Case Report

Penile necrosis in a haemodialysis patient: a rare manifestation of cholesterol crystal embolism

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Introduction

Cholesterol crystals embolism (CCE), an important new diagnosis for the general physician [1], is not so rare as previously considered, particularly in aged patients having erosive atherosclerosis and undergoing vascular surgery, invasive radiological studies, or receiving antiocoagulation [2–9]. The frequency of CCE in autopsy series varies between 1 and 17% [8] and the disease has emerged as a not infrequent cause of subacute or chronic renal failure [10–12].

Renal failure and cutaneous findings are the most frequently observed clinical manifestations of the disease [2–6]. Classically the clinical presentation may be non-specific and can mimic other multisystemic diseases [13–15]. Thus the diagnosis of CCE is often difficult. In a large series reported by Fine et al. [2], only 30% of cases were diagnosed correctly. In a large series reported by Fine et al., the diagnosis was made only in 30% of cases [2].

We report a case in which the diagnosis of CCE was suspected at the time of beginning dialysis but in which confirmation was made only when the patient developed an uncommon complication of the disease.

Case

A 65-year-old white caucasian man was hospitalized in the ophthalmology department of our general hospital for operation on a cataract. The preoperation laboratory examination showed that he had severe renal failure.

The patient had been treated for 3 years for diet-controlled diabetes and hypercholesterolaemia. He also had chronic renal insufficiency (serum creatinine 150 μmol/l 3 years before) and hypertension treated with a beta-blocker for 2 years. During the last 6 months he developed repeated very painful ulcerations of the toes, somewhat like chilblains. He was in poor general state of health (weight loss of 10 kg in the previous 9 months), complaining of asthenia, nausea, and vomiting for 4 weeks. There was no history of smoking but he was known to suffer from alcoholism. At clinical examination he showed a generalized muscular atrophy. Temperature 36.8°C, blood pressure 160/80 mmHg. Livid soles with a livedo reticularis and blue toes were particularly evident in the recumbent position. The peripheral pulses, including foot pulses, were all preserved without murmurs. The left heel had a very painful non-inflammatory dry ulceration. The tendinous reflexes were all present with normal sensibility and pallaesthesia. A Doppler of the arteries of the legs showed physiological pressures, and the transcutaneous oximetry at the back of the feet was normal.

Laboratory results included sedimentation rate 36 mm/h, CRP 47 mg/l, haemoglobin 115 g/l, haematocrit 36 mm/l, leukocytes 9.1 G/l with 7.5% eosinophils. The serum creatinine was 800 μmol/l, blood urea 30 mmol/l, fasting glucose 6.4 mmol/l, serum sodium 146 mmol/l, serum potassium 3.6 mmol/l, ionized calcium 1.16 mmol/l, serum phosphate 1.98 mmol/l, serum phosphate 312 U/l, gamma-GT 288 U/l, HbA1c 4.6%, total cholesterol 4.2 mmol/l, triglycerides 1.28 mmol/l, HDL cholesterol 1.10 mmol/l, and intact parathyroid hormone 86 pg/ml. The serum electrophoresis was normal. The 24-h urine collection contained 0.96 g of proteins (53% albumins) with no Bence Jones protein. Creatinine clearance was 5 ml/min. Urinanalysis showed no erythrocytes or leukocytes. The serologies for HBV, HCV and HIV were negative. The antinuclear factor, anti-ds DNA, anti-RNP, SSA, SSB, cANCA, pANCA, and anti-GBM antibodies were also negative. An abdominal ultrasound showed atrophy of both kidneys and no dilatation of the urinary tract. There was no aortic aneurysm.

An ophthalmoscopic examination of the eyes did not show retinal embolism. A fluorescein angiography showed a diabetic proliferative retinopathy. A renal biopsy was not performed because of the kidney atrophy and the patient refused a skin or muscle biopsy. The diagnosis of cholesterol embolism was suspected but could not be confirmed at that time.

