Surprising diagnosis in a patient with acute coronary syndrome: a case report of acute streptococcal pharyngitis-associated perimyocarditis

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Background
Streptococcal pharyngitis is a common infection, with both suppurative and non-suppurative complications. Most importantly, a streptococcal infection can cause heart disease in different pathophysiological pathways. Acute non-rheumatic perimyocarditis appears to be a more frequent pathological entity associated with streptococcal pharyngitis as once thought, which is poorly understood and explored.

Case summary
We present the case of a middle-aged man with acute chest pain, electrocardiogram (ECG) abnormalities, and elevated cardiac enzymes following a recent episode of pharyngitis in which streptococcal-associated perimyocarditis was diagnosed. Cardiovascular magnetic resonance (CMR) imaging established the diagnosis and allowed cardiac disease monitoring after successful antibiotic therapy resulting in complete clinical recovery.

Discussion
Patients presenting with acute chest pain, ECG abnormalities, and cardiac enzyme elevations do not always suffer from an ischaemic heart attack. A thorough investigation comprising a detailed past medical history and non-invasive imaging such as CMR are the cornerstones for unravelling a correct diagnosis and implementing a proper treatment—as was shown in the present clinical case.

Keywords
CMR • STEMI • SPAM • Rheumatic fever • Case report

Learning points
• In the work-up of acute coronary syndromes, particularly with non-obstructive coronary artery disease, a detailed medical history and multimodality imaging are critical to attain the right diagnosis and administer appropriate treatment.
• Contrast-enhanced cardiovascular magnetic resonance (CMR) allows to distinguish ischaemic from non-ischaemic heart disease. In addition, in non-ischaemic heart disease, CMR distinguishes different aetiologies and allows to monitor the course of disease.
Introduction

First described by Gore and Saphir in 1947, acute non-rheumatic perimyocarditis is a pathological entity associated with streptococcal pharyngitis that is poorly understood and explored. We present the case of a patient admitted with clinical suspicion of myocardial infarction, in which an acute non-rheumatic perimyocarditis was finally diagnosed and accordingly managed.

Timeline

| 2 weeks prior to presentation | Upper respiratory tract infection with pharyngitis |
|-------------------------------|-----------------------------------------------|
| Initial presentation (Day 0)   | Acute chest pain, electrocardiogram with anterior ST-segment elevations, laboratory study with signs of myocardial injury |
|                               | Coronary angiography excludes obstructive coronary artery disease |
| Day 7                         | Increased anti-streptolysin O (1879 IU/mL) and streptococcal anti-DNase B (2000 U/mL) titer indicating recent streptococcal infection |
|                               | Initiation of antibiotic treatment (ampicillin/sulbactam) and non-steroidal anti-inflammatory drug |
| Day 15                        | Recurrence of chest pain and hsTropT elevation (up to 1000 pg/mL) after 3-day interruption of antibiotic for obtaining blood cultures |
| Day 19                        | Cardiovascular magnetic resonance (CMR) established the diagnosis of impressive acute perimyocarditis |
| Day 29                        | Discharge after a complete 10-day course of antibiotic (ampicillin/sulbactam) |
| One month after diagnosis     | Repeated CMR with resolution of wall motion abnormalities and reduction of myocardial damage |
|                               | Drop in anti-streptococcal antibody concentrations (anti-streptolysin O = 989 IU/mL, streptococcal anti-DNase B = 1000 U/mL) |
|                               | No signs of myocardial injury (hsTropT = 6 pg/mL, creatine kinase = 16 U/L) |

Case presentation

A 48-year-old man presented to the emergency department of a regional hospital with acute chest pain and suspected acute coronary syndrome (ACS). The day before, he had visited his general practitioner due to thoracic discomfort with tightness in the chest. A few weeks earlier, he had experienced an upper respiratory tract infection and sore throat. Noteworthy, in the days before, his wife and children (pre-schoolers) suffered also from acute tonsillitis. Physical examination revealed a febrile, generally ill appearing middle-aged man. He had a regular pulse, S1/S2 were normal without murmurs, gallop, or rub. Both lung and abdomen examination were unremarkable. No skin lesions, rash, cyanosis, or oedema were present. The patient had no relevant personal or family past medical history, was a smoker (20 pack-years) and denied any substance abuse or regular medication.

