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Cholesterol embolization syndrome following thrombolysis during acute myocardial infarction

Introduction

The cholesterol embolization syndrome (CES) is the result of atherosclerotic plaque erosion and subsequent dislodgement of cholesterol crystals from the core of the plaque to the peripheral arteries. The source of emboli is usually located in the aorta, whereas the most commonly affected organs are the skin and the kidneys. CES has gained increasing interest as it is considered a complication of invasive vascular procedures. In a large series in 1,786 consecutive patients who underwent left cardiac catheterization the incidence of post-procedural CES was 1.4% [1].

Case presentation

A 69-year-old male, obese patient presented to the emergency department of our center with bilateral painful, cyanotic discoloration of his toes which developed gradually over the past 20 days (**Fig. 1a**). No symptoms of intermittent claudication were mentioned. The patient was an ex-smoker and had a history of essential hypertension, dyslipidemia, and chronic renal insufficiency. About 1 month ago the patient had an inferior ST-elevation myocardial infarction treated with thrombolysis. No cardiac catheterization was performed at that time and the patient was discharged from the hospital on dual antiplatelet therapy, β-blocker, statin, and transdermal nitrates.

Clinical examination was unremarkable. Of note, peripheral pulsation was normal without any evident bruits. Chest X-ray and ECG revealed normal findings. The laboratory examinations on admission showed an increased erythrocyte sedimentation rate (88 mm/h), moderately increased count of eosinophils (472 per mm^3) and elevated serum urea and creatinine levels (77 mg/dl and 2.7 mg/dl, respectively).

On the basis of clinical presentation, the patient was admitted with the diagnosis of lower extremities embolization syndrome. To further investigate the source of emboli the patient underwent a transesophageal echocardiography which revealed an overall normal cardiac anatomy and preserved left ventricular function. However, diffuse, ulcerated atherosclerotic lesions in the course of descending thoracic aorta were visualized. An enhanced magnetic resonance aortography using gadolinium-DTPA further confirmed the echocardiographic findings revealing the presence of multiple, ulcerated atherosclerotic plaques in the descending aorta (**Fig. 1b,c**). No obstructing lesions were found between the aorta and the site of distal embolization. These findings led to the clinical suspicion of embolization of the capillaries of the toes from cholesterol crystals derived from the aortic plaques. To confirm the cholesterol embolization, a deep cutaneous biopsy of the fifth digit of the right foot was carried out which revealed cholesterol crystals in the lumen of the small diameter arteries of the skin (**Fig. 1d**).

The skin lesions and the renal function were progressively deteriorated and the patient had two of his toes amputated due to gangrene. After 30 days of hospitalization, the patient had a second inferior ST-elevation myocardial infarction followed by cardiac arrest and death.

Discussion

Patients with CES have usually complex, unstable atherosclerotic lesions over the entire thoracic aorta [2] Male gender, advanced age, acute coronary syndromes, multivessel coronary artery disease, hypertension, smoking, cerebrovascular disease and aortic aneurysm have been recognized as major risk factors for CES [1, 3]. A triggering event for the clinical development of the syndrome includes invasive procedures of the aorta or large arteries, such as angiography, angioplasty or peripheral vascular procedures, anticoagulation therapy, and thrombolysis [3, 4]. In our case, male gender, advanced age, and a history of hypertension, dyslipidemia, and smoking were present, whereas the patient underwent thrombolysis 1 month previously. Both transesophageal echocardiography and mag-

