Interesting Case

Which type of dialysis in patients with cholesterol crystal embolism?

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Introduction

Cholesterol crystal embolism (CCE) is an increasingly frequent and potentially severe complication of atherosclerotic vascular disease, resulting from embolization of cholesterol crystals from aortic atherosclerotic plaques to various organs. As recently reviewed [1], CCE may occur spontaneously but is usually triggered by a variety of procedures including arteriography, vascular surgery and anticoagulation—resulting from administration of heparin, low-molecular-weight heparin, oral anticoagulants or thrombolysis [1–3]. The diagnosis of CEE may be challenging because both the clinical picture, which ranges from totally asymptomatic to multisystemic disease, and the laboratory findings lack specificity [1]. Diagnostic clues include risk factors for atherosclerosis, characteristic features such as renal, retinal or cutaneous involvement, and laboratory abnormalities such as hypereosinophilia and hypocomplementaemia [1]. In absence of clinical evidence, histological identification of cholesterol crystals in a target organ remains essential for diagnosis and is the only way to distinguish CCE from systemic vasculitis [1]. Despite aggressive supportive treatment, the outcome of CEE remains poor, with first-year mortality rates ranging from 20 to 80% [1,4,5].

Renal involvement is found in > 50% of the patients with CCE [1,6]. Renal failure may occur within a few days after the triggering factor, or appear progressively over several weeks [1,6]. In about one-third of patients, renal function may recover spontaneously or after dialysis support. In 35 to 61% of patients, renal involvement progresses to irreversible end-stage renal failure, requiring renal replacement therapy [1,5,7]. In that setting, haemodialysis (HD), which requires repeated systemic anticoagulation, has been considered as a potentially precipitating factor [8].

We present a case of CCE, which stresses the potential role of HD in precipitating the syndrome. This allows us to discuss the options for dialysis when end-stage renal failure complicates the course of CCE. In addition, this case emphasizes the usefulness of gastroscopical biopsies and eosinophilia in determining the diagnosis and follow-up of CCE.

Case

A 68-year-old man was admitted to the hospital on December 1, 1999, because of abdominal pain and severe deterioration of his general status with a weight loss of 10 kg over the previous 2 months. His past medical history included arterial hypertension, successfully treated by beta-blockers and calcium channel antagonists, and active smoking (totalizing 20 pack-year). Two months before admission, he presented an episode of unstable angina. Coronarography revealed a severe stenosis (90%) of the circumflex artery. Angioplasty followed by stent placement was successfully performed. The patient was discharged with a normal renal function (serum creatinine 1.0 mg/dl).

On admission, physical examination revealed severe arterial hypertension (250/130 mmHg in supine position), epigastric tenderness, blue toes, and livedo reticularis in the lower limbs. Laboratory data showed an increase in serum creatinine (4.7 mg/dl) and urea (192 mg/dl), a normal white blood cell count (9760 /μl) with 10% eosinophils (970 /μl), anaemia (haemoglobin 9.8 g/dl), slightly decreased platelet count (120 000 /μl), and increased levels of C-reactive protein (2.7 mg/dl, normal <0.5 mg/dl) and LDH (825 IU/l, normal 200–393 IU/l). Urinalysis revealed 10 RBC/HPF and significant proteinuria (1.6 g/24 h). C3 and C4 complement levels were within normal limits. Autoimmune disease markers, including ANCA, ANA, and rheumatoid factor were negative.
The diagnosis of subacute renal failure secondary to CCE was suspected on the basis of the clinical and laboratory findings. Funduscopic examination failed to show retinal cholesterol emboli. Abdominal CT-scan demonstrated a 3-cm aortic aneurysm and ruled out mesenteric ischaemia and splenic infarct. Gastroscopy showed diffuse gastritis as well as a bulbar ulcer. The diagnosis of CCE was confirmed by gastric and duodenal biopsies, which revealed cholesterol crystals in submucosal arterioles.

Despite clinical improvement and regression of cutaneous signs, renal function worsened over the following few days and eventually required renal replacement therapy. Continuous ambulatory peritoneal dialysis (PD) was started on December 16, 1999. Two weeks later, the development of a severe dialysate leak through an abdominal wall hernia required surgical repair and temporary transfer to HD. The two first HD sessions, on December 31, 1999 and January 5, 2000, were conducted with systemic anticoagulation (8000 and 6000 IU heparin/session, respectively). On January 6, the patient complained of general malaise, anorexia, and abdominal pain. This was paralleled by recurrence of livedo reticularis and skin necrosis on both feet, together with a striking rise of eosinophilia (2010 μl) (Figure 1). We suspected that the worsening of his clinical condition was caused by recurrence of CCE, triggered by the anticoagulation associated with HD. The two following HD sessions, on January 6 and 17 were conducted without heparin, and PD was resumed on January 19.

