

## Features of the Clinical Course of Invasive Candidiasis in HIV-Infected Patients

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### ABSTRACT

The article presents the results of follow-up of 30 patients with invasive candidiasis who developed against the background of HIV infection during the period 2019-2021. The features of the clinical course of the disease and the risk factors for its occurrence are described. The clinical picture of invasive candidiasis in HIV-infected patients is similar to that of bacterial sepsis, characterized by a severe course and high mortality. Risk factors are severe immunodeficiency, lack of antiretroviral therapy, and the presence of 2 or more foci of superficial candidiasis. The diagnosis of hematogenic dissemination should be performed in all HIV-infected patients in the presence of supporting symptoms.

**Keywords:** Candida pathogen, invasive candidiasis, HIV infection, sepsis, risk factors.

### INTRODUCTION

Candidiasis is the most common opportunistic mycosis caused by fungi of the genus *Candida*. To date, about 160 species of this genus are known, 10 of which are pathogenic to humans. Fungi of the genus *Candida* are widely distributed in the external environment: air, soil, water [1]. Some of them are inhabitants of the human body and are detected by mycological studies of the mucous membranes of the oral cavity and gastrointestinal tract in 30-50% of practically healthy people. When reducing the resistance of the body *Candida* spp. they can cause diseases, and clinical manifestations range from a relatively minor superficial pathological process to a highly lethal invasive lesion of various organs and tissues [2]. The prevalence of candidiasis has increased due to the widespread use of antibiotics, glucocorticosteroids, immunosuppressants, and the pandemic HIV infection. Fungi of the genus *Candida* spp. affect 90% of HIV-infected patients [3].

In recent years, there has been a significant increase in the incidence of invasive candidiasis worldwide. Its rate in economically developed countries is about 200 cases per 1 million population annually. In Europe, *Candida* spp. is 3rd most common pathogens of nosocomial sepsis. The main etiological agents of invasive candidiasis are *C. albicans* (51-62%), *C. glabrata* (18%), *C. parapsilosis* (13%), *C. tropicalis* (10%), and *C. krusei* (3%). At the same time, the shift towards *Candida* non-*albicans* resistant to antimycotics increases [4,10]. In patients with risk factors, invasive candidiasis can occur as an intra-hospital infection, characterized by severe clinical manifestations and high mortality (among certain groups of patients, it reaches 80%). Timely and adequate use of antimycotics largely determines the outcome of the disease. However, it still remains so only in 15-40% of patients with invasive candidiasis. This is due to the difficulties of diagnosis, since the clinical signs of

the disease are often non-specific, and candida fungemia is intermittent and has a low level [5-8]. In addition, there is insufficient data in the literature on the manifestations of invasive candidiasis in HIV-infected patients.

Objective: to conduct detailed microbiological research on the study of invasive candidiasis in HIV-infected patients.

### **MATERIALS AND METHODS**

In the Moscow region Infectious Diseases Hospital from 2019 to 2021, 30 patients were observed with invasive candidiasis: 20 men and 10 women aged 18 to 42 years. The disease developed against the background of 4 B - Stage HIV infection without antiretroviral therapy (according to the clinical classification of V. I. Pokrovsky, 2001). From the epidemiological history, it was found that 18 patients were drug users who were infected by parenteral route. 12 patients were infected during heterosexual and homosexual contacts. Duration HIV infection without treatment ranged from 1 to 10 years. The majority of patients (20 people) were sent to the hospital with primary diagnoses: "pneumonia" and "sepsis". On the basis of a complex of clinical, laboratory and mycological methods, including isolation and identification of candida culture, the diagnosis of acute disseminated candidiasis was established in vivo in 23 and postmortem in 7 patients. Concomitant diseases were chronic hepatitis B and C, type 1 diabetes mellitus, and pulmonary tuberculosis. In 13 cases the genus *Candida* was isolated alone, in 17 cases - with bacteria *Escherichia coli*, *Staphylococcus* spp., *Klebsiella pneumoniae*, *P. aeruginosa*, *P. multocida* and others [11-18].

### **RESULTS AND DISCUSSION**

All patients complained of weakness, myalgia, fever, cough, shortness of breath. Chest pain was observed in 9 patients, headache- 6, dyspeptic phenomena- 2. 17 patients had fever up to 38-41°C with the wrong type of temperature curve. In 5 cases, normothermia and low body temperature were registered. The patients were admitted in an extremely serious condition, the disease was fatal in the first day of their stay in the hospital. A serious condition was recorded in 17 patients, a moderate condition – in 5. The severity of the condition was caused by intoxication, respiratory failure, and hemodynamic disorders. Most of the patients were underweight or emaciated (19 people), the skin was pale, and 3 people had jaundice. Hemorrhagic rash in the distal extremities was observed in 3 patients. The peripheral lymph nodes in all the examined patients were enlarged from 0.5 to 1.5 cm, dense, painless, and the skin above them was not changed. When examining the oropharynx, the mucous membrane of 18 people was moderately hyperemic, edematous, and covered with grayish-yellow spots, curd-like deposits with predominant localization on the tongue, the inner surface of the cheeks, and the soft palate. In 23 patients, hyperkeratosis is expressed on the skin of the feet, cracks in the interdigital spaces, the nails are thickened, with uneven nail plates. When examining the cardiovascular system, all patients had deafness of heart tones, tachycardia (heart rate 86-110 per minute), instability of blood pressure (from 50/30 to 140/80 mm Hg). In 9 cases, a systolic murmur was heard at the top of the heart.

