Cannabis-induced recurrent myocardial infarction in a 21-year-old man: a case report

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Background
Acute coronary syndrome (ACS) is rarely caused by coronary artery disease in young patients unless cardiovascular risk factors are present. Although non-atherosclerotic causes of ACS are rare, they need to be considered in young patients.

Case summary
We report on a 21-year-old patient referred to our institution with ACS. Electrocardiogram showed ST-segment elevation and coronary angiography revealed thrombotic occlusion of the left anterior descending artery. Reperfusion was achieved by thrombus aspiration, glycoprotein IIb/IIIa inhibitors (GPI), and drug-eluting stent (DES). The patient had no cardiovascular risk factors but reported cannabis consumption before symptom onset. Although he was put on dual antiplatelet therapy and strictly advised to avoid consumption, he continued to abuse cannabis and suffered three further ACS events within 18 months: the first 8 months later caused by thrombotic occlusion of a diagonal branch treated by GPI and DES, the second after 17 months due to thrombotic rec-occlusion of the diagonal branch, and the third after 18 months by thrombotic occlusion of the circumflex artery, both events treated by GPI alone (all while still using cannabis). Since then, he stopped cannabis consumption and has been symptom-free for 8 months.

Discussion
This case highlights that cannabis-induced ACS must be considered as a cause of myocardial infarction in young adults. In contrast to ACS in the elderly population, this unusual ACS cause requires specific treatment. The risk of ACS relapse may substantial if cannabis abuse is continued. This potential hazard needs to be taken into consideration when legalization of cannabis is discussed.

Keywords
Acute coronary syndrome • Cannabis • Cardiovascular disease • Case report • Premature myocardial infarction

Learning points
• Differential diagnosis of acute coronary syndrome (ACS) in the younger population is challenging due to a high number of underlying diseases.
• Cannabis-induced ACS must be considered as a cause of myocardial infarction in young adults and its prevalence may increase due to its legalization in some regions.
• Delta-9-tetrahydrocannabinol, the psychoactive component of cannabis, increases the expression of glycoprotein IIb/IIIa on human platelets, which effects the prothrombotic impact of cannabis.

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Introduction

Coronary artery disease (CAD) is one of the most prevalent diseases of the elderly population. Although treatment of patients with CAD and acute coronary syndrome (ACS) is part of clinical routine, ACS in young patients can be challenging due to a wide range of causing differential diagnoses. We report on a 21-year-old man suffering from recurrent myocardial infarction (MI) on persistent cannabis consumption.

Timeline

| Date       | Event                                                                 | Treatment                                                                 |
|------------|------------------------------------------------------------------------|---------------------------------------------------------------------------|
| September 2017 | Presentation with chest pain and ST-segment elevation immediately after cannabis consumption. Thrombotic subtotal occlusion of the left anterior descending artery was diagnosed | Thrombus aspiration, infusion of glycoprotein IIb/IIIa inhibitors (GPI) and drug-eluting stent (DES) implantation |
| May 2018     | Thrombotic occlusion of a diagonal branch despite optimal adaption of the previously implanted stent (still using cannabis) | Infusion of GPI and DES implantation                                      |
| February 2019 | Thrombotic re-occlusion of the diagonal branch after 1 year of event-free survival despite optimal adaption of the previously implanted stent (still using cannabis) | GPI alone                                                                  |
| March 2019   | Thrombotic occlusion of the ramus circumflexus was found (still using cannabis) | GPI alone                                                                  |

