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CASE REPORT
Inherited cardiac conditions/cardiomyopathies

Myocarditis with concomitant tuberculosis infection presenting with solitary ventricular tachycardia: a case report

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Background Myocarditis is an infrequent extrapulmonary manifestation of tuberculosis that confers an unfavourable prognosis.

Case summary A 36-year-old man presented to the hospital with palpitations and dyspnoea. Tests revealed the presence of non-sustained ventricular tachycardia, with mild elevation of troponin and C-reactive protein levels. Coronary angiography showed normal results. A cardiac magnetic resonance (CMR) showed moderate hypertrophy, preserved ejection fraction, and an extensive multisegmental pattern of fibrosis and oedema. An ^{18}F-fluorodeoxyglucose positron emission tomography–computed tomography (^{18}F-FDG-PET–CT) scan revealed multiple hypermetabolic adenopathies and patchy cardiac uptake. A tuberculin skin test and interferon-gamma release assay were both positive. An endomyocardial biopsy (EMB) showed inflammation without granulomas; and microbiological stains were negative. Biopsy of an adenopathy revealed the presence of multiple necrotizing granulomas with Langhans cells. Based on the test results and clinical presentation, the suspected diagnosis was tuberculous myocarditis. Treatment with anti-tuberculosis drugs was started. One month later, the presence of mycobacterium tuberculosis (MT) was detected in the lymph node culture. At 7 months of follow-up, the patient remains asymptomatic, ventricular arrhythmias have ceased, and radiological signs of inflammation have resolved.

Discussion Ventricular arrhythmia is one of the clinical manifestations of tuberculous myocarditis. Cardiac magnetic resonance and ^{18}F-FDG-PET–CT imaging are an essential component of the non-invasive evaluation of inflammatory cardiomyopathy. However, a confirmatory biopsy may be required to identify potentially treatable aetiologies. Although the diagnosis of tuberculous myocarditis requires an isolation of MT by staining or culture in EMB, the diagnostic yield is very low. For this reason, extra-cardiac findings may provide the definitive diagnostic clue.

Keywords Ventricular tachycardia • Myocarditis • Tuberculosis • Cardiac magnetic resonance • Positron emission tomography • Case report

ESC curriculum 2.3 Cardiac magnetic resonance • 2.5 Nuclear techniques • 5.6 Ventricular arrhythmia • 6.5 Cardiomyopathy

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Learning points

- In the differential diagnosis of a patient with ventricular tachycardias and preserved ejection fraction, tuberculous myocarditis should be considered in addition to sarcoidosis, especially if adenopathies coexist.
- The diagnostic process of inflammatory cardiomyopathy is complex and requires a multimodal approach including cardiac magnetic resonance and ^{18}F-fluorodeoxyglucose positron emission tomography–computed tomography, as well as multidisciplinary work, to achieve an accurate diagnosis and precise treatment.
- Atypical presentations of old diseases such as tuberculous myocarditis may become a new reality in a globalized world. Therefore, cardiologists should have an open-minded approach when such new challenges present before them.

Introduction

Tuberculosis (TB) was the leading cause of death from an infectious disease prior to the COVID-19 pandemic, and it is still one of the most common causes of death worldwide.[1] One of the possible extrapulmonary manifestations of TB is cardiovascular involvement, which confers an unfavourable prognosis. The most commonly involved structure is the pericardium, although myocardial and aortic involvement have also been reported.[2,3]

Tuberculous myocarditis accounts for <2% of cases of myocarditis and mainly affects young, immunocompetent males. This rare form of TB manifestation can present as conduction disturbances (ventricular arrhythmias, new-onset or intermittent bundle branch block, long QT syndrome, or cardiac arrest) and heart failure symptoms.[3–7]

Summary figure

−10 years	Moved from India to Catalonia
−2 months	Contact with a tuberculosis-positive person
−1 week	Approximate onset of symptoms (palpitations and dyspnoea)
Day 0	Presentation to the emergency department with dyspnoea and palpitations: electrocardiogram with ventricular extrasystoles and non-sustained ventricular tachycardia Bisoprolol initiation
+7 days	Cardiac magnetic resonance (CMR) reveals moderate hypertrophy in the left ventricle with preserved left ventricular ejection fraction and an extensive non-ischaemic fibrosis pattern with signs of oedema
+8 days	Sustained ventricular tachycardia Amiodarone initiation
+14 days	^{18}F-fluorodeoxyglucose positron emission tomography–computed tomography (^{18}F-FDG-PET–CT) shows multiple supra- and infra-diaphragmatic hypermetabolic adenopathies and patchy cardiac uptake
+15 days	Bronchoscopy with a bronchoalveolar lavage that shows a 1.2 CD4/CD8 ratio and inconclusive result of a fine-needle aspiration of the subcarinal adenopathy
+23 days	An endomyocardial biopsy (EMB) shows inflammation without granulomas. Microbiological stains and cultures are negative, including mycobacterium tuberculosis deoxyribonucleic acid (MT-DNA)
+27 days	Right supraclavicular adenopathy biopsy study identifies multiple necrotizing granulomas and Langhans cells, without any evidence of a lymphoproliferative disorder. Mycobacterium tuberculosis is not found in the Ziehl–Neelsen stain, but copies of MT-DNA are detected Anti-tuberculosis treatment initiation (quadruple therapy)
+2 months	Tuberculosis culture of the supraclavicular adenopathy is confirmed positive, but results are negative in the EMB sample. Clinically, the patient becomes asymptomatic and ventricular arrhythmias cease
+3 months	Switch to bitherapy with isoniazid and rifampicin
+8 months	Resolution of oedema and reduction of fibrosis on CMR and complete resolution of adenopathic and cardiac uptake on ^{18}F-FDG-PET–CT
+10 months	End of anti-tuberculosis treatment

