Acute myocarditis: can novel echocardiographic techniques assist with diagnosis?

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Two-dimensional echocardiography has historically played a limited role in the diagnosis of acute myocarditis because of a lack of specific diagnostic features. The emergence of novel echocardiographic modalities such as strain and myocardial perfusion imaging have greatly augmented the scope of echocardiography, permitting the assessment of myocardial contractility, blood flow, and microvascular integrity. However, the application of these cutting-edge techniques in the diagnosis of acute myocarditis is still at a nascent stage. We present a case of acute myocarditis where echo-based strain imaging/mapping and real-time myocardial contrast echocardiography enabled the detection of regional contractile and perfusion abnormalities, not otherwise apparent with conventional echocardiography. These findings and the final diagnosis were later confirmed by cardiac magnetic resonance imaging. This case highlights the potential utility of novel echocardiographic techniques in the diagnostic workup of acute myocarditis and underscores the need for prospective studies to assess the sensitivity and specificity of these newer technologies. To our knowledge, this is the first report of a multimodality echocardiographic approach towards the diagnosis of myocarditis.

Keywords
Two-dimensional strain imaging • Speckle tracking • Myocardial perfusion echocardiography

Introduction

Myocarditis presents in myriad ways, often mimicking acute coronary syndrome on initial presentation. Conventional two-dimensional (2D) echocardiography has traditionally played a limited role in the diagnostic armamentarium for acute myocarditis.1,2 The advent of novel echocardiographic modalities such as strain and myocardial perfusion imaging have dramatically expanded the scope of echocardiography, providing accurate bedside assessment of regional contractility, myocardial blood flow, microvascular integrity and function.3,4 Whether or not these newer techniques have incremental utility over conventional echocardiography in the diagnosis of myocarditis is unclear. We present a case of acute myocarditis wherein a multimodality echocardiographic approach was adopted. Two-dimensional echocardiographic strain (2D strain) imaging and myocardial contrast echocardiography were performed as part of the initial diagnostic workup, and findings later confirmed with cardiac magnetic resonance (CMR) imaging.

Case report

This is the case of a previously healthy 17-year-old male with a recent viral prodrome who presented to the emergency department with chest pain for 3 days. The pain was precordial, stabbing in nature, and partially relieved by leaning forward. A review of his previous records did not reveal any significant past medical, surgical, or family history. Our patient was a non-smoker and denied history of substance abuse. The physical examination revealed a pericardial rub, but no other significant abnormalities.

At admission, patient’s vitals were stable. Laboratory values showed a WBC count of 27.1 × 10³/mm³, with neutrophilic predominance (81%) and a cardiac troponin-I level elevated at 22.78 ng/mL (Ref normal < 0.40 ng/mL). An electrocardiogram revealed diffuse ST-segment elevation in almost all precordial and limb leads and hyperacute T waves in leads V2 and V3 (Figure 1), and the chest X-ray was unremarkable. The pleuritic chest pain, the pericardial rub, diffuse ST and T wave changes and elevated cardiac troponins in a young previously healthy individual with a recent viral prodrome suggested a working diagnosis of myopericarditis, and an infectious workup to identify the disease aetiology was initiated. Serological testing revealed elevated Cox-sackie A9 titres at 1:16 (IgM); however, a repeat titre could not be measured to show seroconversion. An ANA titre was negative.

Imaging studies

The patient first underwent a 2D transthoracic echocardiography which revealed depressed left ventricular ejection fraction (EF...
35%) and a small pericardial effusion. Disproportionate thickening, echogenicity, and dyskinesis of the inferolateral wall suspicious of oedema were observed (Figure 2; Supplementary data online, Video S1). All echo images were acquired at 70 frames/s using a standard commercial ultrasound machine (Vivid 7, GE Vingmed, Horten, Norway) with a 2.5 or 3.5 MHz multiphased array probe, and the images digitally stored for offline strain analysis (EchoPacPC, GE Healthcare, Waukesha, WI, USA).

Significantly attenuated longitudinal strain in the inferior, inferolateral segments (−3% to −10%), as well as apical segments (−13%) was observed compared with preserved longitudinal strain in the anterior septum (−19%) (Figure 3; Supplementary data online, Video S2). Peak longitudinal strain mapped for all left ventricular segments is represented in polar map format (AFI, Automatic Function Imaging, GE) (Figure 3B). Attenuated radial and circumferential strain were also evident in these segments (Figure 4), with the inferolateral segment exhibiting paradoxical circumferential strain (systolic lengthening).

Real-time low-mechanical-index myocardial contrast echocardiography (RTMCE) with commercially available lipid-encapsulated microbubble Definity (perflutren lipid microspheres, DEFINITY®-Lantheus Medical Imaging, North Billerica, MA, USA) was performed using harmonic imaging (Vivid 7 scanner, GE Vingmed). Time intensity curves were sampled offline (regions of interest of 6.0 mm × 3.0 mm) using the Echo PAC workstation. Real-time myocardial contrast echocardiography revealed attenuated perfusion with delayed contrast replenishment (see wash-in time intensity curves) in the above-referenced segments compared with adjacent unaffected segments. The aforementioned findings were indicative of compromised microvascular integrity and a reduction of capillary bed area in the involved segments (Figure 5; Supplementary data online, Video S3). When viewed in entirety, data were highly suggestive of myocarditis, with the most severe involvement apparent in the inferolateral segments.

