Case Report

Bilateral Endophthalmitis and Symmetrical Peripheral Gangrene in a Patient with Chronic Kidney Disease on Maintenance Hemodialysis

Jishu Deb Nath, Abul Kashem, Ayesha Mohammad Osman, Tapas Das

Departments of Medicine and Nephrology, Chattogram Maa-O-Shishu Hospital Medical College, Chattogram, Bangladesh

ABSTRACT. Dialysis patients have greater number of complications due to multiple comorbidity and access-related infections as well as nosocomial infections due to reduced immunity and more frequent hospitalizations. Endogenous endophthalmitis is a potentially blinding ocular infection occurring in chronically debilitated patients and the use of invasive procedures. Symmetric peripheral gangrene (SPG) is defined as symmetrical distal ischemic damage in two or more sites in the absence of a major vascular occlusive disease. It carries a high mortality rate with a very high frequency of multiple limb amputations in the survivors. However, only a few case reports have described endogenous endophthalmitis in dialysis patients. Concomitant endophthalmitis and disseminated intravascular coagulation (DIC), presenting as SPG, is extremely rare and no such case was found in the literature survey. Herein, we report a very rare association of bilateral endophthalmitis with DIC and SPG in a patient with chronic kidney disease on maintenance hemodialysis.

Introduction

Bacterial endophthalmitis is an infection and inflammation of the posterior segment of the eye that can rapidly evolve into a sight-threatening situation. Endogenous endophthalmitis usually presents with blurred vision and ocular pain, and only less than half of patients have signs of systemic infections such as fever.

Many etiologic organisms (Gram-positive, Gram-negative, and fungal) have been reported to cause endogenous endophthalmitis. During endophthalmitis, bacteria enter the posterior segment following trauma, surgery, or from spread into the eye through the bloodstream from a distant focus of infection. Disseminated intravascular coagulation (DIC) is an acquired syndrome characterized by widespread intravascular activation of coagulation that can be caused by any underlying pathology, such as severe infections, malignancies, trauma, or obstetric complications. DIC itself can be asymptomatic. It can also be associated with bleeding or the signs of systemic thrombosis that may lead to life-threatening
multiple organ failure. Symmetrical peripheral gangrene (SPG) is very rare manifestation of DIC. Chronic dialysis patients have defects in both innate and adaptive immunity, thus predisposing them to infectious disease.

**Case Report**

Informed consent was obtained from the immediate relatives of the patient before reporting the case.

A 57-year-old female with known chronic kidney disease (CKD) undergoing maintenance hemodialysis (MHD) twice weekly for the past seven months was admitted to a private hospital in Chattogram, Bangladesh, with complaints of high-grade intermittent fever with anuria and blurring of vision in both eyes for three days. She had previous history of diabetes and hypertension for 10 years. Initial examination showed that she was confused and febrile, mildly anemic, and had reduced blood flow in the arteriovenous fistula site. She was initially diagnosed with a case of acute kidney injury on CKD with bilateral endophthalmitis due to sepsis. She was treated with intravenous and ocular broad-spectrum antibiotics, and MHD was continuing with a jugular catheter. One day after admission, bluish discoloration followed by blackening of the distal left middle phalanx and swelling and blackening of the right hand and multiple hemorrhagic purpura appeared in soles of both feet (Figures 1 and 2). At the same time, the patient complained of complete loss of vision in both eyes. Ocular examination showed no perception of light, projection of rays. Both radial and dorsalis pedis pulse were palpable. There was no past history of joint pain, hematuria, Raynaud’s phenomenon, and intake of B-blockers. Antibiotics were changed to intravenous piperacillin/tazobactam combination with metronidazole, and she was diagnosed further with bilateral panophthalmitis with SPG due to sepsis. Complete blood count showed neutrophilic leukocytosis, neutrophil was 95%, total count was $20.7 \times 10^9$/L, hemoglobin (Hb) was 11 g/dL, and urine routine analysis and culture were normal. The serum creatinine was 9 mg/dL, fasting blood sugar and 2-h postprandial blood sugar were 119 and 198 g/dL, respectively, glycosylated Hb was 6.4%, serum albumin was 2.71 g/dL, and uric acid was 7 mg/dL. Serum electrolytes showed hyponatremia, sodium was 133 meq/L, calcium was 6.1 mg/dL, and phosphate was 5.8 mg/dL. Blood culture showed the growth of *Serratia* species. The electrocardiogram showed nonprogression of R wave and left ventricular hypertrophy, echocardiography...
showed concentric hypertrophy, mild mitral and aortic regurgitation, and color Doppler imaging of both upper limbs showed no blood flow in the left 4th metacarpal artery, but sparing large arteries on both sides. Prothrombin time was >44 s, P-anti-nuclear cytoplasmic antibodies (ANCA) was 5.6 (<12, normal value), anti-nuclear antibody was 3.9 (<10, normal), C-ANCA was 10.2 U/mL, (<12, normal), Antidouble strand DNA was 14.2 U/mL (<20, normal), and D Dimer was initially 6.31 g/mL (<0.5, normal) which became progressively diminished to 4.1 g/mL and 2.3 g/mL later on, and APTT was 38 s (25–43 s). Unfortunately, the patient died 10 days later as her relatives were reluctant to subject him to any surgical procedure.