Case summary

A 36-year-old man presented to the emergency department of the hospital complaining of palpitations and dyspnoea that started 1 week before presentation. At arrival, he presented with stable vital signs and an unremarkable physical examination. An electrocardiogram (ECG) showed sinus rhythm with frequent monomorphic ventricular extrasystoles and negative T inferior waves (*Figure 1A*). Basal high-sensitivity troponin T levels (23–26 ng/L) were slightly above normal (<13 ng/L). The chest X-ray result was normal (*Figure 2*). A transthoracic echocardiography revealed mild hypertrophy and preserved left ventricular ejection fraction (LVEF) without segmental contractility defects. During cardiac monitoring, we observed symptomatic runs of slow non-sustained ventricular tachycardia (NSVT) (*Figure 1B*).

The patient had no relevant personal or family medical history, no cardiovascular risk factors or history of drug abuse, and did not complain of any previous episode of chest pain, dyspnoea, arrhythmia, or syncope. He had no fever or cough prior to admission. The patient was born in India and moved to Catalonia in 2013. However, he denied having undertaken any recent trips abroad.

Based on this clinical presentation, the repolarization abnormalities, and the mildly elevated troponin levels, the differential diagnosis included the following: NSVT in the setting of an acute coronary syndrome, myocarditis, or idiopathic ventricular tachycardia.

The test result of coronary angiography was normal. The findings of a blood test ruled out electrolyte disturbances and ferritin levels, and the patient's renal and thyroid function were normal. The N-terminal prohormone level of brain natriuretic peptide was also normal (55 ng/L). However, C-reactive protein levels were mildly elevated (7.8 mg/L vs.

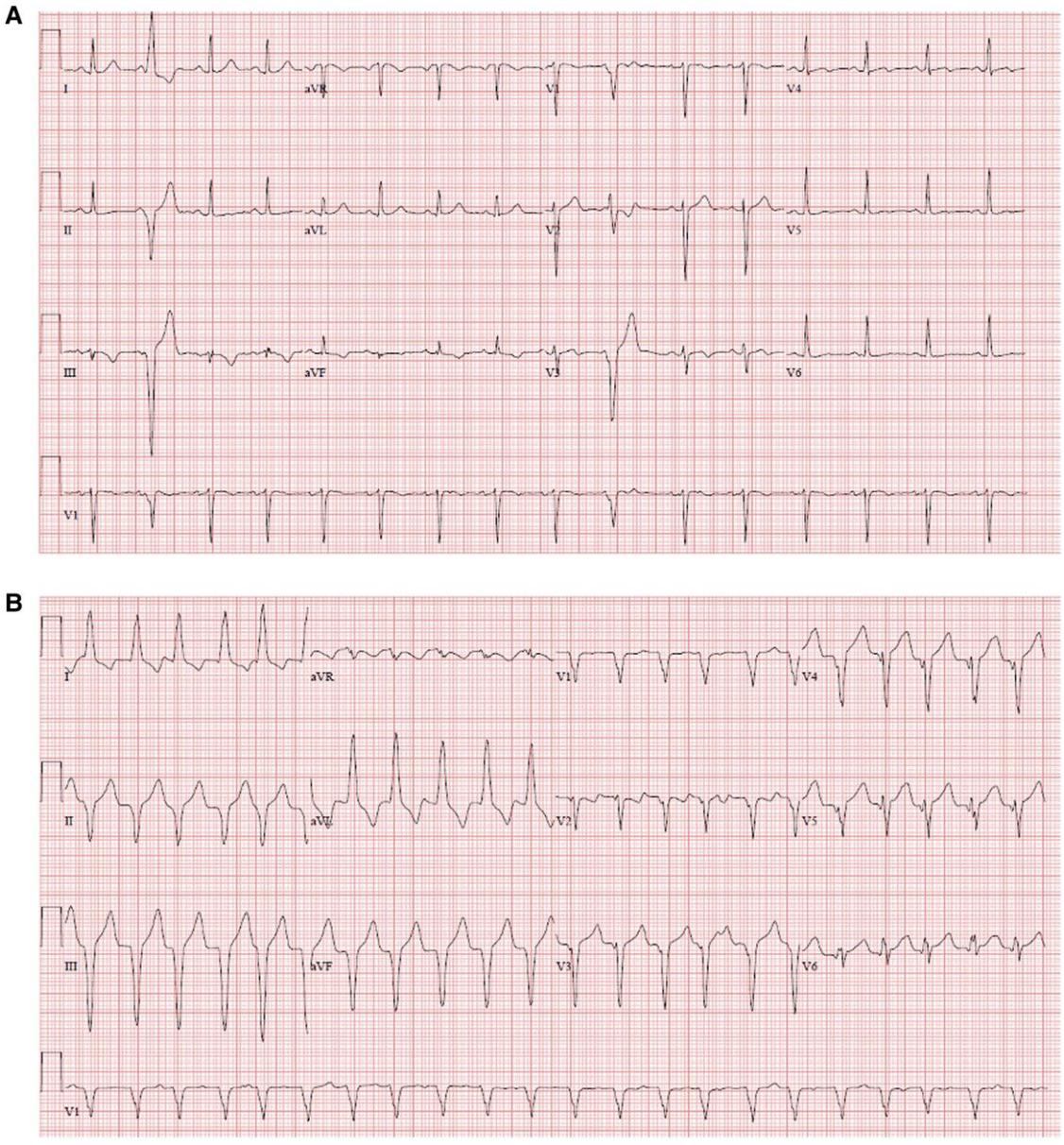

Figure 1 Initial electrocardiogram and electrocardiogram during tachycardia. (*A*) Electrocardiogram at admission showing negative T waves in the inferior leads. (*B*) Electrocardiogram on Day 7 shows a monomorphic non-sustained ventricular tachycardia with a superior axis, left bundle blanch block morphology, and transition at V5, suggesting an inferior-mid-apical septum origin. ECG, electrocardiogram.