The abnormalities detected on echocardiography were later confirmed by gadolinium-enhanced CMR using a 1.5 T whole-body scanner. Cardiac magnetic resonance showed an LVEF of 37% and verified the area of irregular and asymmetric wall thickening involving the inferolateral wall. This area also revealed increased T2-weighted signal (confirming tissue oedema), and post-contrast images showed delayed enhancement which appeared to be
epicardial-based and transmural with sparing of the subendocardium (Figure 6).

Our patient recovered uneventfully with non-steroidal anti-inflammatory agents to follow-up in the cardiology clinic. Follow-up CMR 6 months later showed improved EF of 44%, resolution of the asymmetric wall thickening, and dyskinesis but residual epicardial-based transmural-delayed enhancement of the inferolateral walls, consistent with fibrosis secondary to irreversible myocarditis-associated injury.

Discussion

Accurate diagnosis of myocarditis hinges on an integrated assessment that incorporates historical, electrocardiographic, biomarker, imaging, and endomyocardial biopsy data. No single imaging modality has the capability to diagnose myocarditis with absolute certainty. Conventional echocardiography has traditionally played a limited role in the diagnosis of suspected myocarditis because of the lack of specific distinguishing features and/or apparently normal examinations encountered in less severe forms of myocarditis. Nevertheless, segmental and global wall motion abnormalities do occur, and patterns of hypertrophic, dilated, and restrictive cardiomyopathy have been reported in histologically proven myocarditis.

Our patient had evidence of regional oedema, patchy myocardial perfusion abnormalities, and parallel regional contractile dysfunction as evident from strain mapping. Although oedema was apparent visually in our case, strain and RTMCE
imaging revealed additional areas of dysfunction, not apparent to the naked eye (off conventional echocardiographic images), involving multiple coronary distributions. These abnormalities correlated closely with findings on CMR. In broad terms, perfusion defects that do not conform to a known coronary distribution should raise the clinical suspicion of myocarditis in the appropriate setting. Although areas of necrosis and inflammation have been demonstrated to result in myocardial perfusion defects on nuclear perfusion imaging, to our knowledge, no prior reports of myocardial contrast echocardiography in the setting of acute myocarditis exist in the literature.

Late gadolinium enhancement on T1-weighted images represents necrosis and inflammatory injury. In patients with myocarditis, it typically occurs focally, is subepicardial-based, and extends variably into the ventricular wall, with a predilection for the inferolateral segments. T2-weighted imaging reliably detects

Figure 5 Real-time myocardial contrast echocardiography time intensity curves, showing attenuated perfusion with delayed contrast replenishment in the basal inferolateral segment (yellow), mid-inferolateral wall (blue), apex (red), and mid-anterior septum (green), timed immediately after a high-energy flash ultrasound pulse. Fitted replenishment curves for corresponding areas show attenuated plateau contrast levels and late contrast plateauing in all regions other than the septum (preserved perfusion). Findings suggest disruption of microvasculature in the inferolateral and apical segments.

Figure 6 (A) Short-axis dark blood T2-weighted cardiac magnetic resonance imaging showing asymmetric thickening consistent with extensive myocardial oedema in the inferior and inferolateral segments of the left ventricle. (B) Short-axis delayed enhanced imaging demonstrating extensive enhancement of mid-wall and epicardium with sparing of the subendocardium.
tissue oedema with the long T2 of water-bound protons as the contrast-generating mechanism, generating high signal intensity in oedematous tissue. In our patient, the region of oedema detected on echo correlated with that detected on CMR; these segments exhibited the most severe strain (contractile) dysfunction and perfusion abnormalities on RTMCE. Notably, CMR without (T2-weighted images) and with contrast media (delayed enhancement technique) has emerged as the diagnostic tool of choice for the non-invasive diagnosis of myocardial inflammation and suspected myocarditis. However, the technique is expensive (particularly for serial monitoring), not widely available, and lacks portability.

As illustrated in our case, newer echocardiographic modalities are potentially useful techniques (excellent correlation with CMR) and can provide incremental information, beyond 2D echocardiography, in suspected myocarditis. Although the diagnosis in our patient was evident on conventional echo and electrocardiographic findings, these newer modalities appear to be more sensitive and may be of a particular value when clinical ambiguity in diagnosis exists. Two-dimensional strain echocardiography, in particular, because of its favourable signal-to-noise ratio, angle independence, and ability to differentiate between active and passive myocardial movements could be used to map and quantify regional contractile function in myocarditis. However, caution with the interpretation of RTMCE and strain data needs to be observed, as perturbations similar to those described in our report may be encountered in the setting of acute transmural myocardial infarction.

Finally, the sensitivity and specificity of these newer echocardiographic techniques for the diagnosis of myocarditis are not known at this time, and need to be prospectively studied against CMR/endomyocardial biopsy.

**Supplementary data**

Supplementary data are available at European Journal of Echocardiography online.

**Conflict of interest:** none declared.

**References**