

Misidentification of *Candida parapsilosis* as Large Platelets in an Automated Blood Analyzer

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We experienced a case in which yeasts in blood sample from a patient with cervical cancer with hepatic metastasis and multiple intraperitoneal cysts interfered with platelet morphology flag in automated blood analyzer. The peripheral blood smear was performed to confirm the flag and revealed intracellular and extracellular yeasts, which were subsequently

identified as *Candida parapsilosis* by blood culture. (Korean J Clin Microbiol 2009;12:138-140)

Key Words: *Candida parapsilosis*, Peripheral blood smear, Automated blood analyzer, Large platelet

INTRODUCTION

Yeasts or bacteria may be observed on peripheral blood smears. This may lead to spurious elevation of platelet counts or disturbance of the white blood cell (WBC) differential counts when they clump[1-3]. In present, automated cell counters play a central role in the hematology part of the clinical laboratory. Although it is generally agreed that automated cell counters have improved the quality of routine blood analysis, a number of interfering factors have been identified for these instruments[4,5]. We experienced a case in which yeasts, confirmed as *Candida parapsilosis* by blood culture, interfered with platelet morphology flag in an automated blood counter, ADVIA2120 hematology system (Bayer Healthcare, Diagnostic Division, Tarrytown, NY, USA).

CASE REPORT

A 50-year-old woman was suffering from cervical cancer with hepatic metastasis and multiple intraperitoneal cysts. She had been receiving chemotherapy with hospice care. The findings of her initial blood analysis included a WBC count of 10,680/ μ L, a hemoglobin concentration of 12.7 g/d, and a platelet count of 248,000/ μ L. *C. parapsilosis* was first isolated in blood and cystic fluid 4 weeks after the admission. At this time the results of blood analysis were as follows: WBC count, 12,760/ μ ; hemoglo-

bin, 8.8 g/dL; platelet count, 285,000/ μ L; and CRP, 15 mg/dL (0 ~0.5 mg/dL) with a D-dimer concentration of 4.3 μ g/mL (<0.4 μ g/mL) (Table 1). She also began to develop pulmonary edema, hydronephrosis, and metabolic acidosis. About a week later, her peripheral blood analysis by the ADVIA 2120 Hematology System revealed decreased platelet counts (59,000/ μ L) with morphology flags as many large platelets and aggregates. A peripheral blood smear (PBS) was performed to review the abnormal flag. The PBS showed numerous yeast cells within neutrophils and monocytes (Fig. 1) and also yeast clumps extracellularly (Fig. 2), which were enumerated as large platelets in ADVIA 2120. WBC counts seemed to be the same as in blood analysis when calculated by a manual method. Platelet counts were within normal limits without any giant forms or aggregates. The PBS was carefully followed afterward but candidemia could not be detected anymore, even though blood and cystic fluid cultures continued to grow *C. parapsilosis*. The follow-up blood analysis showed a WBC count of 7,400/ μ L, a hemoglobin count of 6.8 g/dL, a platelet count of 39,000/ μ L and CRP 18 mg/dL. She became more acidic metabolically and had poor general condition. Her family refused to receive any further medical treatments, except for hospice care.

She was initially treated with intravenous fluconazole for a week for candidemia, which was changed to itraconazole and then to amphotericin B due to severe side-effects including fever and drug rash. She then received caspofungin for several days but died soon after because of sepsis and respiratory failure due to aggravated underlying severe conditions.

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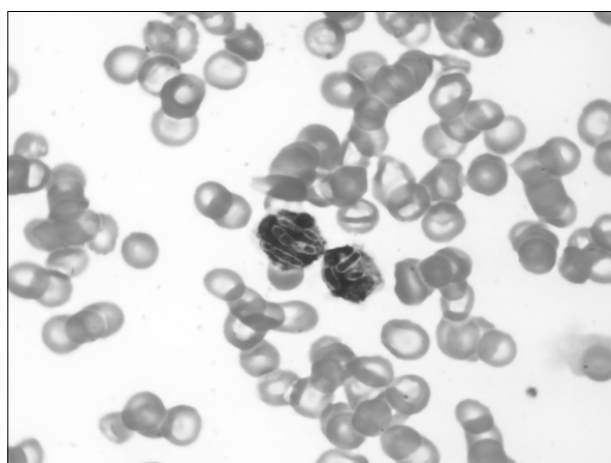
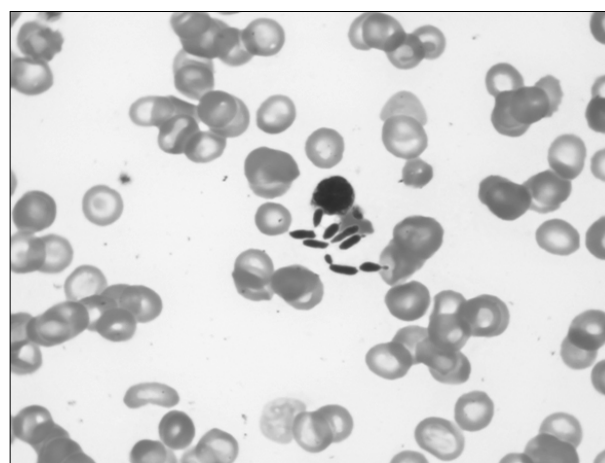
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Table 1. Sequential laboratory findings of this patient

	Dec 16	Dec 23*	Dec 29	Jan 5	Jan 14*	Jan 21 [†]	Jan 28*	Jan 29	Feb 4	Feb 6
WBC count ($\times 10^3/\mu\text{L}$)	10.7	9.9	8.5	14.4	12.8	15.4	6.0	6.2		7.4
Neutrophil (%)	61	70	74	80	94	80	62	68		79
Hemoglobin (g/dL)	12.7	7.7	9.4	7.5	8.8	6.9	5.2	8.3		6.8
Platelet count ($\times 10^3/\mu\text{L}$)	248	289	300	321	285	59	56	86		39
CRP (mg/dL)				15.4	15.0	14.0				18.2
Blood culture				NG	CPA	CPA	CPA		NG	
AF culture					CPA	CPA	NG		PAE	

*Date of a transfusion of packed red cells; [†]Date of detection of Candidemia by peripheral blood smear.

