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Identifying Myocarditis in Severe Scrub Typhus

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CASE VIGNETTE

A 55-year-old previously healthy woman was admitted with a 15-day history of fever, 5 days of jaundice, abdominal pain, vomiting, and 4 days of shortness of breath. She developed an altered sensorium for the last day. Her daughter denied dependences, and history of sudden cardiac death in the family.

On examination, her Glasgow Coma Scale (GCS) was E3V3M5. She had a temperature of 102°F, a pulse rate of 149 bpm, blood pressure of 80/62 mm of Hg, and a respiratory rate of 38/min and required oxygen support to maintain saturation. Bilateral pedal edema was observed, with decreased air entry and fine inspiratory crackles noted in the axillary region upon chest auscultation. Arterial blood gas analysis revealed respiratory acidosis, and endotracheal intubation was done for airway protection and respiratory distress. Point-of-care ultrasonography revealed bilateral diffuse bilateral B lines and a non-collapsing inferior vena cava. The chest X-ray and 12-lead electrocardiogram are shown in the image 1a & 1b. Troponin I levels were measured at 59 ng/L (reference range: 10 – 23 ng/L), NT-pro BNP levels were noted at 6107 ng/L (reference range: 70 – 133 ng/L), and CRP levels were significantly elevated at 106.9 mg/L (reference range: 0 - 1 mg/L). The tropical fever workup was positive for scrub typhus, and she was started on intravenous doxycycline along with azithromycin.

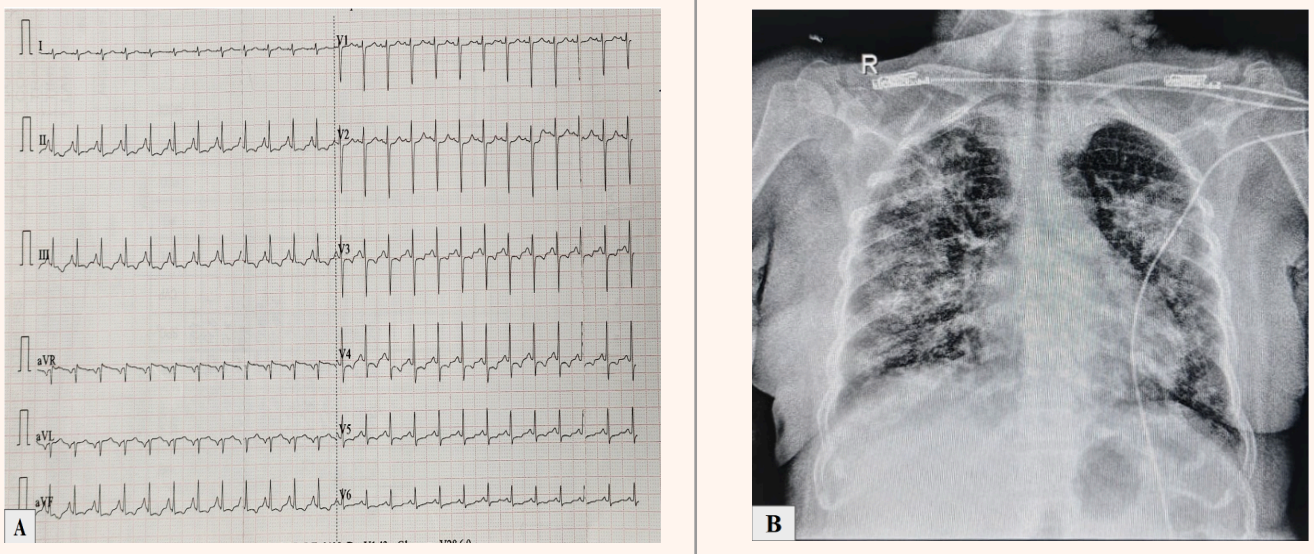

Image: 1A: 12-lead electrocardiogram taken in emergency department; **1B**: portable chest x-ray antero-posterior view.

Ques. Which of the following features does not point towards myocarditis?