normal levels of <5 mg/L). The patient was hospitalized under continuous cardiac monitoring. Despite the administration of increasingly greater doses of bisoprolol, he presented a haemodynamically well-tolerated and self-limited episode of sustained ventricular tachycardia (42 s). Consequently, high doses of amiodarone were initiated, which significantly reduced the arrhythmic burden.

A cardiac magnetic resonance (CMR) showed a moderately hypertrophied left ventricle with a preserved LVEF and an extensive non-ischaemic pattern of fibrosis [subepicardial in the basal-anterior septum and almost transmural in the inferior-mid-apical septum (*Figure 3A*)] with signs of oedema (*Figure 3B*). Fibrosis burden was calculated to be 12.24 g (18.8% of the total LV mass). We also observed a non-dilated right ventricle with a slightly depressed systolic function (44%) without fibrosis, a normal pericardium, and the presence of subcarinal and right perihilar adenopathies.

Given these signs and symptoms, there was a high suspicion of a granulomatous disease. Consequently, an ^{18}F-fluorodeoxyglucose positron emission tomography–computed tomography (^{18}F-FDG-PET–CT) scan with protocol to display inflammation was performed, showing multiple supra- and infra-diaphragmatic hypermetabolic adenopathies and patchy cardiac uptake (*Figure 4A* and *B*).

Based on these findings, we performed a dedicated/focused/thorough medical history/anamnesis, during which the patient reported having had one contact with a TB-positive person 2 months before onset of symptoms (they shared a dinner together for ∼2 h in a closed room). He denied experiencing weight loss, fever, night sweats, asthenia, or

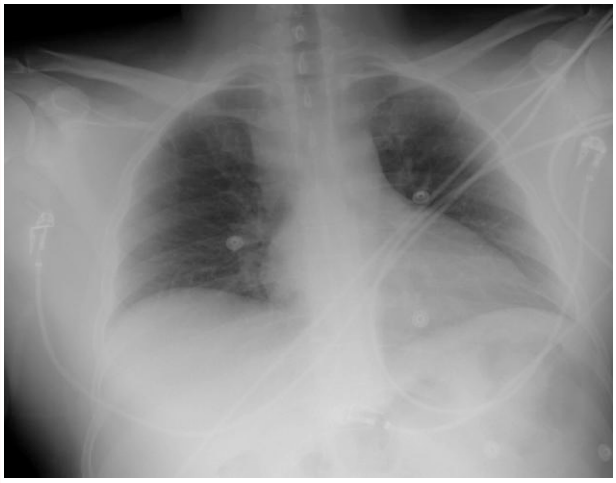

Figure 2 Chest X-ray at admission. Anteroposterior supine chest X-ray performed with a portable machine on Day 0 showed normal results with no signs of vascular redistribution or notable alterations in the lung parenchyma.

other systemic symptoms. A tuberculin skin test and interferon-gamma release assay (IGRA) were performed, both of which were positive for TB. Serum angiotensin-converting enzyme activity was slightly elevated (74 U/L vs. normal levels <60 U/L). A test done for the presence of human immunodeficiency virus (chemiluminescent microparticle immunoassay method) showed a negative result.

An endomyocardial biopsy (EMB) revealed the presence of inflammation without granulomas, and the results of microbiological stain and culture tests were negative, including a test result of mycobacterium tuberculosis deoxyribonucleic acid (MT-DNA). A bronchoalveolar lavage was performed, which showed a CD4:CD8 ratio of 1.2. Fine-needle aspiration of the subcarinal adenopathy showed inconclusive findings. Finally, a biopsy of a right supraclavicular adenopathy identified the presence of multiple necrotizing granulomas and Langhans cells, without any evidence of a lymphoproliferative disorder (*Figure 5*). Although no evidence of MT was found in the Ziehl–Neelsen stain, copies of MT-DNA were detected.

Once the diagnosis of acute myocarditis was confirmed, and given the high suspicion of TB, anti-tuberculosis therapy was started (with daily doses of isoniazid 375 mg, rifampicin 750 mg, pyrazinamide 2000 mg, and ethambutol 1375 mg).

The findings of the culture of the affected node were received ∼1 month after discharge. The culture test result was positive for TB, but in the EMB sample, the result was negative. After the initiation of anti-TB treatment, the ventricular arrhythmias ceased, and the patient remained asymptomatic. He maintained good adherence to the treatment regimen and had no tolerability issues.