Case presentation

In September 2017, a 21-year-old male patient was referred to our emergency room with constant substernal chest tightness, unrelated to breathing, with radiation into the left shoulder, lasting for 2 h before admission. Physical examination was unremarkable; there were no additional heart sounds on auscultation and no pulmonary rales. The heart rate was 67 b.p.m. and blood pressure 130/75 mmHg. Jugular venous pressure was not elevated and no pitting oedema was present. On electrocardiogram (ECG), sinus rhythm with ST-segment elevation in the precordial leads and in leads II, III, and aVF was noted (Figure 1A). Laboratory measurements showed elevation of the cardiac biomarkers troponin (0.239 ng/mL; upper limit of normal <0.1 ng/mL) and creatine kinase (initial 469 U/L, peak 1563 U/L; upper limit of normal <169 U/L). Treatment with aspirin 250 mg intravenously was initiated, a heparin infusion started and a loading dose of 180 mg ticagrelor administered. Subsequent coronary angiography showed thrombotic subtotal occlusion of the left anterior descending artery (LAD) at the take-off of the first diagonal branch (Figure 1B: Supplementary material online, Video S2). No other lesions were observed and the remaining coronary arteries did not show any atherosclerotic alterations (Supplementary material online, Video S1). Because coronary blood flow could not be fully re-established by thrombus aspiration (Supplementary material online, Video S3) and infusion of glycoprotein IIb/IIIa inhibitors (GPI), implantation of a drug-eluting stent (DES; 4.0 × 18 mm) was necessary after pre-dilatation of the lesion (Figure 1C and D, Supplementary material online, Videos S4 and S5). During intervention, we used a FilterWire EZ™-system (Boston Scientific, Marlborough, MA, USA) to protect the peripheral vessels from thrombotic occlusion (Supplementary material online, Videos S4 and S5, Figure 1). The culprit lesion was reopened successfully and TIMI III flow could be established (Figure 1E, Supplementary material online, Video S6). The culprit lesion was reopened successfully (Figure 1E, Supplementary material online, Video S6). No peri-procedural arrhythmias occurred and the patient recovered quickly. Dual antiplatelet therapy (100 mg aspirin once daily and 90 mg ticagrelor twice daily), a betablocker (47.5 mg metoprolol once daily), and a statin (40 mg atorvastatin once daily) were prescribed. Transthoracic echocardiography revealed hypokinesia of the anterior wall resulting in overall mildly reduced left ventricular ejection fraction but no other abnormalities.

To rule out an embolic source for the thrombotic coronary occlusion in this young patient, we additionally performed transoesophageal echocardiography with echo contrast but could not find any evidence for an intracardiac shunt or any other source of cardiac embolism. Moreover, laboratory testing for thrombophilia did not show any abnormalities and testing for autoimmune diseases was negative. Blood lipid and glucose levels were within the normal range. The patient had a history of frequent cannabis abuse but denied cigarette smoking. He had no family history of CAD and did not regularly take any medication. Urine toxicology revealed elevated levels of delta-9-tetrahydrocannabinol but was negative for any other drugs. Thus, we considered cannabis abuse as the most likely cause of the MI and strictly advised the patient to avoid further cannabis consumption. The patient was discharged from the hospital in good clinical status under optimal medical treatment. However, the patient continued his cannabis abuse and suffered from three ACS relapses within 2 years, although medication was continued. The first MI occurred 8 months later and was caused by thrombotic occlusion of a diagonal branch despite optimal adaption of the previously implanted stent in the LAD which was visualized by optical coherence tomography (Figure 2A–C). This occlusion was treated by GPI and implantation of another DES into the diagonal branch (Figure 2D–F). The second relapse was a non-ST elevation ACS in February 2019 and was due to...
thrombotic re-occlusion of the diagonal branch, again despite optimal stent adaptation. One month later, the patient again presented with angina at rest, this time without cardiac enzyme release, caused by thrombotic occlusion of the proximal circumflex artery. Both events were treated by GPI alone. Coronary angiography did not reveal any evidence of coronary dissection in any of the ACS relapses. Cannabis consumption was continued during the whole period. After the fourth ACS, left ventricular ejection fraction was still only mildly reduced. Since the last relapse, the patient stopped cannabis abuse and has been symptom-free for 8 months, i.e. until the last follow-up in November 2019.

**Discussion**

This case highlights an unusual cause for the overall rare occurrence of an ACS in young patients. In the fourth universal definition of MI consensus document by the European Society of Cardiology, MI was defined as myocardial injury with elevation of cardiac biomarkers and evidence of myocardial ischaemia indicated by ECG changes, specific symptoms or evidence of myocardial damage in imaging. MI can be caused by either plaque rupture/erosion (Type 1), usually affecting patients with underlying CAD, or by an imbalance between oxygen supply and demand (Type 2), which often includes young patients with other aetiologies of MI. In contrast to ACS in the elderly population, MI is rarely caused by plaque rupture with underlying CAD in young patients unless a certain number of cardiovascular risk factors are already present. Differential diagnosis of ACS in the younger population is challenging due to a high number of potential and rare aetiologies. There is limited evidence how to effectively assess the cause of MI in younger patients and knowledge is based on a few case series only. Table 1 summarizes diseases that have been implicated as causative factors for an ACS in young patients. Thus, in a young patient presenting with ACS a thorough investigation for potential causes of MI is mandatory to enable adequate treatment of the underlying disease and improve prognosis. Careful patient history and physical examination often help to limit differential diagnoses and reach the correct diagnosis.