Both general status and skin lesions improved dramatically, and the patient was discharged on January 21, 2000. The patient was followed-up over the subsequent few weeks in the outpatient clinic. He remained asymptomatic, and cutaneous signs, including blue toes and livedo reticularis, disappeared. In parallel, his eosinophil count normalized (490 μl). The patient was then followed-up by his physician at home, where he suddenly died from a heart attack 2 months later.

Discussion

We report here a classical case of CEE in a 68-year-old white male patient, with a history of arterial hypertension and heavy smoking, occurring 2 months after a coronary angiography. The course of CCE was complicated by rapidly progressive renal failure, ischaemia of the lower limbs and a bulbar ulcer. The diagnosis of CCE, which was suspected on the basis of the clinical course and laboratory abnormalities, was proven by light microscopy evidence in four gastro-duodenal biopsies.

Gastrointestinal involvement is found in 20–50% of patients with CCE, depending on the series [9]. A common mode of presentation is abdominal pain or gastrointestinal bleeding, which may range from occult blood loss and anaemia to frank haemorrhage. Rare complications such as pancreatitis, pseudo-polyp, hepatitis and acalculous cholecystitis have also been reported. Fiberoptic endoscopy may reveal diffuse gastritis, gastric or duodenal ulcerations as well as mucosal infarcts and angiodysplasia [9]. In their series of 67 patients with CCE, Belanfant et al. found cholesterol crystals in the gastric mucosa of nine symptomatic patients [5]. Thus, as illustrated here, endoscopy of the digestive tract may be a precious tool to confirm the diagnosis of CCE, especially in absence of skin lesions.

The clinical course of this patient with CCE was marked by renal failure necessitating renal replacement...
therapy. PD was the first-choice modality of dialysis, because it does not require systemic anticoagulation and induces less haemodynamic variations than HD. A dialysate leak through a hernia unfortunately required a temporary transfer of the patient to HD. The subsequent HD sessions conducted with classical heparinization were followed by recurrence of both clinical features and eosinophilia, characteristic of CCE. The regression of these symptoms after discontinuation of HD suggests a causal relationship between the recurrence of CCE and HD-associated anticoagulation (Figure 1).

It is interesting to note that eosinophilia is often found in the active phase of CCE and could have a role in the pathogenesis of the disease. Indeed, atheromatous material induces polymorphonuclear leucocyte aggregation and the subsequent release of C5a chemotactic factor and oxygen free radicals that alter endothelial cells [10]. Whereas the extremely transient nature of hypocomplementaemia limits its diagnostic utility in CCE, hypereosinophilia is considered as the most common diagnostic marker of CCE, with a prevalence ranging from 15 to 70% of the cases [5,7]. However, it is by no means specific [1].

The temporal relationship between the clinical and biological features of the patient’s disease and the modality of dialysis raises the important question of the ideal mode of renal replacement therapy in CCE. As mentioned earlier, PD offers a handful of advantages and might be the preferred option [8]. However, there are also some theoretical contra-indications to PD in CCE—such as mesenteric ischaemia, which can lead to tissue-repair processes and bowel fragilization [5]. In addition, PD may have to be withdrawn because of technical failure, including recurrent peritonitis, protein malnutrition, or a dialysate leak as illustrated here. When indicated in patients with CCE, HD should be performed without systemic anticoagulation. Obviously, such HD is associated with the potential risk of repeated coagulation events of the extracorporeal circuit and subsequent anaemia—a potentially serious complication in CCE patients with gastrointestinal involvement. Practically speaking, high blood flow rates and frequent flushing of the dialyser with saline will help prevent clotting. Anticoagulation with very low doses of heparin (1000 IU/session), which may be adjusted based on clotting time, is another possibility to avoid the recurrence of CCE [1,5]. The use of low-molecular-weight heparin during HD has also been suggested. However, low-molecular-weight heparin can also trigger CCE and its use at the beginning of HD has been associated with the recurrence of CCE as well [2,11]. A potentially interesting alternative for CCE patients requiring dialysis would be daily, short HD sessions using no anticoagulation at all.

Conclusion

Because an impairment of renal function frequently complicates CCE, dialysis treatment may be required. PD should be the preferred treatment modality because it does not require systemic anticoagulation and induces less HD variations. When HD is chosen, one should be aware of it being a potentially precipitating factor of CCE. In this case, HD should be conducted without or with only minimal systemic anticoagulation. One should also note the theoretical advantage of short daily HD sessions without heparin.

References