Imaging and laboratory tests confirmed the absence of signs of inflammation. A CMR performed 7 months after discharge showed resolution of the oedema and a decrease in fibrosis (6.92 g, −10.6% LV mass). Complete resolution of adenopathic and cardiac uptake was evidenced on the ^{18}F-FDG-PET–CT scan (*Figures 4* and *6*). After 2 months of quadruple therapy, a course of isoniazid and rifampicin was continued for 7 more months because of the good tolerability to this treatment (total duration: 9 months). In addition, two 24 h Holter ECGs were performed and no arrhythmias were documented. Because of the patient's excellent clinical and radiological response, we decided not to implant a defibrillator (ICD).

Discussion

In this study, we described the case of a patient with myocarditis presenting with ventricular arrhythmias and a concomitant diagnosis of TB infection. After anti-TB treatment, no arrhythmias were documented, evidence of inflammation disappeared, and late gadolinium enhancement (LGE) burden decreased. Consequently, it was decided not to implant an ICD. The multimodal approach to the case (combining magnetic resonance imaging, ^{18}F-FDG-PET–CT scan, and histology) was crucial in arriving at the final diagnostic orientation. Even though isolation of MT in the myocardial tissue was not possible, the final diagnostic judgement was based on evidence of non-invasive myocardial inflammation and extra-cardiac MT isolation, together with good clinical response, after specific treatment initiation.

Certainty diagnosis of tuberculous myocarditis requires isolation of MT by staining or culture of the myocardial tissue obtained by EMB. However, no cases of TB myocarditis with microbiological isolation on EMB have been published.[4–8] Endomyocardial biopsy is a highly complex procedure with potentially lethal complications, and it is available only at tertiary care centres. For this reason, diagnosis is usually made by using non-invasive techniques (such as CMR) with extra-cardiac isolation of MT. In fact, CMR has become a cornerstone in the assessment of inflammatory cardiomyopathy. Our patient met two of the main updated (2018) Lake Louise diagnostic criteria.[9] ^{18}F-fluorodeoxyglucose positron emission tomography–computed tomography has proved useful for detecting asymptomatic MT infection in other organs (e.g. lymph nodes) and for the definitive diagnosis of TB by guided biopsy.

In the differential diagnosis of inflammatory cardiomyopathy with adenopathies, it is important to consider sarcoidosis and lymphoproliferative diseases.[8] Angiotensin-converting enzyme levels are neither sensitive nor specific, and the presence of TB can lead to false positives. In this patient case, the absence of tuberculin anergy, the CD4/CD8 ratio, and the type of granuloma were not suggestive of sarcoidosis. In patients in whom other tests are not diagnostic, a confirmatory biopsy is essential, because treatments as different as corticosteroids or antimicrobials may be indicated. In patients with unexplained ventricular arrhythmias refractory to treatment, EMB may be indicated to identify potentially treatable aetiologies.[10]

In our patient, antibacterial treatment was started based on the high suspicion of tuberculous myocarditis, prior contact with another TB patient, positive tuberculin and IGRA skin tests, positive MT-DNA, and a histopathologic pattern on the nodal biopsy suggestive of TB. However, both idiopathic myocarditis with concomitant extra-cardiac TB and necrotizing sarcoid granulomatosis could not be ruled out. Although the presence of a negative culture and negative MT-DNA in the EMB represent a notable gap in confirming the diagnosis of tuberculous myocarditis, it is important to note that the diagnostic yield of these techniques is unknown; moreover, to our knowledge, MT has not been isolated in EMB to date. In contrast, the positive TB culture obtained from the supraclavicular node, together with good response (clinical, radiological, and blood parameters) after tuberculostatic treatment, clearly supports our diagnostic judgement.

Although a good response to standard anti-tuberculosis treatment has been described in patients with tuberculous pericarditis, no specific treatment regimen has been proposed for myocardial involvement. Similarly, while the role of corticosteroid therapy for the treatment of acute tuberculous pericarditis has become increasingly well established, its role in myocarditis remains unclear.[2,3,11]

With regard to the indications for ICD implantation, evidence is lacking in myocardial TB and scarce in inflammatory cardiac diseases.[12] In our patient, arrhythmias were haemodynamically well tolerated and confined to the initial inflammatory phase, and remission of inflammation was observed both analytically and by CMR and ^{18}F-FDG-PET–CT. Furthermore, the LGE burden was reduced, and no further arrhythmias

