Myocardial infarction with non-obstructive coronary arteries (MINOCA) complicating myocarditis

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Abstract
Myocarditis can lead to myocardial infarction in the absence of coronary artery obstruction. We report a case of probable myocarditis, complicated by myocardial infarction with non-obstructive coronary arteries. A 19-year-old man presented with chest pain typical of myocarditis. He was a smoker but was otherwise well. Electrocardiogram revealed diffuse ST-elevation and echocardiography revealed a thin, akinetic apex. Troponin-T levels on admission were raised leading to an initial diagnosis of myocarditis being made. However, late gadolinium enhancement study on cardiac magnetic resonance imaging demonstrated transmural enhancement typical of ischaemia. Coronary angiogram was normal, leading to a likely diagnosis of myocardial infarction with non-obstructive coronary arteries. It is important to highlight that coronary assessment remains important when working up for myocarditis, as myocardial infarction with non-obstructive coronary arteries can often complicate myocarditis in cases of normal angiography. Another important lesson was on how cardiac magnetic resonance imaging provided vital evidence to support underlying ischaemia despite normal coronary angiogram, leading to a diagnosis of myocardial infarction with non-obstructive coronary arteries. Myocardial infarction with non-obstructive coronary arteries remains a broad ‘umbrella’ term and cardiac magnetic resonance imaging, as well as more invasive coronary imaging techniques during angiography, can further assist in its diagnosis. Our case provides a reminder that myocardial infarction with non-obstructive coronary arteries, although increasingly recognised, remains under-diagnosed and can often overlap with peri-myocarditis, highlighting the need to employ multi-modality imaging in guiding management.

Keywords
Myocardial infarction with non-obstructive coronary arteries, MINOCA, myocarditis, case report

Introduction
Myocarditis is an under-reported entity with variable clinical presentation and can mimic myocardial infarction. However, myocardial infarction with or without obstructed coronary arteries following myocarditis can also occur concomitantly. We report an unexpected case of probable myocarditis, complicated by myocardial infarction with non-obstructive coronary arteries (MINOCA), supported by both a suggestive cardiac magnetic resonance imaging (MRI) and a normal coronary angiography.

Case report
A 19-year-old man presented to our emergency department with episodes of chest pain. He described it as being sharp in nature, worse on both inspiration and lying down, and relieved on sitting forward. This was preceded by 2 days of feeling feverish. He was a heavy smoker (5 pack-years since the age of 14 years) but was otherwise well prior to this admission. There was no significant family history of sudden cardiac death or major adverse cardiac events.

His vitals on arrival included a blood pressure of 120/76 mmHg, heart rate of 110 beats per minute, respiratory rate of 16 per minute, oxygen saturation of 96% on room air, and
temperature of 36.5°C. Cardiorespiratory examination was unremarkable. Initial electrocardiogram performed revealed coved ST-segment elevation and associated PR segment depression in most leads aside from aVL, with ST-segment depression in aVR and V1. There were also T-wave inversions in leads V1 to V6 (Figure 1). Bedside echocardiography revealed low-normal ventricular systolic function (ejection fraction 52%) and demonstrated an akinetic apex (Figure 2). Peak troponin-T levels during this admission were 1678 ng/L (normal <14 ng/L).

Due to the patient’s age, clinical presentation and investigative findings, an initial diagnosis of myocarditis was made. The patient was commenced on oral ibuprofen 600 mg three times a day and admitted for observation and a cardiac MRI.

Figure 1. Electrocardiogram performed revealed coved ST-segment elevation and associated PR segment depression in most leads aside from aVL, with ST-segment depression in aVR and V1. There were also T-wave inversions in leads V1 to V6.

Figure 2. Cardiac imaging, including (a–d) echocardiography on apical four-chamber (a, b) and two-chamber (c, d) view in (a, c) diastole and (b, d) systole demonstrating apical akinesia, and (e–g) coronary angiography at (e) left anterior oblique and caudal view, (f) right anterior oblique and caudal view, and (c) right anterior oblique view revealing normal coronaries. LMS: left main stem; LAD: left anterior descending; LCx: left circumflex; RCA: right coronary artery.
Table 1. Blood investigations.

| Test                              | Results | Test                              | Results |
|-----------------------------------|---------|-----------------------------------|---------|
| Haemoglobin (g/L)                 | 110     | Hepatitis B serology              | Negative|
| White cell count (10⁹/L)          | 6.5     | Hepatitis B serology              | Negative|
| Platelet (10⁹/L)                  | 350     | HIV serology                      | Negative|
| Sodium (mmol/L)                   | 140     | C-reactive protein (mg/L)         | 117.2   |
| Potassium (mmol/L)                | 4.9     | Erythrocyte sedimentation rate (mm/h) | 13     |
| Urea (mmol/L)                     | 3.6     | Rheumatoid factor (IU/ml) (0-20)  | 8       |
| Creatinine (mmol/L)               | 86      | Anti-nuclear factor titre         | Negative|
| Troponin-T (<14 ng/L)             | 16.78   | Antineutrophil cytoplasmic antibodies titre | Negative|
| Aspartate aminotransferase (U/L)  | 48      | Lupus anticoagulant               | Negative|
| Creatine kinase (U/L)             | 356     | Cardiolipin antibody              | Negative|
| Total cholesterol (mmol/L)        | 4.4     | Factor V activity                 | Negative|
| Low-density lipoprotein (mmol/L)  | 2.5     | Protein C activity                | Negative|
| High-density lipoprotein (mmol/L) | 1.3     | Protein S activity                | Negative|
| Triglycerides (mmol/L)            | 1.4     | COVID-19 nasopharyngeal polymerase chain reaction | Negative|
| Fasting blood glucose (mmol/L)    | 5.1     | Complement C3 (mg/dL)             | 1.55    |
| Prothrombin time (s)              | 13.5    | Complement C4 (mg/dL)             | 0.4     |
| International normalised ratio    | 1.1     | Free thyroxine, FT4 (pmol/L) (12.0–22.0) | 16.6    |
| Activated prothrombin time (s)    | 37.3    | Thyroid-stimulating hormone (mIU/L) (0.55–4.78) | 4.16    |