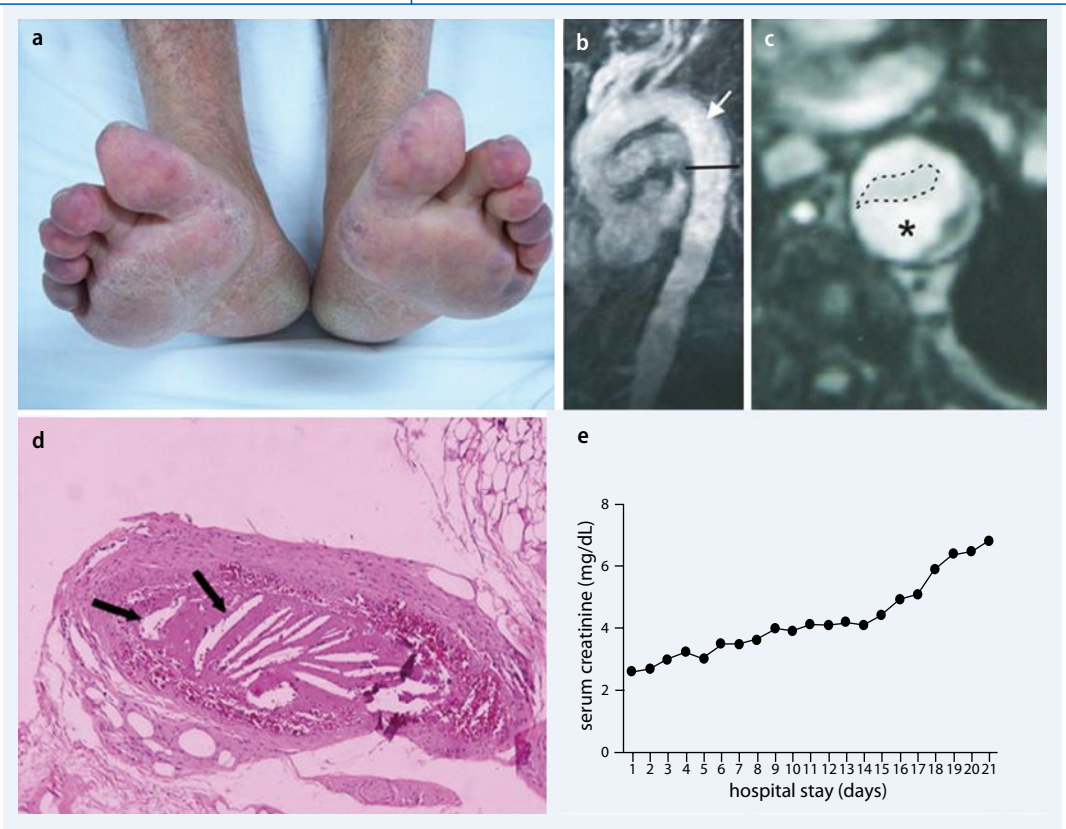

Fig. 1 ◀ **a** Blue toes, **b** gadolinium-enhanced magnetic resonance aortography showing irregular walls and atherosclerotic degeneration of the thoracic aorta (*arrow*) without any obstructing lesions between the aorta and the site of embolization, **c** cross-sectional view of the atherosclerotic aorta at the section indicated with the black line in **b** (*asterisk* denotes the plaque and *dashed lines* the lumen), **d** the skin biopsy specimen contained cholesterol crystals within the occluded small vessel (*arrows*: cholesterol crystals), **e** in-hospital course of serum creatinine levels

netic resonance aortography demonstrated a complex, ulcerated, atherosclerotic plaque in the course of descending thoracic aorta.

The most common clinical findings of the syndrome are cutaneous lesions, such as livedo reticularis, blue toe syndrome or digital gangrene more often affecting lower extremities, renal failure, and eosinophilia [3]. Considering renal involvement three types of atheroembolic renal disease have been described [4]. Our patient fulfilled the criterion of skin lesions and mild eosinophilia. Although the patient's baseline serum creatinine levels were already elevated due to preexisting chronic renal insufficiency, during the course of the hospital stay, a further deterioration in renal function occurred (◘ **Fig. 1e**). According to the pattern of renal impairment, our case matches the second type of atheroembolic renal disease which is characterized by a subacute time course with a gradual deterioration of renal function and with longer latent period of few weeks from the triggering event.