A) Elevated CRPH, troponin, and NT-pro BNP levels

B) Sinus tachycardia

C) Hypotension with tachycardia

D) Respiratory distress, and bilateral fine inspiratory crepitations

E) Leucocytosis and thrombocytopenia

ANSWER: **E.** Leucocytosis and thrombocytopenia

COMMENTS

The clinical presentation of a 55-year-old lady with a 15-day history of fever, followed by jaundice, abdominal pain, vomiting, dyspnea, and examination findings such as tachycardia, hypotension, bilateral pedal oedema, decreased air entry with fine inspiratory crackles, and respiratory acidosis. These findings along with positive IgM ELISA for scrub typhus and raised cardiac biomarkers suggest a diagnosis of scrub typhus complicated by myocarditis leading to acute heart failure. The electrocardiogram (ECG) indicative of sinus tachycardia in the case of scrub typhus may be indicative of myocardial inflammation. Other causes can be respiratory distress and hypotension. Leucocytosis and thrombocytopenia are not directly indicative of myocarditis; rather, they are components of the inflammatory response and multiple organ dysfunction syndrome (MODS) in scrub typhus.

Scrub typhus causes endothelial dysfunction, leading to T cell, macrophage, and monocyte activation, which may result in uncontrolled cytokine release and multiple organ dysfunction syndrome (MODS). Raised C reactive protein reflects the ongoing inflammation and elevated cardiac troponin reflects the myocardial injury. Whereas nT pro-BNP is a sensitive marker of heart failure released due to ventricular dysfunction and wall stress.

Cardiac complications of scrub typhus include myocarditis, pericarditis, endocarditis, heart failure, arrhythmias, and myocardial ischemia. Risk factors for myocarditis paroxysmal atrial fibrillation, elevated bilirubin, short duration of symptoms before presentation, liver disease, elevated CRPH, and creatinine levels. The incidence of myocarditis is 4.3%-14%, and it presents with chest pain, palpitations, and heart failure; it has a high mortality rate (up to 24%) and is diagnosed using ECG, echocardiography, troponin, cardiac MRI, and endomyocardial biopsy (EMB).[1]

The ECG is commonly used as an initial screening tool for diagnosing myocarditis, even though it has a low sensitivity of 47%. In patients with myocarditis, ECGs often show a variety of nonspecific findings, such as sinus tachycardia, nonspecific ST/T-wave changes, low voltage, and PR-segment depression. However, none of these findings are specific to myocarditis.[2] The most common ECG finding in scrub typhus-associated myocarditis is sinus tachycardia followed by T-wave and ST-T segment abnormalities. Atrial fibrillation can be seen which is associated with a 1.3-fold increase in mortality over three months.[1] Cardiac MRI is the gold-standard non-invasive imaging technique for diagnosing myocarditis. Updated 2018 Lake Louise Criteria increased its sensitivity from 74% to 87.5% and specificity from 86% to 96.2% for diagnosis of acute myocarditis. However, EMB remains the gold standard for confirming myocarditis and identifying the underlying aetiology.[2]

A high index of suspicion should be kept for the diagnosis of scrub typhus myocarditis. Approach and treatment depend upon the condition of the patient, and are summarised in the illustration (image 2).[3] The symptoms of scrub typhus myocarditis can resemble those of a secondary bacterial infection or a hospital-acquired infection. In such cases, it is important to use antibiotics judiciously while adhering to antibiotic stewardship principles. Additionally, one should always monitor electrolytes such as calcium, potassium, and sodium, as well as potential drug interactions, to prevent life-threatening arrhythmias.