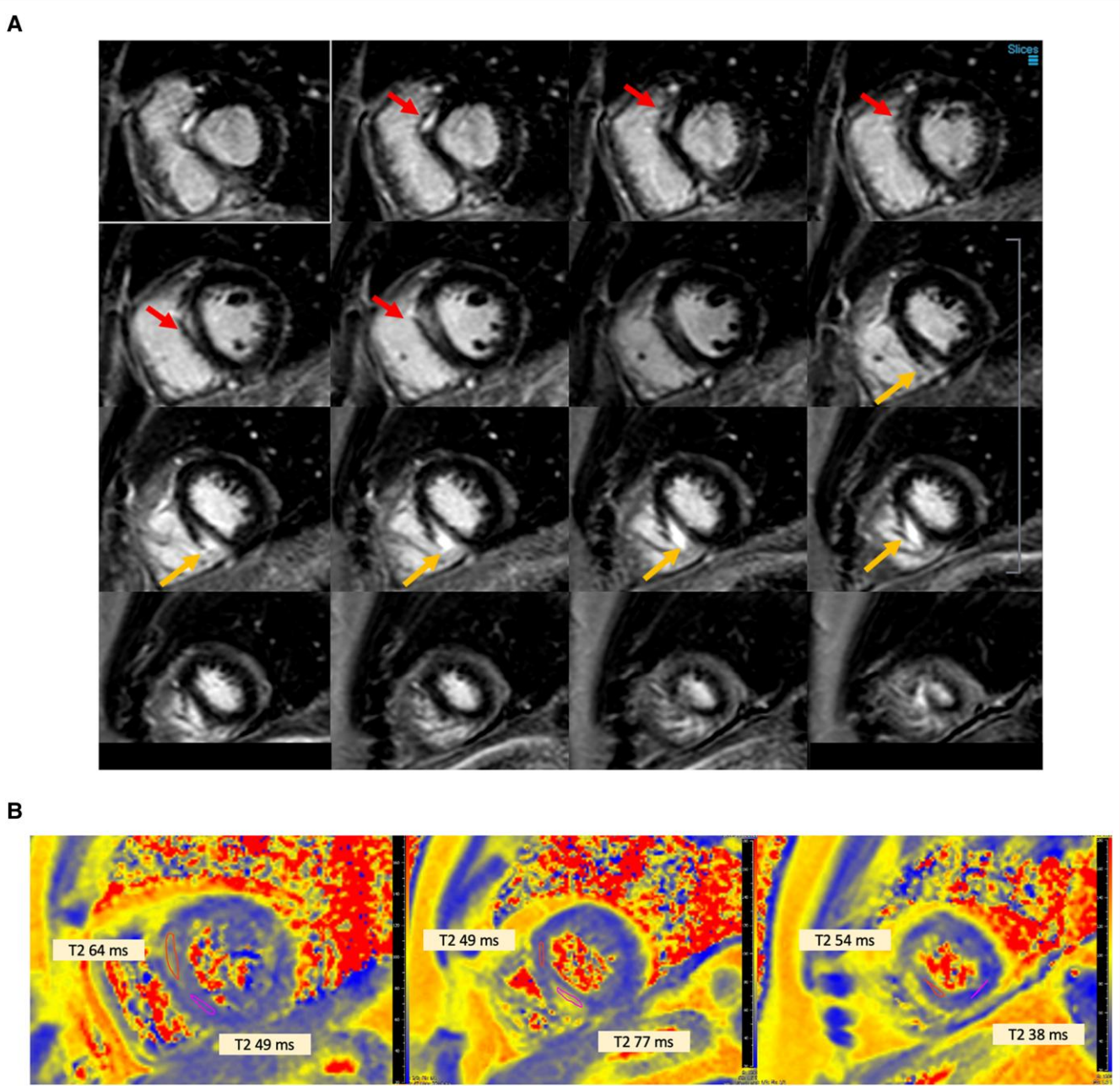

Figure 3 Cardiac magnetic resonance findings performed on Day 7 of admission (acute phase). (*A*) The late gadolinium enhancement in short-axis view shows a non-ischaemic pattern with diffuse patchy hyper-enhancement in the anteroseptal basal wall (red arrows) and in the mid inferoseptal and septal apical wall (yellow arrows). (*B*) Quantitative T2 map in the basal, mid, and apical short axis, respectively. The T2 mapping sequence shows elevated values of T2 time in the anteroseptal (64 ms) and inferoseptal (77 ms) segments consistent with the presence of myocardial oedema (normal <55 ms). CMR, cardiac magnetic resonance.

