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Uremia as an immunosuppressive factor in a patient with acquired immunodeficiency syndrome: A case report and review

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Abstract

We report a case of a patient with AIDS and non-dialytic renal failure who presented a spontaneous abscess in the thigh and progressed with sepsis. Non-typical infectious disease of a cellular immunodeficiency characteristic of AIDS, but rather from a phagocytic disorder and very probably caused by uremia. Patients with defects in cellular immunity, such as AIDS patients, have intracellular pathogen infections while phagocytosis defects are characterized by the formation of abscesses and sepsis. In this article, we explain the possible mechanisms caused by uremia that impair phagocytosis and may trigger abscesses and sepsis.

Keywords

Uremia; AIDS; Immunosuppression; Phagocytic dysfunction.

Introduction

In recent decades, relevant evidence has accumulated concerning the immunosuppressive effect of uremia on the immune system. This effect has been studied very little compared with what is known about the impact of uremia on metabolism and other systems. Infections are known to be the leading cause of morbidity and mortality in chronic kidney patients, but the mechanisms that trigger these processes are poorly elucidated. The literature contains reports of phagocytic disorders triggered by uremia. These disorders cause abscess formation and sepsis. We report a case of a patient with chronic renal failure and AIDS who spontaneously presented a large abscess on the thigh and later presented sepsis, a severe condition that suggests that it was caused by phagocytic dysfunction rather than by defective T cells [1]. In this report, we present evidence that characterizes our patient's uremia as the causative agent of this clinical condition.

Case Report

The patient was aged 51 years old and has been a carrier of the AIDS virus for 28 years (1992). He has been prescribed antiretroviral treatment since 1995. He has followed several antiretroviral regimens, established undetectable viral load and began presenting CD4+ levels of 550 to 777 cells/mm^3 from 2007 onwards. The patient had neurotuberculosis in 1996 and presented necrosis of the femoral head bilaterally, in 2000. In 2006 and 2007, an operation for bilateral femoral prostheses was performed. Even though his AIDS was successfully controlled with antiretroviral treatment, in 2011, the patient showed progressive renal failure, which was under investigation, but its etiology was not established. This could be due to the human immunodeficiency virus (HIV) or by regular use of tenofovir, which was replaced but did not prevent its progressive loss of renal function; In December 2017, our patient had chronic renal parenchyma nephropathy with normal renal Doppler flowmetry, a normal venous blood gas analysis (pH 7.39, PCO_2 43 mmHg, PO_2 31 mmHg, BE 2.5, $satO_2$ 57%), and uremia. In december 2019, he had no complaints when he began to feel pain in his right thigh and progressive swelling. He was evaluated by an orthopedist and infection or some other problem in the prosthesis was discarded. After three days of intense progressive pain, he was hospitalized for fever and increased right thigh volume and showed difficulty walking. At the time, he had undetectable viral load for HIV and CD4+ of 777 cells/mm^3 and CD8+ 1535 cells/mm^3. He was being prescribed fosamprenavir + lamivudine + raltegravir + ritonavir. A diagnosis was made of bulging abscess collection in the right thigh, sepsis and worsening of chronic renal failure. A large amount of purulent secretion (about 900 ml) was drained. Gram stain and culture of the secretion presented negative growth for yeasts and bacteria. Blood culture showed gram-positive cocci. Daptomycin + clindamycin was prescribed for 21 days. The patient was hospitalized for 30 days and dialysis was initiated due to worsening renal function during hospitalization. He is currently on hemodialysis three times per week. The dihydrorhodamine assay performed after hospitalization was normal. Their antibody levels were normals. IgG: 1018 mg / dL; IgA: 394 mg / dL.

Discussion

Our patient spontaneously presented a large pyogenic abscess collection in the right thigh, with no associated trauma or injury at the site, which evolved to sepsis. The severe and unusual evolution strongly suggests it was caused by immunosuppression, and given that the patient has AIDS, this initially led us to consider that the condition was likely caused by his underlying disease. AIDS causes cellular immunodeficiency when CD4+ lymphocyte levels are greatly reduced, commonly below 350 cells/mm^3. Cellular immunodeficiencies cause infections by intracellular pathogens, such as mycobacterioses, systemic fungal infections and others, including pneumocystosis, cerebral toxoplasmosis, and disseminated viral infections. However, this type of opportunistic infection is not expected in patients presenting normal CD4+ cell levels of 777 cells/mm^3 and undetectable viral load, as was the case in our patient. Even if he were presenting abnormal CD4+ levels, the dysfunction or decrease in CD4+ cells would not explain how this abscess formed nor the subsequent sepsis. Immunological defects characterized by the formation of spontaneous abscesses and sepsis are suggestive of phagocytic disorders, rather than cellular immunodeficiency [1].