On the part of the lungs, 21 patients had dry and wet wheezing, weakening of breathing in the lesion. Dyspnea was observed in 11 people (BH 22-42 per minute). Three patients required respiratory support (extended ventilator). All patients showed a significant increase in the size of the liver, and 12 patients had splenomegaly. One third of the patients had meningeal

symptoms (rigidity of the muscles of the back of the neck, symptoms of Kernig, Brudzinsky), one-insufficiency of the 7<sup>th</sup> pair of cranial nerves.

The number of CD4-lymphocytes in the blood varied from 3 to 660 cells/ $\mu$ l (on average, 168 cells / $\mu$ l). The viral load was 80 000-300 000 copies HIV RNA in 1 ml of blood.

In the hemogram of the vast majority patients were found to have hypochromic anemia, left shift of the formula, lymphopenia, and high COE. Leukocytosis was observed in 14 patients ( $9,0-35,8 \cdot 10^9/l$ ), leukopenia-in 4 ( $1,1-3,3 \cdot 10^9/l$ ). In general analysis in the urine of all the observed patients, proteinuria occurred (up to 0.794 g/l), in one third – leukocyturia and erythrocyturia.

The study of biochemical blood analysis in 15 patients revealed an increase in the levels of bilirubin (25-150mmol/L), urea (8.8–36.6 mmol/l) and creatinine (up to 0.68). A third of the patients were diagnosed with cytolysis syndrome (transaminase indices from 49 up to 135 units), 7 people have hyperglycemia (6.3-20.9 mmol/l).

For diagnostic purposes, 10 patients underwent spinal puncture. Meningitis was detected in 7 patients. There was an increase in the pressure of the cerebrospinal fluid, clear cerebrospinal fluid, pleocytosis from 10 to 278 cells/ml (average 120 cells/ml).

Lung radiography was performed in all 25 patients, pneumonia was detected in 18 (2-sided in 10 cases). In addition, lung abscess, pneumothorax, hydrothorax, and calcified pleurisy were diagnosed. Changes in the ECG - electrocardiogram - were observed in 9 patients in the form of a decrease in the voltage of the teeth and a violation of the ventricular conduction.

Fungi of the genus *Candida* spp. were isolated in 19 patients during mycological examination of sputum and smears from the pharynx, of which *C. albicans* in 12 people, *C. glabrata* in 2, and in the remaining cases *Candida* spp. was not identified. In 9 cases, *C. albicans* were detected in urine cultures.

To confirm the diagnosis of invasive candidiasis, the study material was blood, cerebrospinal fluid, as well as pieces of cadaveric material from deceased patients. In order to isolate the culture and identify the pathogen, a mycological study was conducted. Identification of fungi of the genus *Candida* spp. from the blood occurred in 17 human. On the Saburo medium, they formed smooth, small, shiny, cream-colored colonies. After the identification of micromycetes, the following results were obtained: *C. albicans*-19, *C. albicans* + *C. glabrata*-4, *C. albicans* + *C. lusitania*-1. In one case – *Candida parapsilosis*. In 9 cases, there was a combination of fungi of the genus *Candida* and various bacteria (*Escherichia coli*, *Staphylococcus* spp., *Klebsiella pneumonia*)[19-25].

Etiotropic antimycotic therapy according to the clinical recommendations was prescribed to all patients in the hospital. Also all patients received broad-spectrum antibiotics.

The outcomes of the disease were different. In 18 cases, positive dynamics were achieved. Despite the treatment, 7 patients died from septic shock, multiple organ failure and manifestations of DIC syndrome. Death occurred within 10 to 50 days of treatment.

The analysis of the results of the study revealed the features of the course of invasive candidiasis in patients with HIV-infected patients. The disease occurs in the form of an acute disseminated process, characterized by a severe course and high mortality. Thus, the clinical picture of systemic candidiasis is similar to that of bacterial sepsis: antibiotic-resistant fever, broad spectrum of action, lung damage, multiple organ failure with a predominance of hepatic-renal and manifestations of DIC-syndrome. This causes difficulties in the diagnosis and

adequate treatment of the disease. Complicating the task is the fact that in a third of patients, the etiological cause of the disease was an association of fungi and bacteria. This led to a late diagnosis and did not allow for adequate and timely treatment.

## CONCLUSION

The results of the studies indicate that invasive candidiasis in HIV-infected patients occurs as an acute disseminated process, characterized by a severe course and high mortality. In one third of cases, the etiological cause of the disease is mixed fungal-bacterial flora. The clinical picture of invasive candidiasis is similar to bacterial sepsis, which leads to difficulties in diagnosing the disease. Risk factors for invasive candidiasis in HIV-infected patients are: severe immunodeficiency, no antiretroviral therapy and the presence of foci of superficial candidiasis. The diagnosis of hematogenic dissemination of candidiasis should be carried out in all HIV-infected patients with supporting symptoms: fever, resistant to broad-spectrum antibiotics; acute respiratory failure and lung damage. In 13 cases the genus *Candida* was isolated alone, in 17 cases - with bacteria *Escherichia coli*, *Staphylococcus* spp., *Klebsiella pneumoniae*, *P. aeruginosa*, *P. multocida* and others.

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## Competing Interests

The authors declare that they have no competing interests.

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