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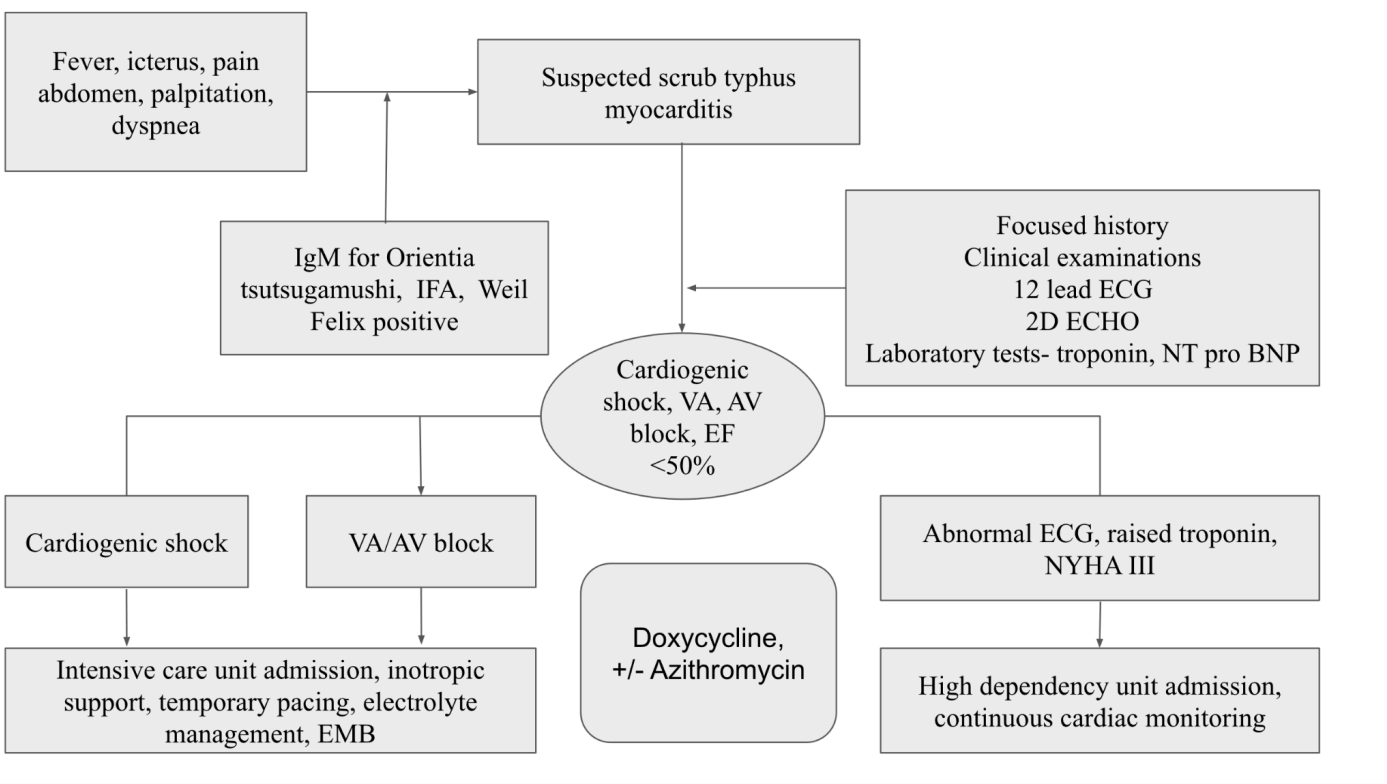

Image 2: Illustration showing the outline of management of scrub typhus myocarditis.
AV block: atrioventricular block; ECG: electrocardiogram; EMB: endomyocardial biopsy; ECHO: echocardiogram; NYHA: New York heart association; IgM: immunoglobulin M; IFA: indirect immunofluorescence assay; VA: ventricular arrythmia.

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Managing TB and HCV in DCLD (CTP B): A Balancing Act Between ATT and DAA

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CASE VIGNETTE

A 51-year-old woman with type 2 diabetes and chronic HCV infection presented with a 3-month history of productive cough, fever, abdominal distension, and dyspnea. Evaluation revealed **decompensated chronic liver disease (DCLD), Child-Pugh B (score 9)** with high HCV viral load (7,12,000 IU/mL). Imaging showed bilateral pleural effusion and ascites, and sputum CBNAAT confirmed **rifampicin-sensitive pulmonary tuberculosis**.

