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Original article

High rate of *Candida* deep-seated infection in patients under chronic hemodialysis with extended central venous catheter use

Ana Paula Jafet Ourives[a], Sarah Santos Gonçalves[a], Ricardo Andreotti Siqueira[a], Ana Carolina Remondi Souza[a], Maria Eugenia F. Canziani[b], Silvia Regina Manfredi[c], Luci Correa[d], Arnaldo Lopes Colombo[a,*]

[a] *Laboratório Especial de Micologia, Disciplina de Infectologia, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, SP, Brazil*
[b] *Disciplina de Nefrologia, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, SP, Brazil*
[c] *Hospital do Rim e Hipertensão-Fundação Oswaldo Ramos, Brazil*
[d] *Hospital Israelita Albert Einstein, Brazil and Escola Paulista de Medicina, Universidade Federal de São Paulo, SP, Brazil*

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ABSTRACT

Background: Hemodialysis has been described as an important risk factor for the development *of* candidemia in patients suffering from chronic renal failure.
Aims: The aim of this study was to evaluate the epidemiology of candidemia in outpatients with renal replacement therapy (RRT) by hemodialysis where the fungemia clearly represents a healthcare-associated infection.
Methods: We retrospectively collected clinical and laboratory data from patients undergoing at least 3 months of RRT by hemodialysis who developed candidemia within 48 h of hospital admission.
Results: We identified 14 patients with candidemia with central venous catheters (CVC) in place for 11–277 days before developing fungemia. Deep-seated infection was documented in 6 out of 14 candidiasis cases (43%), including 5 cases of endocarditis (36%).
Conclusions: CVC in patients under RRT should be promptly replaced by fistulas and grafts to avoid bloodstream infections. Facing a case of candidemia, adequate source control and prompt initiation of antifungal therapy are mandatory to avoid morbidity and mortality.

Altas tasas de infección profunda por *Candida* en pacientes en hemodiálisis crónica con catéter venoso central de uso prolongado

Palabras clave:
Candidemia comunitaria adquirida
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Candida parapsilosis

RESUMEN

Antecedentes: La hemodiálisis se ha descrito como un importante factor de riesgo para el desarrollo de candidemia en pacientes con insuficiencia renal crónica.
Objetivos: El objetivo de este estudio fue evaluar la epidemiología de la candidemia en pacientes en hemodiálisis con terapia renal sustitutiva (TRS), en la que la fungemia representa claramente una infección asociada a los cuidados hospitalarios.
Métodos: Se recogieron retrospectivamente datos clínicos y microbiológicos de pacientes con, al menos, 3 meses de hemodiálisis con TRS que desarrollaron candidemia dentro de las primeras 48 horas tras la admisión hospitalaria.
Resultados: Identificamos a 14 pacientes con candidemia asociada con el uso de catéter venoso central (CVC) durante períodos de 11 a 277 días previos al desarrollo de la fungemia. En 6 de los 14 casos de candidemia, el diagnóstico fue de candidiasis invasiva (43%), incluidos 5 casos de endocarditis (36%).

* Corresponding author.
E-mail address: arnaldolcolombo@gmail.com (A.L. Colombo).

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Conclusiones: Los CVC en pacientes con TRS deberían ser sustituidos inmediatamente por fístulas o injertos arteriovenosos para evitar infecciones del torrente sanguíneo. Ante los casos de candidemia, un control adecuado de las posibles fuentes de infección y el comienzo inmediato de la terapia antifúngica deberían ser imperativos para reducir tanto la morbilidad como la mortalidad.

Nosocomial bloodstream infections due to *Candida* species represent a frequent complication in patients submitted to invasive medical procedures, including major surgeries, the use of central venous catheters (CVCs) and hemodialysis.[8,23] Indeed, invasive fungal infections represent a substantial cause of morbidity and mortality in patients with chronic renal failure.[7,25]

Chronic renal failure is a medical condition with an increasing incidence worldwide.[16,29] It is estimated that by 2020, two thirds of end-stage renal disease (ESRD) patients in the United States will require hemodialysis, which makes this population highly susceptible to bloodstream infections.[7] Brazil, United States, Germany, Italy and Japan are home to 12% of the world's population, and more than half of all patients with ESRD are now being treated in these countries.[18] Arteriovenous fistulas are the ideal permanent vascular access method for patients under renal replacement therapy (RRT) by hemodialysis to avoid bloodstream infections.[2,3] However, in Brazil, there is a delay in constructing the fistula, which leads to the prolonged use of central venous catheters for hemodialysis and an increased risk of infections.[4]

Several studies have reported the occurrence of candidemia in chronic renal failure patients during their hospitalization, where hemodialysis represents one among several other risk conditions and comorbidities that may contribute to patient outcomes.[25,27,28] The focus of our study was to evaluate the epidemiology of candidemia in outpatients with RRT by hemodialysis where the fungemia clearly represents a healthcare-associated infection.