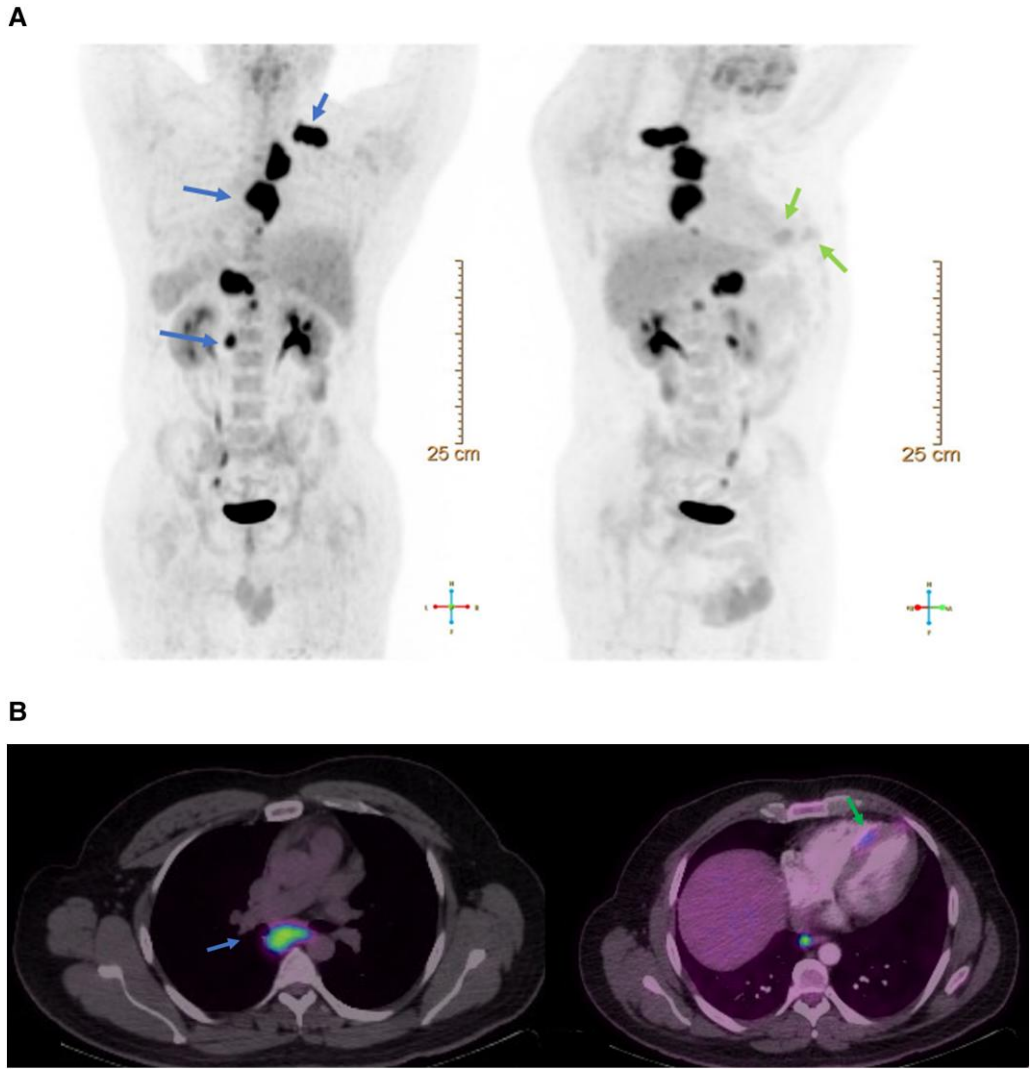

Figure 4 Comparative ^{18}F-fluorodeoxyglucose positron emission tomography–computed tomography findings (baseline and follow-up). (*A*) ^{18}F-fluorodeoxyglucose positron emission tomography images (anterior view in the left, and right semilateral in the right) performed on Day 10 showing the distribution zones of uptake of the radiotracer ^{18}F-fluorodeoxyglucose: multiple supra- and infra-diaphragmatic hypermetabolic adenopathies (blue arrows) and patchy cardiac uptake (green arrows). (*B*) In these ^{18}F-fluorodeoxyglucose positron emission tomography–computed tomography images, we can identify one of the paratracheal hypermetabolic adenopathies (blue arrow) and the myocardial uptake in the septal region (green arrow). (*C*) ^{18}F-fluorodeoxyglucose positron emission tomography performed after 7 months under anti-tuberculosis treatment shows a complete resolution of the uptakes. ^{18}F-FDG-PET–CT, ^{18}F-fluorodeoxyglucose positron emission tomography–computed tomography.