Abbreviations: CRP, C-reactive protein; NG, no growth after 5 days; CPA, *Candida parapsilosis*; PAE, *Pseudomonas aeruginosa*; AF, ascitic fluid.

**Fig. 1.** Phagocytized yeasts within neutrophils (Wright stain, $\times 1,000$).**Fig. 2.** Multiple budding yeast cells observed on peripheral blood smear (Wright stain, $\times 1,000$).

DISCUSSION

Automated cell counters have improved the quality of routine blood analysis in modern clinical laboratories. However, a number of potential interfering factors have been identified for these instruments, including spuriously elevated platelet counts caused by cytoplasmic fragments of RBCs and WBCs or by bacteremia[1,2]. Other reports of interference with the platelet counts on automated hematology analyzers include autoagglutinins, cryoglobulins, cold agglutinins, platelet clumps, giant platelets, malaria infected RBCs, and leukemic cell fragments in the tumor lysis syndrome[5,6]. It is also well known that yeast is an interference factor of blood cell count in automated hematology systems. Arnold et al[7] and Latif et al[8] reported that *C. glabrata* fungemia can lead to a falsely elevated platelet count on the H*2 (Bayer HealthCare, Diagnostics Division, Tarrytown, NY, USA) and on the Cell-DYN 4000 (Abbott Diagnostics, Santa Clara, CA, USA) hematology analyzers in thrombocytopenic patients.

Candida spp. can be a common pathogen of fungal infections in blood stream. The most common isolate is *C. albicans* followed by *C. parapsilosis* and *C. glabrata*. Latif et al[8] revealed

that *C. glabrata*, which has a mean volume of 12 fL, can be confused with a large platelet in an automated blood analyzer that uses an optical scatter or electrical impedance method to detect the blood cells. Large size yeasts such as *C. albicans* or *C. parapsilosis* do not show similarity with platelets[8]. Therefore, candidemia by *C. parapsilosis* would not cause any numerical changes in platelet counts in ADVIA but just result in abnormal flag, because yeasts clumped together and also resided within WBCs (Fig. 1 and 2). As in our case, candidemia by *C. parapsilosis* caused only size abnormalities like platelet clumps and giant platelets, but not a numerical change in platelet counts, since platelet counts remained decreased while *C. parapsilosis* was present in blood cultures. We also evaluated WBC counts by a manual method to determine whether WBC count was falsely elevated or not, but WBC counts by the manual method were similar with those found with the automated blood analyzer.

Branda et al[9] discovered that yeast have to be at least greater than $1\sim 5\times 10^6$ CFU/mL of blood to be counted as falsely increased platelets in automatic blood analyzers and thus was concentration-dependent to effect blood analysis. Also Branda et al[10] stated that detection of candidemia by PBS requires a con-

centration of the yeast to be at least 1 to 5×10^5 CFU/mL, which would be quite unusual. In our case, we carefully followed the PBS after the first time, but there was only one episode of abnormal platelet flag in the ADVIA 2100, even though the patient had persistent candidemia for more than a week. This could be explained that *C. parapsilosis* appeared on PBS at the first time when the blood concentration of the yeast was high. However, a low level of candidemia still remained in our patient afterward and thus only blood cultures continued to be positive. Contrarily, Heo et al[11] reported that they incidentally found the fungemia of *Pichia anomala* in a child on the PBS first before they identified *P. anomala* in blood and pleural effusion cultures. Buchman et al[12] also reported *Candida* fungemia that was first diagnosed by PBS. These 2 cases probably had severe fungemia with the concentration of the yeast being high enough to be appeared on PBS as to the result of Branda et al[10].

Blood samples containing yeast or bacteria may give erroneous abnormal flags in automated blood analyzers such as abnormal morphology flags in platelet or high WBC and platelet counts. Therefore one could review PBSs by microscopy when a patient shows continuous positive blood culture with candidemia. The candidemia would appear on the PBSs dependent on the concentration of the yeast in the blood.

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=국문초록=

자동혈액분석기에서 거대 혈소판으로 인식된 *Candida parapsilosis* 1례

계명대학교 의과대학 진단검사의학교실, ¹내과학교실
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간으로 전이된 자궁경부암과 복막강 내 다낭종을 가진 환자의 혈액검사 결과 자동혈액분석기에서 혈소판 모양 이상 소견을 보였다. 이상소견의 확인을 위해 말초혈액도말검사를 실시한 결과, 세포 내와 세포 외에서 다수의 효모균이 발견되었고 혈액배양검사서 *Candida parapsilosis*로 동정된 1례를 경험하였기에 보고하는 바이다. [대한임상미생물학회지 2009;12:138-140]

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