Given her advanced liver dysfunction, initiating both **anti-tubercular therapy (ATT)** and **direct-acting antivirals (DAA)** posed a significant challenge. ATT (especially isoniazid and rifampicin) carries a high hepatotoxic risk, and the use of DAAs in decompensated cirrhosis also requires caution. Following stewardship principles, the team opted to **initiate ATT first**, with close monitoring of liver function, and **defer DAA therapy** until completion of the intensive TB phase or stabilization of hepatic parameters.

Ques. In a patient with decompensated chronic liver disease (Child-Pugh B) who has active TB and HCV co-infection, which of the following best describes the recommended approach to initiating therapy?

A. Start ATT and DAA concurrently regardless of liver function.

B. Initiate ATT first and delay DAA until liver function stabilizes (usually after the intensive phase of TB treatment).

C. Begin DAA first to improve liver function before starting ATT.

D. Defer both therapies until liver enzymes normalize completely.

ANSWER: B. Initiate ATT first and delay DAA until liver function stabilizes (usually after the intensive phase of TB treatment).

COMMENTS

In patients with DCLD (CTP B), the risk of drug-induced liver injury is high. As a stewardship principle, it is generally recommended to **prioritise anti-tubercular therapy**—given the urgency of treating active TB—and delay DAA initiation until liver function stabilizes. Concurrent initiation of ATT and DAA is generally not advisable in this setting due to:

- **Increased Hepatotoxicity:** The combined hepatotoxic effects of ATT (particularly isoniazid) and DAA may exacerbate liver injury.
- **Drug-Drug Interactions:** Rifampicin, a cornerstone of ATT, is a potent enzyme inducer and can reduce the efficacy of DAAs.
- **Clinical Stability:** Patients with CTP B have limited hepatic reserve, making them more vulnerable to additional insults.
- However, in rare scenarios where TB is less severe or liver function remains relatively stable despite DCLD, and where rapid HCV clearance is critical (for example, to qualify for liver transplant), concurrent initiation may be considered under close monitoring and in a multidisciplinary setting. Such decisions must be individualized, with rigorous surveillance of liver enzymes and clinical status.
- Factors Influencing Treatment Prioritization in HCV–TB Co-infection

Start ATT First	Start DAA First	Start Both Together
- **Active TB with significant symptoms** or radiological evidence of progression	- **Compensated or early DCLD** with high HCV viral load and relatively **mild TB**	- **Stable Child-Pugh B** patient with **mild TB and HCV**, needing rapid viral suppression (e.g., transplant listing)
- Child-Pugh B/C with **limited hepatic reserve**	- HCV-induced hepatic decompensation where **TB is latent** or indolent	- When both infections are active but **drug interactions can be managed** and patient is under **close monitoring**
- ATT is **life-saving** and delays increase mortality risk	- DAA can potentially **improve liver function** and **enable safer ATT** later	- Managed in **high-resource settings** with access to therapeutic drug monitoring (TDM) and expert hepatology input
- High risk of hepatotoxicity from isoniazid/rifampicin **requires deferral of DAAs**	- When rifampicin **not immediately needed** or replaced with a DAA-compatible ATT regimen	- **Multidisciplinary care** available and regular LFT surveillance possible

Stewardship Interventions:

- **Sequence Therapy Based on Urgency and Tolerance:**Prioritize the initiation of **ATT** to control the active TB infection, as delayed treatment can be life-threatening. DAA therapy should be **deferred until hepatic function stabilizes**, typically after the intensive phase of TB therapy (first 2 months), or once liver enzymes normalize.
- **Multidisciplinary Coordination:**Collaborate with hepatologists, infectious disease specialists, and the antimicrobial stewardship team to ensure therapeutic decisions are individualized and evidence-based.
- **Rigorous Monitoring:**Implement close and frequent **liver function monitoring** during ATT. This helps detect early signs of hepatotoxicity and guides the safe introduction of DAAs at an appropriate time.
- **Tailored Treatment in Special Scenarios:**In selected cases—such as those being evaluated for **liver transplantation**, or where TB is clinically less severe—**simultaneous initiation of ATT and DAA** may be considered. This must occur under **strict monitoring**, with clear clinical justification and consensus among specialists.

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