On admission, resting electrocardiogram (ECG) demonstrated ‘saddle-shaped’, anterior ST-segment elevations; PR interval was normal (Figure 1A). Transthoracic echocardiography showed a hypercontractile left ventricle without wall motion abnormalities (Figure 2). Laboratory studies revealed signs of inflammation with elevated leucocytes (15.85 × 10^9/L); normal values: 4–10 × 10^9/L) and C-reactive protein (CRP) (6.28 mg/dL; normal values: <0.50 mg/dL) as well as of acute myocardial injury [high-sensitive cardiac troponin T (hsTropT) = 589 pg/mL initially with increase up to 1009 pg/mL; normal values: <14 pg/mL, creatine kinase (CK) = 410 U/L, creatine kinase - myocardial band (CK-MB) = 15 ng/mL; normal values: <174 U/L and <5 U/L, respectively]. Chest X-ray was unremarkable.

Due to the suspicion of acute ST-elevation myocardial infarction (STEMI) 500 mg aspirin and 5000 units of heparin (IV) were administered and the patient immediately underwent coronary angiography (Figure 3) which revealed normal coronary arteries. Additional laboratory tests showed no signs of infection with potential cardiotropic viruses [Coxsackie A/B, Echoviruses immunoglobulin A (IGA) negative] and no flu infection (Influ-A/-B PCR negative). Moreover, testing for Lyme disease [anti-Borrelia burgdorferi immunoglobulin G (IgG)/immunoglobulin M (IgM)] was negative. There was no sign of an autoimmune cardiac disease (anti-cardiac-muscle-, myo-lemm-, sarcolemm-antibodies negative). Noteworthy, an increased anti-streptolysin O (1879 IU/mL; normal values: <200 IU/mL) and streptococcal anti-DNase B (2000 U/mL; normal values: <200 U/mL) titer indicated a recent streptococcal infection. Repeated blood cultures (aerobic and anaerobic) turned negative. The patient was put on a trial of ampicillin/sulbactam due to suspected streptococcal pharyngitis-associated inflammatory disease with consecutive obvious clinical improvement. Concurrently, ST-segment elevation slowly resolved over days and was followed by T-wave inversion without development of Q waves (Figure 1B).

Interestingly, during a 3-day interruption of antibiotic—to obtain blood cultures, marked recurrent chest pain and hsTropT elevation (up to 1000 pg/mL) occurred. To elucidate the respective cause, a cardiovascular magnetic resonance (CMR) study was performed and established the diagnosis of acute perimyocarditis with impressive myocarditis and mild corresponding pericarditis. Presence of marked, subepicardial to transmural, late gadolinium enhancement (LGE) together with pronounced myocardial oedema, as indicated by increased signal intensity on T2-weighted imaging, was documented in the mid-ventricular anterior- and anterolateral wall segments; corresponding focal hypo- to akiniesia was noted; pericardial involvement with mild oedema and LGE over the anterior wall, but without substantial pericardial fluid, was also seen (Figure 4). Interestingly, this pattern did not match the patchy subepicardial LGE in the inferolateral left ventricular wall,
typically seen in ‘viral myocarditis’—but suggested a rather different, more confluent, myocardial damage.

A full 10-day course of antibiotic (ampicillin/sulbactam) and non-steroidal anti-inflammatory (ibuprofen 600 mg/t.i.d.) was prescribed, in view of streptococcal pharyngitis-associated acute perimyocarditis (SPAM) with persistent chest pain. Due to pronounced regional myocarditis—confirmed by CMR, despite limited evidence in case of a preserved global left ventricular systolic function, a beta-blocker (bisoprolol 2.5 mg/day) was started to suppress ventricular ectopy and an angiotensin-converting enzyme inhibitor (ramipril 1.25 mg/day) to prevent adverse left ventricular remodelling. In the same context, a 3- to 6-month wearable cardioverter defibrillator (LifeVest®, ZOLL Medical Corporation, USA) was discussed and finally indicated on discharge. Restriction of physical activity for the same time period was recommended. In the absence of valvular injury, long-term antibiotic prophylaxis was deemed unnecessary.

One month after first CMR, the patient was referred to our centre for follow-up. The aforementioned wall motion abnormality had resolved and the extent of LGE and myocardial oedema had markedly decreased (Figure 4). A complete normalization of the ECG was documented (Figure 1C). The anti-streptococcal antibody concentrations significantly dropped (anti-streptolysin O = 989 IU/mL, streptococcal anti-DNase B = 1000 U/mL) and there was no sign of ongoing myocardial damage (hsTropT = 6 pg/mL, CK = 16 U/L).

