrophages [6]. A case is reported in which technetium-99m (^{99m}Tc)-depreotide scintigraphy aided in the assessment of viral myocarditis.

Case report

An 18 years old male was admitted in our hospital with acute chest pain of 5h duration and a 5mm ST-segment elevation in leads II, III, aVF with reciprocal changes in leads aVL, V1-V4 in the electrocardiogram. The pain started on exertion and was accompanied by nausea and vomiting. The patient was afebrile, he had no manifestations of a recent viral or other infection and his previous medical history was unremarkable. On admission he was experiencing mild chest pain, he had tachycardia (105bpm) and his blood pressure was 90/50mmHg. In angiography coronary arteries were normal and there was no evidence of apical ballooning in ventriculography [7]. All cardiac biomarkers were markedly elevated (with a cardiac troponin I value of 16.10ng/mL, normal limits <0.03) and an echocardiographic examination showed a slightly dilated left ventricle with diffuse wall hypokinesis, septal akinesis and an ejection fraction of 40%. Subsequent toxicologic examination excluded drug abuse (cannabinoids, opiates, benzodiazepines, cocaine, amphetamines, barbiturates and methadone) as a cause of coronary artery spasm, serologic examinations for a plethora of viruses and other microorganisms related with acute myocarditis (cytomegalovirus, Epstein-Barr virus, adenovirus, mycoplasma pneumoniae, chlamydia pneumoniae, coxiella burnetti, rickettsia typhi, rickettsia rickettsii, bartonella henselae and bartonella quintana) were negative and also autoimmune disease related vasculitis was ruled out. Acute myocarditis was deemed the most likely diagnosis, although an acute myocardial infarction with normal coronary arteries remained a concern, mainly because of the exercise related onset of chest pain with territorial ST segment elevation, in the absence of evidence of a recent infection. Cardiac magnetic resonance imaging was performed and the findings were compatible with myocarditis, although cardiomyopathy could not be ex-

cluded (Fig. 1). The patient received treatment for acute heart failure possibly related with acute myocarditis (carvedilol, an angiotensin converting enzyme inhibitor and eplerenone) and improved clinically. Cardiac biomarkers decreased to nearly normal values within 7 days of hospitalization and the patient was discharged.

One month later, the patient presented with worsening heart failure. At that time point tomographic somatostatin receptor imaging with ^{99m}Tc -depreotide, which was readily available in our site, was suggestive of persisting inflammatory reaction (Fig. 2). Carvedilol was titrated to higher doses and the patient gradually improved. Taking into account the clinical manifestations together with imaging findings it was decided to proceed with endomyocardial biopsy. A subsequent polymerase chain reaction amplification of the RNA was consistent with herpes virus VII myocarditis.



Figure 1. Cardiac magnetic resonance imaging (mid-ventricular slices presented) showed diffuse subepicardial late gadolinium enhancement in T1-weighted pulse sequences, which involved 35%-50% of left ventricular wall thickness (white arrows), together with localized mid-myocardial enhancement in the interventricular septum (black arrows). No subendocardial late gadolinium enhancement was noted, which would indicate an ischemic etiology of myocardial injury.

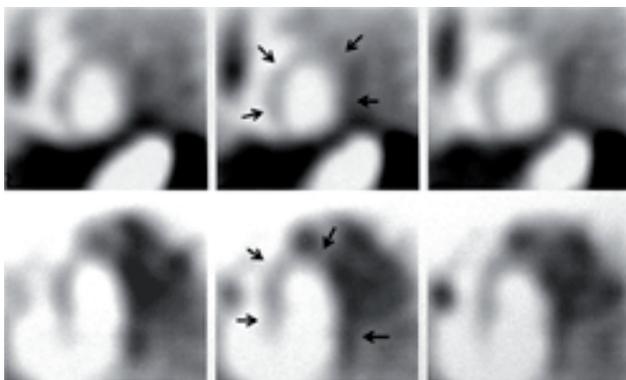


Figure 2. ^{99m}Tc -depreotide tomography. Mid-ventricular short axis slices in the top row and horizontal long axis slices in the bottom row showed diffuse myocardial tracer uptake (arrows).