Currently, there is no widely acceptable treatment for CES. Various therapeutic strategies have been proposed including conservative, invasive or surgical measures; however, none of them has been tested in the clinical setting. Most authors agree that withdrawal of anticoagulants is beneficial [5]. Corticosteroids have been also used in many cases either as monotherapy [6] or in combination with statins [5] or cyclophosphamide therapy aiming to reduce the inflammatory burden of the affected capillaries [7]. Statins are also considered as a key therapeutic measure. The rationale behind statin treatment is that these agents apart from LDL-lowering properties demonstrated the ability of stabilizing vulnerable plaques and decreasing plaque inflammation [1]. Our patient was initially treated with atorvastatin 40 mg which subsequently titrated to 80 mg daily. For patients having focal stenoses, angioplasty and stent placement has been reported to be effective with a good mid-term prognosis [8]. Filter-assisted angioplasty has been also applied in order to ensure that no further embolization will take place during the procedure [9]. Surgical repair of the atheromatous aorta by passing the diseased area has also been described [10]. However, our patient was not considered as a candidate for any invasive or surgical therapeutic procedure because of the diffuse distribution of atherosclerotic plaques along the course of the descending aorta.

Conclusion

CES is an under-diagnosed clinical entity which is often related with increased in-hospital mortality. Since treatment options are limited without proven efficacy, increased awareness by the clinicians is needed. Except for statins, treatment is mainly supportive and close monitoring of renal function is required.

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Conflict of interest. The corresponding author states that there are no conflicts of interest.

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Abstract · Zusammenfassung

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Cholesterol embolization syndrome following thrombolysis during acute myocardial infarction

Abstract

Background. Cholesterol embolization syndrome (CES) is the result of atherosclerotic plaque erosion and subsequent dislodgement of cholesterol crystals from the core of the plaque to the peripheral arteries. The source of emboli is usually located in the aorta, whereas the most commonly affected organs are the skin and the kidneys.
Case report. The case of a 69-year-old male with cyanotic painful discoloration of his toes following thrombolysis for acute myocardial infarction 1 month previously is presented. Both transesophageal echocardiography and magnetic resonance aortography showed a diffuse ulcerated atherosclerotic plaque in the course of descending thoracic aorta, while a skin biopsy of the cyanotic toes revealed cholesterol crystals in the lumen of the small diameter arteries.
Conclusion. Cholesterol embolizations from the aorta are difficult to treat and may end in renal failure. Since treatment options are limited without proven efficacy, increased awareness by the clinicians is needed.

Keywords

Cholesterol embolization syndrome · Cyanotic toes · Thrombolysis · Atheroembolic renal disease

Cholesterinkristallemboliesyndrom nach Thrombolyse beim akuten Myokardinfarkt

Zusammenfassung

Hintergrund. Das Cholesterinkristallemboliesyndrom (CES) ist das Ergebnis der Erosion von atherosklerotischen Plaques und der anschließenden Verschiebung von Cholesterinkristallen vom Kern der Plaque in die peripheren Arterien. Die Quelle der Embolie ist meistens in der Aorta lokalisiert, wobei die am häufigsten betroffenen Organe die Haut und die Nieren sind.
Fallbeschreibung. Ein 69-jähriger Mann stellte sich mit schmerzhaften, zyanotisch verfärbten Zehen 4 Wochen nach Thrombolyse eines akuten Myokardinfarkts vor. Sowohl die transösophageale Echokardiographie als auch die kernspintomographische Aortographie zeigten eine diffus ulzerierte atherosklerotische Plaque im Bereich der thorakalen Aorta descendens, während die Hautbiopsie aus den zyanotischen Zehen Cholesterinkristalle im Gefäßlumen der kleinkalibrigen Arterien zeigte. Der Patient entwickelte eine progrediente Niereninsuffizienz, wahrscheinlich aufgrund von Kristallembolien auch in das Kapillarstromgebiet der Nieren, und verstarb nach dem 2. Infarkt.
Schlussfolgerung. Die Therapieoptionen bei Kristallembolie sind eingeschränkt und ohne nachgewiesene Wirksamkeit; erhöhte Aufmerksamkeit durch die klinischen Ärzte ist erforderlich.

Schlüsselwörter

Cholesterinkristallemboliesyndrom · Zyanotische Zehen · Thrombolyse · Atheroembolische Nierenerkrankung