Chronic haemodialysis was started because of the ureaemic syndrome. His general condition progressively improved, but the patient continued to complain of
his painful cutaneous lesions. Four months later he was hospitalized for an upper gastrointestinal hemorrhage. Shortly after he developed a necrosis of the two distal centimetres of the penis. An amputation of the necrotic zone was performed and examination of the histological slides disclosed the presence of cholesterol embolism within the arterioles of the penis (Figure 1). Six months later the patient died of infection.

Discussion

CCE is characterized by the embolization in different organs of cholesterol crystals from the arteriosclerotic plaques lining the walls of major arteries. Once considered a rare disease, in recent years CCE has been shown to be more frequent than was previously thought [1–9]. Autopsy reports indicate a frequency varying from 1 to 17% [8]. A large Dutch study estimated the frequency of six to eight cases per million inhabitants per year [3]. However, as already suggested by several authors, these figures probably underestimate the real frequency of the disease [7–9]. CCE may be asymptomatic, may present with non-specific symptoms, or may mimic other multisystemic diseases, and is thus often undiagnosed antemortem [8]. Fine et al. considered that premortem diagnosis was made in only 30% of cases [2]. Most authors emphasize that the premortem diagnosis of CCE may be quite difficult. According to data from the literature, CCE may have two distinct clinical forms: acute/subacute, and ‘chronic indolent’ [8,9]. The former occurs mainly in patients having undergone invasive procedures or thrombolytic therapy and includes multisystemic manifestations, while the latter often presents with a progressive worsening of renal function in patients with long-lasting hypertension, often without any other associated symptom [8]. CCE occurs mainly in aged patients having erosive atherosclerosis either ‘spontaneously’ or—in 10–35% of cases—following vascular surgery, invasive radiological studies, thrombolytic therapy, or during anticoagulation [1–12]. The major clinical manifestations of CCE are progressive renal failure in 30–50% of cases, skin lesions with typically a livedo reticularis and blue toes (with normal peripheral pulses) in 15–35% of cases, and gastrointestinal symptoms in 10–20% of cases [2,3].

Our case report summarizes several aspects of the clinical presentation and of diagnostic problems of CCE. During the clinical course the patient had several symptoms and signs, as well as biological abnormalities, focusing the diagnosis on CCE. However, it was not possible to confirm this diagnosis until he developed a quite uncommon complication of the disease. To our knowledge this is the first case of penile necrosis due to CCE reported. Moolenaar and Lamers mentioned a case of cholesterol embolism in the corpus cavernosum [3] and Scholten et al. reported a case of preputial necrosis as an unusual cutaneous manifestation of CCE [16].

The diagnosis of CCE depends on a high degree of clinical suspicion [7–9] and should ideally be confirmed by a biopsy specimen. The recommended sites of biopsy are the muscle, skin, and/or kidneys. Unfortunately the sensitivity of these diagnostic procedures is low. Actually, as CCE is a patchy non-uniform lesion, cholesterol emboli may be missed on histological slides [9]. The presence of retinal emboli is a useful non-invasive diagnostic index, but one must be aware that retinal cholesterol emboli may be found in asymptomatic patients who will never develop clinical manifestations of CCE [17].

Many authors focused on an unfavourable clinical course of CCE, with a high mortality rate, up to 81% [2]. However, a less severe evolution has also been reported particularly in patients presenting with the ‘chronic indolent’ form of the disease [8]. It appears that some patients with renal insufficiency may in time partially recover their renal function [10–12]. The treatment is disappointing, even if some beneficial effects have been occasionally reported with various therapies, including steroids, lovastatin, pentoxifylline, low-dose dopamine, or ticlodipine [8,9,18,19]. Anticoagulation should be discontinued [1,6,8]. Prevention is also important, and all not strictly necessary invasive manoeuvres or surgical procedures should be avoided in aged patients with atherosclerosis.

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