Discussion

Myocarditis is defined as myocardial inflammation in the absence of ischemia or infarction [1]. Numerous agents may cause myocarditis, but viruses are the most common cause in the industrialized world [2, 3]. The clinical manifestations of myocarditis may range from an asymptomatic condition to fulminant acute heart failure, occasionally accompanied by conduction system disturbances or ventricular arrhythmias, and it may even mimic an acute myocardial infarction [1, 3, 8].

A major limitation to the accurate diagnosis of myocarditis is the lack of sufficiently sensitive and specific routine

cardiac tests. Endomyocardial biopsy may secure the diagnosis. Apart from its invasiveness, however, because of the patchy nature of the inflammatory infiltrates it suffers in sensitivity and its use is reserved for patients likely to have specific myocardial disorders [3, 5, 9]. Hence, the diversity of clinical manifestations together with the limited diagnostic performance of the usual cardiac tools, have led to the introduction of novel approaches [10].

Cardiac magnetic resonance imaging is regarded a powerful noninvasive modality for detecting myocarditis and it has been reported also that it may help in directing endomyocardial specimen collection [2, 3, 5, 11]. This technique can evaluate 3 markers of myocardial injury, namely intracellular and interstitial edema, hyperemia and capillary leakage, and necrosis and fibrosis [12]. A recent consensus statement recommended that cardiac magnetic resonance imaging should be performed in symptomatic patients with a clinical suspicion of myocarditis, if the imaging results would be expected to affect clinical management [12]. Three imaging criteria have been proposed for determining myocarditis (the "Lake Louise Criteria": signal increase in T2-weighted images, increased early gadolinium enhancement in T1-weighted images and a non-ischemic distribution of a lesion in late gadolinium enhancement in T1-weighted images). Two or three positive criteria can predict myocardial inflammation quite reliably, but late gadolinium enhancement findings alone, as in our case, are associated with a drop in diagnostic accuracy [12].

Concerning radionuclide imaging, ^{67}Ga -citrate and ^{111}In -antimyosin scintigraphy have been found efficient in detecting myocardial inflammation and necrosis, respectively, but their use in the assessment of myocarditis has declined mainly because of a relatively low specificity and availability issues [2, 5, 13, 14]. The radiopharmaceutical ^{99m}Tc -depreotide is a synthetic somatostatin analogue which has been approved for the assessment of solitary pulmonary nodules and has been tested successfully also in various malignant and inflammatory disorders [15-20]. Depreotide binds with somatostatin receptors (subtypes 2, 3 and 5) which are over-expressed on the cell surfaces of activated lymphocytes and macrophages and thus this agent allows the visualization of inflammatory processes.

Earlier reports concluded on myocardial inflammatory involvement in two patients with sarcoidosis and one patient with thrombotic thrombocytopenic purpura using ^{99m}Tc -depreotide scintigraphy [18, 21]. More recently, three more cases were presented with increased myocardial depreotide uptake, which was attributed to myocarditis secondary to orchitis-epididymitis, peripartum cardiomyopathy, and immune or interferon induced myocarditis [22]. However, in none of those publications was there histopathological confirmation of disease in the myocardium, whereas the diagnoses were made on clinical grounds, supported also by laboratory and cardiac imaging findings.

In the present case, the heart abnormality in ^{99m}Tc -depreotide imaging was consistent with the overall clinical impression, reinforced cardiac magnetic resonance findings, suggested persistent inflammatory reaction and facilitated the decision to proceed with right-heart catheterization and cardiac tissue sampling. More importantly, the abnormality in somatostatin receptor imaging was substantiated by an endomyocardial biopsy established diagnosis (of herpes virus myocarditis). As such, this is a new addition to the lit-

erature and furthers previous reports. Admittedly, management decisions in our patient may have been affected somehow by local experience and availability of imaging facilities. Nevertheless, this case corroborates the concept of cardiac nuclear imaging with somatostatin analogues as an adjunct in the evaluation of patients likely to suffer from myocarditis. However, assigning a particular clinical role and determining an optimal time window for somatostatin receptor scintigraphy in the course of the disease are open to clinical investigation.

In conclusion, this case report supports the utility of somatostatic analogues imaging in myocarditis by linking positive scintigraphic findings with myocardial inflammation of a viral origin, which was established with endomyocardial biopsy.

The authors declare that they have no conflicts of interest.

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