Materials and methods

Study setting

We retrospectively collected the clinical and laboratory data of patients undergoing at least 3 months of RRT by hemodialysis who developed candidemia within 48 h of hospital admission during a four-year period. This study was conducted in the Hospital do Rim e Hipertensão, a center of excellence and world leader in kidney transplantation with approximately 150 beds located in São Paulo (Brazil).

Definitions

An episode of candidemia was defined as the incident isolation of *Candida* from one or more blood cultures (BACTEC System) of a patient under RRT by hemodialysis. Candidemia occurring more than 30 days after the incident isolation was defined as a new episode. Patients were followed for 90 days after the diagnosis of candidemia. Endocarditis was defined according to the DUKE criteria.[11] The diagnosis of endophthalmitis was based on clinical features observed on dilated fundoscopy performed by an ophthalmologist.

For all episodes of candidemia, we collected clinical and laboratorial data using a standard clinical form, including the following variables: age, gender, date of candidemia, date of admission, exposure to invasive medical procedures, use of antibiotics or corticosteroids, clinical management of candidemia (antifungal treatment and time of CVC removal), and outcome (mortality). The presence of comorbidities, including diabetes mellitus, arterial hypertension, autoimmune diseases, hepatitis (B and C), cardiac, pulmonary, and neurologic diseases documented within the previous 3 months, was also recorded. The presence of vascular devices was recorded and classified as tunneled catheters, short-term catheters and fistulas with grafts for dialysis. The protocol was approved by the local ethics committee.

Incidence of candidemia was calculated using the number of episodes of candidemia as numerator, and total of hemodialysis sessions per year as denominator, multiplied per 1000.

Yeast identification

Blood samples were aseptically collected and processed for culture by the BACTEC automatic system. All the species of *Candida* recovered from the blood cultures were initially identified by conventional methods (ID32C®, bioMérieux, France) at the routine laboratory of Hospital São Paulo (Escola Paulista de Medicina, Universidade Federal de São Paulo). Isolates stored in the routine laboratory were further sent to the Laboratório Especial de Micologia, Universidade Federal de São Paulo, São Paulo, Brazil, for further molecular identification. Sequencing of the internal transcribed spacer (ITS) region of ribosomal DNA was used for the molecular identification of *Candida* species.[13] The nucleotide sequences generated in this study were deposited in the GenBank database (http://www.ncbi.nlm.nih.gov/GenBank) [GenBank: JQ585710, GenBank: JQ989500, GenBank: JQ585713, GenBank: KP659256, GenBank: KP659257, GenBank: KP659258, GenBank: KP659259 and GenBank: KP659260].

Results and discussion

Initially, we screened 29 patients with candidemia undergoing hemodialysis along the period of our study. A total of 15 patients were excluded because they developed candidemia before a 3 month-period of RRT was completed or were hospitalized for more than 48 h. Consequently, our casuistic consisted of 14 outpatients with candidemia and RRT by hemodialysis. The incidence of candidemia ranged from 0.04 to 0.32 cases per 1000 hemodialysis sessions per year, and the highest rate was recorded in 2006, suggesting the occurrence of a possible outbreak (Fig. 1).

Demographics, clinical characteristics, underlying conditions and outcomes are summarized in Table 1. Most patients (57%) were female, and the median age was 45.5 years, ranging from 22 to 79 years. We noted the occurrence of previous episodes of bacteremia in 5 patients (35.7%), diabetes mellitus in 4 patients (28.6%) and kidney engraftment failure in 4 patients (28.6%). Other predisposing conditions for candidemia included the presence of central venous catheters in 13 cases (92.9%), previous exposure to antibiotics in 7 cases (50%) and corticosteroids in 6 cases (43%).

CVCs are a major risk factor for candidemia in patients under chronic hemodialysis.[6,27] In our study, 13 out of 14 patients with candidemia were under hemodialysis through CVC, included tunneled catheters in 10 cases (71.4%) and short-term catheters in 3 cases (21.4%) (see Table 1). It is relevant to mention that those