This raised an intriguing question regarding the mechanism causing the probable phagocytic disorder. About twelve years earlier, the patient began developing progressive renal failure and became dialytic following sepsis. In 2016, the patient presented a creatinine of 3.19 mg/dL and urea of 128 mg/dL, i.e. he already presented an important uremia. Numerous studies in the literature show evidence of the harmful impact of uremia on immunity. It is known that uremic patients have a higher susceptibility to severe bacterial infections and are the main cause of morbidity and mortality [2-4]. In recent decades, several studies have shown that uremia triggers deleterious action on neutrophil phagocytosis [5] and monocytes [6], in addition to other immunological defects. The first line in the fight against bacteria is polymorphonuclear cells, which move to the infection zone by chemotaxis and phagocytose and destroy the microorganisms through proteolytic enzymes and toxic oxygen radicals produced by oxidative burst. Defects in polymorphonuclear function significantly increase the chance of bacterial infections [1]. The susceptibility of uremic patients to infections is caused by a defect in phagocytosis due to a range of causes, including uremic toxins, iron overload, kidney disease anemia, and dialyzer biocompatibility [6]. Anding et al. demonstrated that the phagocytic capacity of neutrophils in uremic patients on hemodialysis is diminished [7]. Another study reported that following the worsening of uremia in nephropathic patients, neutrophils presented progressive impairment of phagocytic capacity due to a deterioration in oxygen-dependent microbicidal mechanisms due to decreases in the production of O_2- and H_2O_2 [8]. Jin et al. investigated the expression of the gp91phox and IL-8 genes and the neutrophil function of patients with chronic dialysis renal failure. A decrease in gp91phox gene expression was verified in the neutrophils of these patients, indicating compromise of the NADPH-oxidase system. This causes a defect in the formation of superoxides, which are fundamental to the intracellular digestion of phagocytosed pathogens. They also reported a decrease in the expression of IL-8 expression in neutrophils, which causes the suppression of phagocytosis and intracellular killing capacity, since this cytokine has the important property of attracting immune cells, like neutrophils, to the inflammatory site through CXCR1 and CXCR2 receptors [9]. A decrease in IL-8 expression impairs this property. Other studies suggest that the accumulation of uremic toxins may accelerate the apoptosis of lymphocytes, monocytes and polymorphonuclear cells, and this can significantly reduce the immune response of uremic patients and favor infections [10]. Cendoroglo et al. demonstrated that uremic neutrophils undergo apoptosis in vitro and uremic plasma accelerates neutrophil apoptosis in normal individuals [11]. In murine models and in humans, Rossaint et al. have shown that acute loss of renal function reduces of leukocyte recruitment by abolishing selectin-induced slow leukocyte rolling on E-selectin/ICAM-1 and P-selectin/ICAM-1 and reduced transmigration without affecting chemokine-induced arrest. The abolition of selectin-mediated slow leukocyte rolling occurred due to a reduction in the phosphorylation of spleen tyrosine kinase (Syk), Akt, phospholipase C (PLC) γ2, and p38 MAPK and with no change in the expression of adhesion molecules on the surface of neutrophils [12]. Our patient presented a normal dihydrorhodamine assay. This assay shows that the level of superoxides in neutrophils was normal, thus ruling out a defect in oxidative burst and, consequently, in the production of superoxides. However, this test was performed after the patient began hemodialysis and, therefore, he presented decreased urea levels. Some authors have observed defects in opsonization in patients with uremia [2]. Opsonization facilitates phagocytosis, is critical in the defense against encapsulated bacteria, and can result in susceptibility to serious infections among uremic patients. As discussed in this article, numerous studies

show that uremia causes harmful effects in migration and oxide and superoxide production, thus increasing neutrophil apoptosis and decreasing opsonization. It is highly likely that the clinical condition presented by our patient was caused by the harmful effect of uremia on phagocytic cells. This case may contribute to understanding the relationship between uremia and phagocytosis, but further studies should be conducted to more clearly understand the phenomenon.

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