Discussion

In patients with chest pain and signs of acute myocardial injury, it is critical to elucidate the underlying cause and to differentiate coronary artery disease (CAD)-associated myocardial ischaemia from other causes, since there are essential differences regarding therapy. Acute chest pain with concomitant ST-elevation on resting ECG is always a red flag for the physician and immediate coronary angiography is of utmost importance. In case of invasive exclusion of a culprit lesion, the diagnosis of ischaemia-driven STEMI has still to be considered since an unneglectable proportion of myocardial infarctions (1–14%) occur in the absence of obstructive CAD. Moreover, for the diagnosis of myocardial infarction with non-obstructive coronary arteries (MINOCA) no specific cause of the patient’s symptoms needs to be present. Therefore, a detailed past medical history and further tests are required. Besides, the presence of MINOCA can be elegantly confirmed or ruled-out by CMR—as done in this case.

Our patient had recently suffered from an acute tonsillitis episode. Streptococcal pharyngitis is common, with both supplicative and non-suppurative complications. Interestingly, a streptococcal...
infection can affect the human heart in different ways. Bacterial-induced myocarditis is a life-threatening disease, which affects almost exclusively immunodeficient patients. Post-streptococcal rheumatic fever is a well-known cause of pancarditis due to an autoimmune response to group A streptococcus infection and typically affects patients at young ages.

Notably, the incidence of rheumatic fever has declined dramatically in high-income countries in the last decades.

Despite febrile presentation with elevated inflammation markers and anti-streptococcal antibodies, 2 weeks after streptococcal pharyngitis, our patient did not meet any major criteria for acute rheumatic fever due to absence of clinical/subclinical valvular regurgitation. In contrast, the presentation mimicking STEMI is compatible with a non-rheumatic SPAM, except for a slightly longer latency (usually reported as <7 days). Streptococcal pharyngitis-associated acute perimyocarditis appears to be a more frequent as thought, pathological entity associated with streptococcal pharyngitis. Its pathophysiology is yet to be clarified but is suggested to differ from acute rheumatic fever. Importantly, contrary to rheumatic fever, the beneficial effects of β-lactam antibiotics are unclear in this setting. In our case, antibiotic therapy showed an indisputable effect on disease course, with initial improvement followed by recurrence of chest pain and hsTropT elevation during the aforementioned 3-day interruption—supporting the diagnosis of SPAM in this case. Notably, in the setting of SPAM there is no evidence-based recommendation regarding long-term anti-streptococcal prophylaxis, as in rheumatic fever. Nevertheless, a definite differentiation between a rheumatic and non-rheumatic mechanism of myocarditis in this case is difficult.

Typically, a diagnosis of acute viral myocarditis is made in young males presenting with an ACS, history of recent infection and normal coronary arteries. The differential diagnosis of acute chest pain is, however, much more comprehensive and demands a thorough investigation with detailed past medical history and non-invasive methods such as CMR.

Noteworthy, to the best of our knowledge, the current case comprises the oldest patient (48 years old) with a diagnosis of SPAM.

Figure 2 Two-dimensional transthoracic echocardiography images obtained upon admission in apical four-chamber (A and B) and two-chamber views (C and D) at end-diatole (A and C) and end-systole (B and D). Normal systolic function with no wall motion abnormalities are depicted.
Figure 3 Coronary angiography images on admission in left anterior cranial (A) and right anterior caudal (B) oblique views depicting the right (A) and left (B) coronary arteries. No coronary abnormalities are present.

Figure 4 Late gadolinium enhancement and T2-weighted short-tau inversion recovery cardiovascular magnetic resonance images in the acute phase (top row) and 1 month thereafter (bottom row) in four-, two-chamber, and mid-ventricular short-axis views. A pronounced subepicardial enhancement on late gadolinium enhancement (*) with corresponding oedema on T2-weighted short-tau inversion recovery (#) images in the anterior and antero-lateral mid-ventricular myocardial segments can be seen on first examination (top row). A marked regression of the above aforementioned findings is depicted one month later (bottom row).
Lead author biography

Grigoris Chatzantonis was born on 12 April 1989 in Athens, Greece. He graduated the Hellenic-American Educational Foundation (HAEF) 2007 with high honours (19/20) and the medical school of Democritus University 2013 with honours (8.17/10). His cardiology fellowship began November 2013 in Germany. From August 2016, he works in the University of Munster (UKM) where he specialized in cardiovascular imaging and acute patient care. As of September 2018, he trains in cardiovascular magnetic resonance (CMR) in a Level 3 certificated medical centre under the guidance of Professor Ali Yilmaz. His medical interests are cardiovascular imaging, cardiomyopathies, and microvascular dysfunction.

Supplementary material

Supplementary material is available at European Heart Journal - Case Reports online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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