

Peripheral Blood Smear: Hematologist Buddy to Catch Dangerous Budding: A Report of Two Cases

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Abstract

The incidence of nosocomial infections has been reported as 12%–18% in various studies from India, with bloodstream infections amounting 15%. Fungal pathogens have become a major cause of nosocomial bloodstream infections. Detection of fungemia by blood culture often requires 2 or 3 days of incubation. Few studies have reported the detection of *Candida* species (*Candida albicans*, *Candida glabrata*, and *Candida parapsilosis*) by review of routinely stained blood smears, often days earlier than diagnosis being possible by culture. These can be seen as round–oval extracellular as well as intracellular budding yeast organisms which show pink-magenta staining with periodic acid Schiff stain. We report here the detection of *Candida* spp. in the peripheral blood smear.

Keywords: Budding yeast, *Candida*, fungal infection, nosocomial infection, peripheral blood smear

INTRODUCTION

The incidence of nosocomial infections has been reported as 12%–18% in various studies from India with bloodstream infections amounting 15%.^[1,2] Fungal pathogens have become a major cause of nosocomial blood stream infections.^[1] Detection of fungemia by blood culture often requires 2 or 3 days of incubation.^[3] Few studies have reported the detection of *Candida* species (*Candida albicans*, *Candida glabrata*, and *Candida parapsilosis*) by review of routinely stained blood smears, often days earlier than diagnosis being possible by culture.^[3,4] We report here the detection of *Candida* spp. in the peripheral blood smear (PBS).

CASE REPORT

First case is of a 25-year-old male admitted in the intensive care unit (ICU) in view of cervical spine injury and quadriplegia. Contrast-enhanced computed tomography (CT) abdomen revealed pancreatic body transection. Following an exploratory laparotomy, the patient was managed in the ICU on continuous mechanical ventilation, intravenous (IV) fluids, broad-spectrum antibiotics, and total parenteral

nutrition (TPN). Complete blood counts (CBCs) at the time of admission were hemoglobin (Hb) - 10.8 g%, total leukocyte count (TLC) - 14,500/mm³, platelet count - 152,000/mm³. During the hospital stay over 2 months, the patient's condition deteriorated in view of underlying sepsis. Hb reduced to 7.9 g%, TLC to 8290/mm³, and platelet count to 13,000/mm³, and no differential count was given by Coulter. On PBS, numerous round–oval extracellular as well as intracellular budding yeast organisms inside neutrophils and monocytes were seen [Figure 1a], which showed pink-magenta staining with periodic acid Schiff stain [Figure 1b]. Differential leukocyte count could not be done manually, as well as most of the leukocytes were morphologically damaged due to phagocytosis of yeast cells. An impression of bicytopenia with fungemia with organisms morphologically consistent with *Candida* spp. was given. Next day, the patient developed septic shock and expired.

Second case is of a 65-year-old male, a native of Bhagalpur, Bihar, and a known case of diabetes mellitus for the past 10 years presented with fever, headache, and altered

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Table 1: Pathogens detected in peripheral blood smear

Pathogens detected in peripheral blood smear	
Fungi (intracellularly within leucocytes and extracellularly)	Bacteria (intracellularly within leucocytes)
<i>Histoplasma capsulatum</i>	<i>Neisseria meningitidis</i>
<i>Cryptococcus neoformans</i>	<i>Streptococcus pneumoniae</i>
<i>Penicillium marneffei</i>	<i>Staphylococcus aureus</i>
<i>Candida albicans</i>	<i>Staphylococcus epidermidis</i>
<i>Candida parapsilosis</i>	<i>Bacteroides distasonis</i>
<i>Candida glabrata</i>	<i>Clostridium welchii</i>
<i>Hansenula anomala</i>	<i>Clostridium perfringens</i>
	<i>Klebsiella pneumoniae</i>
Protozoa	<i>Filaria</i> (extracellular)
<i>Plasmodium</i> species (within RBCs)	<i>Loa loa</i>
<i>Babesia</i> species (within RBCs)	<i>Wuchereria bancrofti</i>
<i>Trypanosoma</i> species (extracellular)	<i>Brugia malayi</i>
Rickettsiae	Spirochetes
<i>Ehrlichia</i> species (intracellularly in leucocytes)	<i>Borrelia</i> genus

