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Acute myocardial injury, MINOCA, or myocarditis? Improving characterization of coronavirus-associated myocardial involvement

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This commentary refers to 'Acute myocarditis presenting as a reverse Tako-Tsubo syndrome in a patient with SARS-CoV-2 respiratory infection', by S. Sala *et al.*, doi:10.1093/eurheartj/ehaa286.

In severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, acute myocardial injury, mainly defined as troponin release, has been associated with adverse outcome, as well as male gender, older age, and cardiovascular comorbidities. The underlying mechanisms are yet to be elucidated; myocarditis has been proposed as a possible explanation.

In clinical practice, when myocardial injury is associated with typical chest pain, an acute coronary syndrome should be suspected. If subepicardial coroanary artery disease (CAD) is ruled out, alternative causes of myocardial infarction with non-obstructive coronary arteries (MINOCA) should be investigated (e.g. microcirculatory endothelial dysfunction and procoagulant states). Myocarditis with pseudo-infarct presentation is a differential diagnosis of MINOCA.

According to the WHO definition,[1] myocarditis is an inflammatory disease of the myocardium diagnosed by established histological, immunological, immunohistochemical, and molecular criteria; endomyocardial biopsy (EMB) is necessary to achieve a diagnosis of certainty and identify its cause.[1] Cardiac magnetic resonance (CMR) provides non-invasive morphofunctional and tissue characterization, but it does not identify aetiology, e.g. SARS-CoV-2 viral myocarditis.[1] So far, EMB has been performed in two COVID-19-positive cases from Italy;[2,3] diagnostic criteria for myocarditis were met in only one.[2] Both studies failed in demonstrating SARS-CoV-2 localization within cardiomyocytes, thus conclusive proof that SARS-CoV-2 infects the cardiomyocytes leading to direct virus-induced necrosis and troponin release, i.e. viral myocarditis, is still lacking.[2,3] The only histologically confirmed case, who presented with an inverted Takotsubo pattern in the course of SARS-CoV-2 infection, turned out to be a virus-negative immune-mediated myocarditis, which constitutes a relevant proportion of myocarditis cases.[2] Takotsubo syndrome (TTS) is a possible cause of MINOCA, but again a diagnosis of certainty of TTS requires histological exclusion of myocarditis, which can mimick TTS,[1] as shown by another case of acute myocarditis presenting as TTS:[4] fluctuations in troponin, recovery of systolic function, and CMR signs of oedema are features that can be found in both myocarditis and TTS.[2,4]

In conclusion, in the setting of COVID-19 infection, we strongly encourage the use of the term 'myocarditis' referring only to EMB/autopsy-proven diagnosis.[1] We think that indication of EMB/CMR should be restricted to selected young COVID-19 patients with life-threatening presentations and few or no cardiovascular comorbidities, after excluding CAD, MINOCA, and other possible causes of secondary myocardial injury, such as the cytokine storm or hypoxia. More EMB/autopsy data are needed to establish the mechanisms of myocardial injury in COVID-19, including its potential role as a new cause of viral myocarditis. A recent autopsy report in a series of COVID-19 patients describes endothelial cell infection in several organs, including the heart vessels, with no sign of lymphocytic myocarditis.[5] The authors suggest that COVID-19 endothelialitis could lead to endothelial cell dysfunction. This would explain acute myocardial injury and its prognostic relevance, particularly in vulnerable COVID-19 patients with pre-existent endothelial dysfunction, due to old age, male gender, smoking, hypertension, diabetes, obesity, and established cardiovascular disease. This observation, if confirmed, could provide the missing link between acute myocardial injury in COVID-19 and dismal prognosis.

Conflict of interest: none declared.

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