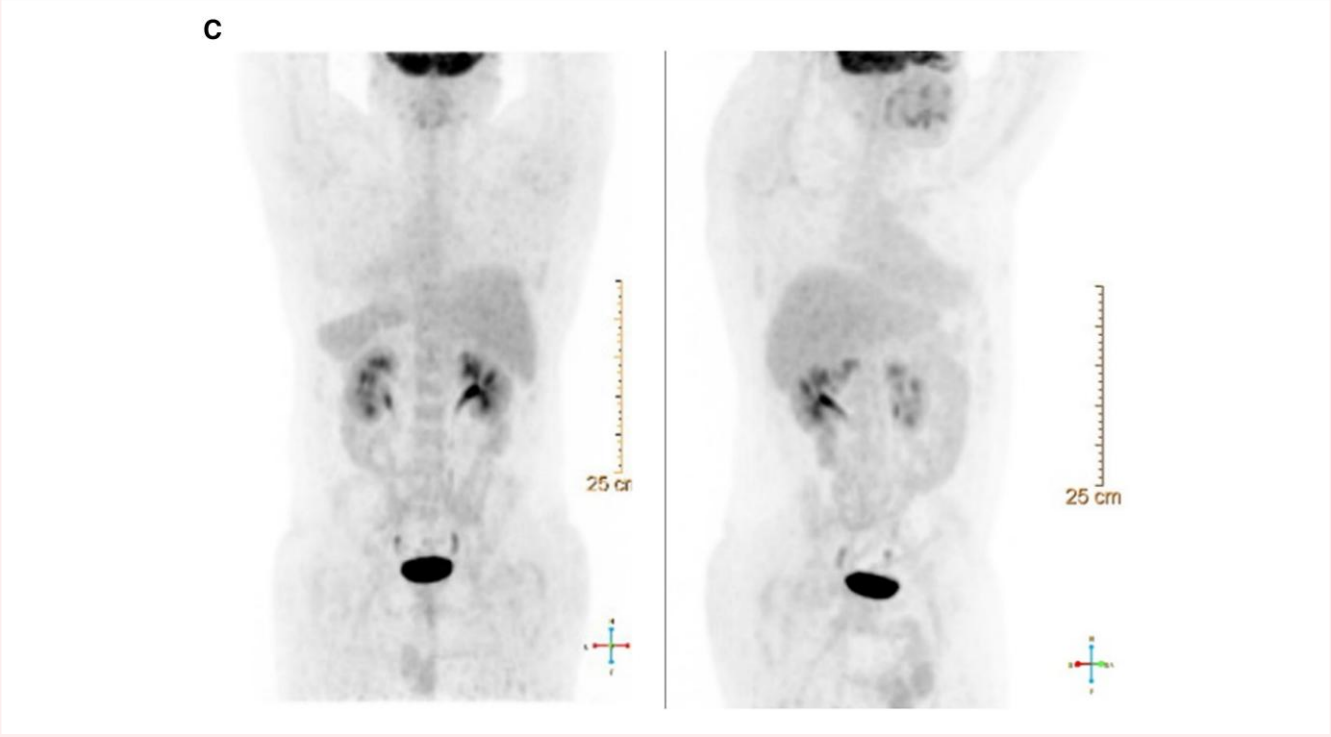

Figure 4 Continued

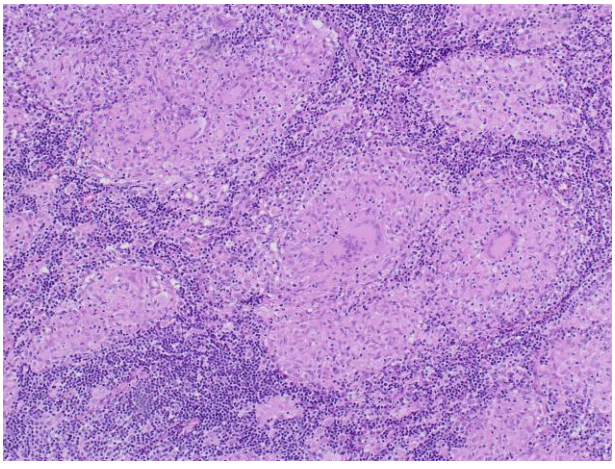

Figure 5 Supraclavicular adenopathy biopsy. Lymph node with effacement of the node architecture at the expense of multiple granulomas and occasional multinucleated giant cells (Langhans cells).