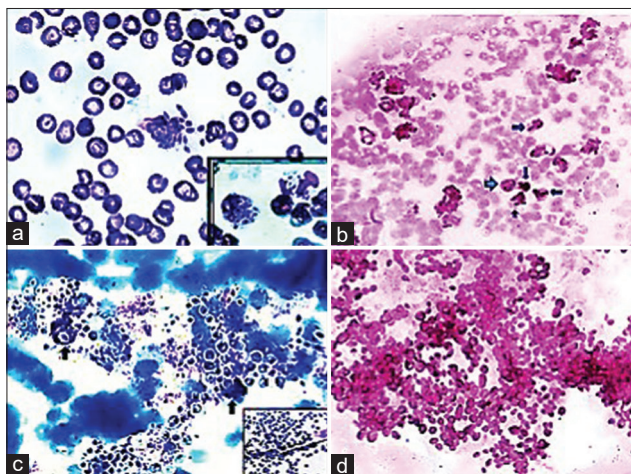


Figure 1: Case 1: (a) Numerous budding yeast organisms seen (Giemsa-stained PBS, $\times 400$). Inset: Intracytoplasmic presence within a neutrophil with a deformed nucleus. (b) Intracytoplasmic (arrows), pink-colored budding yeast forms (PAS, $\times 400$). Case 2: (c) Numerous budding yeast organisms seen and intracytoplasmic (arrows) presence within a neutrophil with a deformed nucleus (Giemsa-stained PBS, $\times 1000$). Inset: Microfilaria. (d) Numerous pink-colored budding yeast forms (PAS, $\times 1000$). PAS: Periodic acid Schiff, PBS: Peripheral blood smear

sensorium for the past 4–5 days. Lymphadenopathy and hepatosplenomegaly were absent. CBC revealed bicytopenia with leukocytosis (Hb: 10.8 g/dL, TLC: 14,900/ μ L, and platelet count 44,000/ μ L) with differential count of 90% neutrophils, 8% lymphocytes, and 2% monocytes. PBS showed the presence of round–oval extracellular as well as intracellular budding yeast organisms in neutrophils and monocytes along with the presence of microfilaria in PBS [Figure 1c and d]. Fasting blood sugar was raised (220 mg/dL). Nonenhanced CT of the head showed hydrocephalus with parietal infarct. Cerebrospinal fluid (CSF) examination was within normal limits. Tridot test and cryptococcal antigen in the CSF were negative. An impression of bicytopenia with leukocytosis with

fungemia with organisms morphologically consistent with *Candida* spp. and microfilariasis was given. The patient went into a sudden cardiopulmonary arrest and expired the same day.

DISCUSSION

Fungal pathogens are a major cause of nosocomial bloodstream infections.^[1] Fungal species and other pathogens that can be detected in the PBS are given in Table 1. *Candida* spp. is the second-most common cause of fungemia after *Histoplasma capsulatum*. It has been attributed as a causative agent in 8%–15% of all nosocomial bloodstream infections.^[1,5,6] The predisposing factors for disseminated candidiasis include neutropenia, immunosuppression, chemotherapy, indwelling catheters, multiple antibiotic treatment, TPN, prolonged ICU stay, and major cardiovascular or abdominal surgery.^[4–6] However, the most important risk factor for invasive candidiasis is prolonged stay in the ICU.^[6] Mortality rates for systemic candidiasis are reported to be as high as 50%–80%, despite appropriate treatment.^[7,8] Because clinical signs are nonspecific, diagnosis of systemic candidiasis remains difficult.^[5]

In the present study, one of the patients was on broad-spectrum antibiotics, TPN, and IV fluids for 2 months during stay in the ICU, and the other had prolonged uncontrolled blood sugar. The diagnosis of candidemia is rarely made by PBS because the pathogen is usually too small for visual detection; however, in the present cases, the budding yeast organisms and pseudohyphae were so numerous that they were easily seen in PBS.^[6] Budding yeast on the PBS is considered a contaminant, but their intracytoplasmic presence is indicative of their pathological nature.^[6] Marshall *et al.* in their study concluded that a possibility of circulating organisms should be considered when abnormal white cell flags are observed with Coulter and the presence of microorganisms in the peripheral blood can result in spurious WBC counts or electronic differentials.^[9] Hence, a manual screening of PBS should be done in cases with abnormal flags/differentials given by the analyzer.^[10]

Similar findings were observed in the first case where PBS was screened in view of absent Coulter differentials. Before we could do a blood culture, which requires 2–3 days of incubation, and start appropriate antifungal treatment, both the patients had expired. Hence, rapid detection methods besides blood culture are needed as also suggested by Hirai *et al.*^[8]

To be visually detectable in the PBS, the minimum blood concentration of yeast required is 10^5 – 10^7 CFU/ml.^[3] This degree of fungemia is unusual; therefore, PBS examination will be diagnostic only in a small proportion of cases and is a rare finding. Such detection suggests fulminant infection with uncontrollable complications, indicative of a dismal prognosis. However, in all these cases, PBS could be lifesaving, yielding a speedy diagnosis and timely initiation of treatment.

CONCLUSION

This study highlights the importance of early and meticulous examination of the PBS for detection of fungal organisms. Furthermore, the co-existence of fungal organisms and microfilaria in PBS as seen in the second case is an unusual finding. In immunocompromised patients with clinical suspicion of sepsis, a search for fungal organisms in PBS should always be specifically thought of. This could accelerate the diagnosis of fungemia before blood cultures become positive and may potentially benefit the patient with an immediate treatment.

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Conflicts of interest

There are no conflicts of interest.

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