Discussion

CKD is associated with poor outcomes including an increased risk of cardiovascular disease and mortality. These associations may result from the presence of traditional risk factors as well as biochemical abnormalities such as increased inflammatory factors, endothelial dysfunction, and enhanced coagulation. Increased risk for infections is linked to alterations in the immune system in CKD, since uremia is associated with a state of immune dysfunction characterized by immunodepression that contributes to the high prevalence of infections among these patients, as well as by immune-activation resulting in inflammation.

Endogenous endophthalmitis (also known as metastatic endophthalmitis) results from the spread of the organism into the eye from an infection elsewhere in the body. Compared with endophthalmitis following trauma or surgery, endogenous endophthalmitis is relatively rare, accounting for only 2%–8% of all reported endophthalmitis cases. The prevalence of endogenous endophthalmitis is higher than exogenous endophthalmitis in chronic dialysis patients. However, endogenous endophthalmitis carries with it the danger of bilateral infection in 15%–25% of cases. Fungal organisms account for at least 50% of all endogenous cases, with Candida albicans (75%–80% of fungal cases) being the leading causative agent. Gram-negative organisms cause 32%–37% of all cases of endogenous endophthalmitis and typically have poor visual outcomes because these infections are difficult to treat.

Only a few case reports have described endogenous endophthalmitis among dialysis patients in the literature. These case reports highlight that vascular access should be considered as a possible and unique source of infection in the dialysis population. Serratia marcescens was earlier considered to be an innocuous, nonpathogenic organism, but over the past two decades, it has become an opportunistic pathogen causing nosocomial infections. A broad range of hospital-acquired infections caused by S. marcescens including respiratory tract infections, urinary tract infections, septicemia, meningitis, pneumonia, conjunctivitis, wound and eye infections, keratitis, endophthalmitis, and endocarditis have been reported. Reports have shown rare cases of S. marcescens in nonhospital settings.

Severe systemic infections or sepsis are the most common causes of DIC. About 35% of cases of severe sepsis may be complicated by DIC. Classically, infection with Gram-negative microorganisms has been associated with DIC. Systemic infections with other microorganisms, including fungi or parasites, may lead to DIC as well. For example, high parasitemia, primarily of Falciparum malaria, may be associated with DIC and high mortality.

The initiation and propagation of procoagulant pathways with simultaneous impairment of natural anticoagulant systems and suppression of endogenous fibrinolysis as a result of systemic inflammatory activation lead to platelet activation and fibrin deposition. Important mediators that regulate these processes are cytokines, such as interleukin-1 (IL-1) and IL-6 and tumor necrosis factor-α.

Purpura fulminans, a severe form of DIC, is characterized by diffuse microthrombi of the skin leading to hemorrhagic necrosis. This is classically seen in meningococcemia.

SPG is characterized by symmetric necrosis of the skin and distal extremities, following
which two or more distal sites become gangrenous in the absence of large artery occlusion.\textsuperscript{8,9} SPG is described as multiple extremity ischemia at two or more sites in the absence of large vessel obstruction. It is well established that the digital perfusion will drop to zero in the presence of persistently low perfusion pressures of 35–60 mm Hg.\textsuperscript{10}

SPG is known to present with pallor or cyanosis, coldness, and pain in the extremity in the initial phases. If appropriate care is not provided at this stage, the digits may progress to become erythematous with dusky discoloration of the skin followed by the development of bullae or blisters that subsequently result in the formation of gangrene.\textsuperscript{11}

SPG is associated with a high rate of amputation (auto-amputation or surgical amputation) of the limbs in the survivors. In a prospective case series from Eastern India, six patients had amputation out of the nine survivors of SPG. In another retrospective case series from the USA, eight patients had amputation out of the nine survivors.\textsuperscript{12} The mortality rate of SPG is also very high. About one-third of the patients of different case series had died.

Calciphylaxis is a serious, uncommon disease in which calcium accumulates in small blood vessels of the fat and skin tissues. Lesions begin characteristically as a livedo reticularis pattern of mottling with violaceous, superficial, tender nodules, and presentation can be mistaken for cellulitis. In this case, presentation was so florid with the lack of this discoloration. Hence, SPG was diagnosed clinically by the exclusion of calciphylaxis.\textsuperscript{13}

Conclusion

A high degree of suspicion is necessary to make an early diagnosis of endogenous endophthalmitis with patients commonly complaint of eye pain and blurring of vision. Surgical intervention is generally recommended for patients infected with virulent organisms. Even with aggressive treatment, outcome is very disappointing.

Conflict of interest: None declared.

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