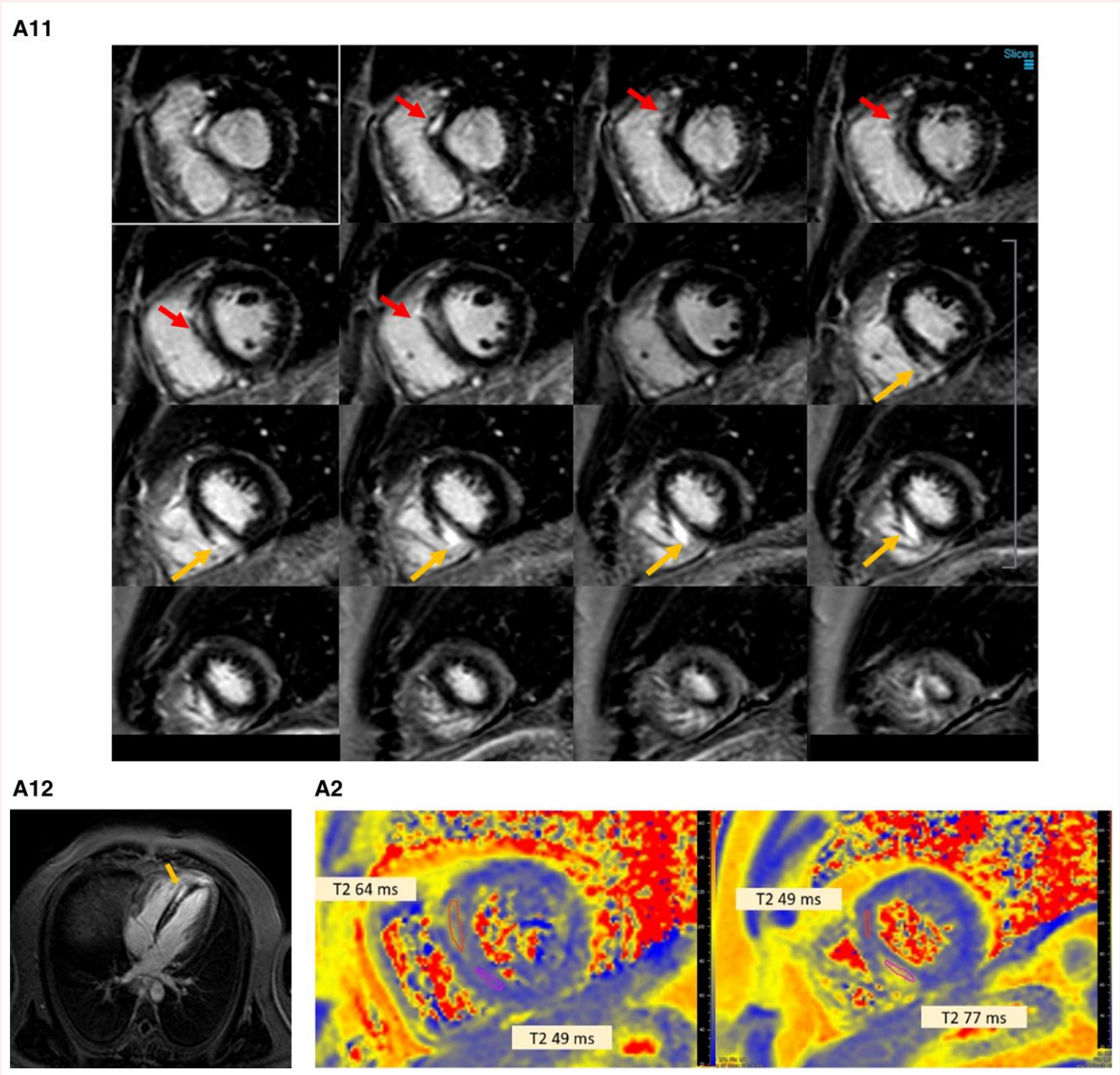

Figure 6 Comparative CMR findings (baseline and follow-up). (*A*) Baseline: The LGE in short-axis view (A11) and A4C view (A12) show a non-ischaemic pattern with diffuse patchy hyper-enhancement in the anteroseptal basal wall (red arrows) and in the mid inferoseptal and septal apical wall (yellow arrows). Quantitative T2 map in the basal and mid short axis, respectively (A2). The T2 mapping sequence shows elevated values of T2 time in the anteroseptal (64 ms) and inferoseptal (77 ms) segments consistent with the presence of myocardial oedema (normal <55 ms). (*B*) Follow-up: after 7 months with anti-tuberculosis treatment, CMR shows a decrease in transmurality and extension of LGE in short-axis view (B11) and A4C view (B12) both in the anteroseptal basal wall (red arrows) and in the mid inferoseptal and septal apical wall (yellow arrows). A resolution of the myocardial oedema is also observed compared with the acute phase (B2). The T2 mapping sequence shows normal values of T2 time in the anteroseptal (48 ms) and inferoseptal (52 ms) segments (normal <55 ms). CMR, cardiac magnetic resonance; LGE, late gadolinium enhancement; A4C, apical four chamber view.

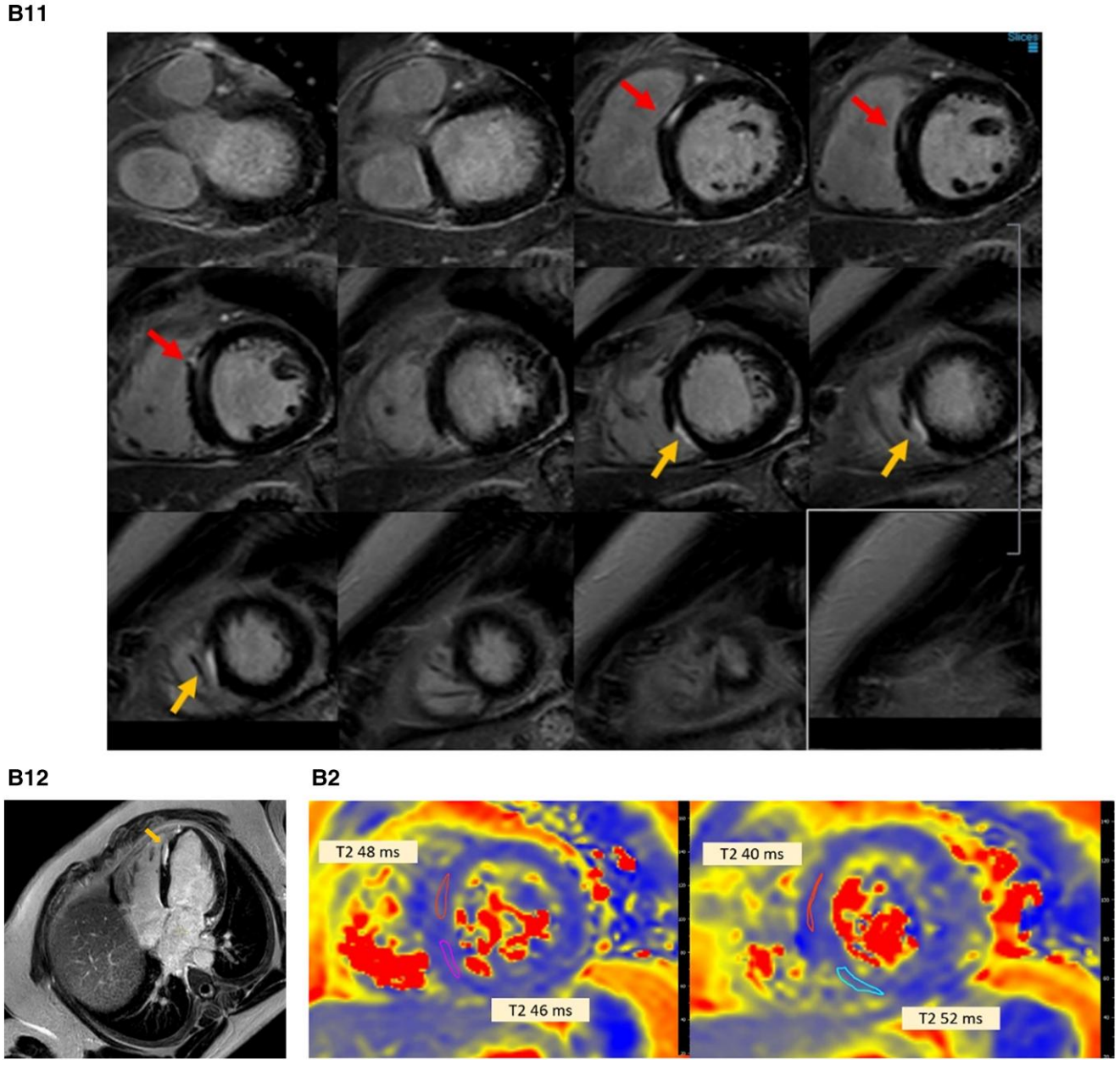

Figure 6 Continued

were found on follow-up Holter-ECG. Therefore, it was decided not to implant an ICD at this time.

Conclusions

This case report raises questions about how to address the situation where myocarditis and suspected TB coexist, and highlights the need for a multimodal diagnostic approach that includes CMR, ^{18}F-FDG-PET–CT, and histology in patients with inflammatory cardiomyopathy.

Lead author biography

David Belmar Clivillé is a cardiology resident at Hospital de la Santa Creu i Sant Pau in Barcelona. His areas of interest are in Clinical Cardiology, Cardiology, and Inherited Cardiac Diseases.

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Consent: The authors confirm that written consent for submission and publication of this case report, including images and associated text, has been obtained from the patient in accordance with COPE guidelines.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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