Blood tests, including polymerase chain reaction for coronavirus disease 2019 (COVID-19) via nasopharyngeal swab, were essentially unremarkable or non-specific (Table 1). Cardiac MRI supported the echocardiographic findings of low left ventricular ejection fraction (48%) with akinesia at the apex. In addition, there was hypokinesia in the apical anterior and anteroseptal regions. However, unexpectedly in the late gadolinium enhancement study, there was transmural enhancement seen at the apical septal, apical anteroseptal, and true apex regions suggestive of an ischaemic pathology. There was also a visible 18 mm × 6 mm apical thrombus seen (Figure 3). Due to the unexpected findings on cardiac MRI, a coronary angiogram was performed. However, the coronary angiogram failed to reveal any obstructive lesions, plaque ulceration or evidence suggestive of spontaneous coronary artery dissection (Figure 2). Further investigations of the coronaries, including coronary functional assessment (with acetylcholine or fractional flow reserve (FFR)) or coronary vascular imaging (via intravascular ultrasound (IVUS) or optical coherence tomography) were not performed due to financial constraints on the patient’s part.

On day 5 of admission, the patient’s electrocardiogram revealed resolution of earlier mentioned ST-segment changes, although with evidence of Q-waves in leads V1 to V3 suggesting transmural infarction (Figure 4). The patient was eventually discharged with smoking cessation advice, and was commenced on oral warfarin, bisoprolol 2.5 mg once a day and perindopril 2 mg once a day, and awaits a repeat echocardiogram and risk stratification to decide on the use of long-term antiplatelet or anticoagulation.

Discussion

Myocarditis is often difficult to diagnose due to heterogeneity in clinical presentation. Although endomyocardial biopsy remains the gold standard for diagnosis, accumulation of supportive demography, signs and symptoms, and investigations including suggestive cardiac MRI findings can be useful to guide diagnosis.1,2 Aside from demonstrating myocardial involvement in a non-coronary distribution, myocarditis differs from ischaemia by demonstrating sub-epicardial localisation with variable intramyocardial extension, whereas ischaemia often demonstrates subendocardial up to transmural involvement.2 In myocarditis, however, it is important to highlight that coronary assessment, to rule out significant coronary disease, remains an integral part in diagnosis and has been given mention in major guidelines.3 In our case, the decision to diagnose myocarditis was due to the patient’s age and lack of comorbidities, although we noted a significant smoking history (which has been shown to be an important, independent predictor in the development of myocardial infarction in those aged 30 years or younger).4

Another important lesson from our case was on how cardiac MRI provided evidence to support an ischaemic pathological taking place which made us consider a diagnosis of concurrent MINOCA complicating the myocarditis. MINOCA remains a broad ‘umbrella’ term that encapsulates various pathophysiology including coronary artery spasm, microvascular dysfunction, thrombophilia-prone conditions, cardiomyopathy and even myocarditis itself.5 Although not performed in our case, guidelines do recommend the use of luminal imaging, either via IVUS or optimal coronary tomography (to provide evidence of plaque rupture, coronary thrombus or dissection) or physiological assessment via FFR or provocation using acetylcholine (to guide diagnosis of vessel spasm or microvascular disease) in MINOCA.6

Conclusion

Coronary assessment and evaluation for ischaemia remains pertinent in diagnosing and managing myocarditis, even in the most ‘barndoor’ of cases. Our case provides a reminder that MINOCA remains an uncommon, but significant complication following myocarditis, although multi-modality imaging including intra-coronary assessment can provide useful information to help with diagnosis and management.
Figure 3. Cardiac magnetic resonance imaging on (a) parasternal long-axis and (b) apical four-chamber, demonstrating late gadolinium enhancement at the true apex, apical septal and anteroseptal, with evidence of a filling defect suggestive of a 18 mm × 6 mm apical thrombus. On (c–h) parasternal short-axis view moving from the base to the apex of the heart, the enhancement appears transmural in the apical cap (g, h).

Figure 4. Electrocardiogram performed 5 days from initial admission revealed right bundle branch block, with changes in the inferior lead axes versus the electrocardiogram on arrival. There are also T-wave inversions in leads V1 to V6, with Q-waves in leads V1 to V3, suggestive of old infarction.
Acknowledgements

The author(s) would like to acknowledge Universiti Teknologi MARA (UiTM) for supporting the submission of the following article.

Authors’ contributions

REFRS: Data collection and analysis, drafting of manuscript
HAZA: Data collection and analysis, image analysis, drafting of manuscript
RNK: Data collection and analysis, drafting of manuscript
SS: Drafting or manuscript, revision of manuscript

Availability of data and materials

The data that support the findings of this study are available from UiTM Sungai Buloh but restrictions apply to the availability of these data, which were used under licence for the current study, and so are not publicly available. Data are, however, available from the authors upon reasonable request and with permission of UiTM Sungai Buloh.

Conflict of interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval to report this case/these cases was obtained from the Universiti Teknologi MARA (UiTM) Ethics Committee. The manuscript does not report on any animal data or tissue.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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