Our report underlines that cannabis-induced MI should be considered as a rare cause of ACS in young adults. This is emphasized by the fact that the patient was free of events since he stopped cannabis consumption, although there is still a chance that the patient may develop similar symptoms without association to recent cannabis abuse in the future.

Three mechanisms of cannabis-associated ACS have been reported in the literature: coronary vasospasm, thrombus formation, and coronary artery dissection. In the case presented coronary angiography revealed coronary thrombosis without any evidence for
vasospasm or dissection. Therefore, calcium channel blockers or nitrates were not used in this specific circumstance. A prothrombotic effect of delta-9-tetrahydrocannabinol, the psychoactive component of cannabis, caused by an increase in the expression of glycoprotein IIb/IIIa on human platelets has been discussed as the underlying mechanism resulting in thrombotic occlusion of non-atherosclerotic coronary arteries. Infusion of GPI may be beneficial in this setting but is often not sufficient as in the case presented. There is no clear recommendation for the optimal drug regimen after the acute intervention. We decided to prescribe dual antiplatelet therapy for

Table 1  Underlying diseases and findings in patient history and physical examination for differential diagnoses of premature myocardial infarction

| Underlying disease                                      | Findings in patient history and physical examination                                                                 |
|--------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------|
| Anomalous coronary artery9                             | Prior syncope                                                                                                          |
| Autoimmune and vasculitis8                            | Skin abnormalities, involvement of other organs                                                                       |
| Vasospasm10                                            | Often female, anamnesis of smoking, drugs                                                                             |
| Cardiomyopathies (e.g. takotsubo11)                    | Positive/negative stress                                                                                              |
| Coronary endothelial dysfunction7                      | Presence of several cardiovascular risk factors                                                                      |
| Embolism12                                              | Atrial fibrillation, patent foramen ovale                                                                             |
| Intoxications (e.g. amphetamines, cannabis, cocaine)3   | Anamnesis, conspicuous mental state                                                                                   |
| Myocarditis13                                           | Fever, myalgia                                                                                                          |
| Sickle cell disease14                                   | Country of origin                                                                                                      |
| Spontaneous aortic or coronary artery dissection15      | History of Marfan syndrome or Syphilis, malperfusion of organs or limbs, pregnancy                                     |
| Thrombophilia16                                         | Family history                                                                                                          |
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Discharge medication, which is recommended in the current guidelines after percutaneous coronary intervention in ACS. In the ATLAS ACS 2–TIMI 51 trial, low-dose rivaroxaban has shown beneficial effects in patients with ACS. A non-vitamin K-dependent oral anticoagulant was not administered in our patient. It may be speculated that low-dose rivaroxaban may have been particularly useful in the setting of repeated intracoronary thrombosis induced by cannabis use although there are yet no data to support this regimen in this specific clinical setting.

This case additionally highlights the potential hazards of cannabis especially for patients maintaining consumption despite complications. A previously published case series illustrated the potential problem of cannabis-induced ACS in early adulthood. Legalization of cannabis may lead to more widespread use of the drug which may potentially increase the incidence of ACS in young patients.

**Conclusion**

This case report highlights the potential difficulties in the differential diagnosis of ACS in early adulthood. Prevalence of premature MI caused by cannabis consumption in early adulthood is low but may increase with cannabis legalization.

**Lead author biography**

Dennis Lawin achieved his license to practice medicine at RWTH Aachen University, Germany. After internship at the university hospital of Bern (heart surgery), Switzerland, he finished his doctoral thesis at RWTH Aachen, University, Germany. At present, he is a junior physician for cardiology and internal medicine at Klinikum Bielefeld, Germany. His scientific interest is in cardiac resynchronization therapy, emergency care, and electrophysiology.

**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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