증례보고
Lab Med Online
Vol. 11, No. 3: 191-193, July 2021
https://doi.org/10.47429/lmo.2021.11.3.191

진단혈액학 LMO

자동혈구분석기 Sysmex XN에서 낮은 값으로 잘못 측정된 백혈구수에 대한 증례: WNR 채널과 WDF 채널 간 차이

A Case of Spuriously Decreased White Blood Cell Count on an Automated Sysmex XN Hematology Analyzer: The Difference Between the WNR and WDF Channels

김한주 · 남궁승 · 박찬정
Han Joo Kim, M.D., Seung Namgoong, M.T., Chan-Jeoung Park, M.D.

울산대학교 의과대학 서울아산병원 진단검사의학과
Department of Laboratory Medicine, University of Ulsan College of Medicine and Asan Medical Center, Seoul, Korea

Most clinical laboratories utilize automated hematology analyzers for complete blood cell count (CBC). The CBC, including white blood cells (WBCs), is critical to determine patients' clinical status; therefore, these results should be accurate and precise. We encountered a case that showed spurious WBC count from a Sysmex XN hematology analyzer (Sysmex Corporation, Japan). A 56-year-old man visited our center in October 2018 for follow-up of hepatocellular carcinoma with lung metastases. The initial WBC count measured by the Sysmex XN was 0.02×10^3/μL and the differential count was not available. A blood smear slide was automatically prepared and reviewed according to the laboratory protocol. The WBC count in the blood smear was within normal limits, much higher than that of CBC result, and there was no WBC aggregation. We also reviewed the raw data from the equipment, and we found the big difference between two channels (WBC and nucleated red blood cells [WNR] and white cell differential [WDF]) of the analyzer. The WBC count of the WNR channel was very low, but that of the WDF channel was 7.16×10^3/μL, consistent with that of the peripheral blood smear slide. The viscosity of the blood and the neutrophil respiratory burst activity were within normal limits. In conclusion, clinical laboratories operating hematology analyzers should be alert for this phenomenon. If the analyzer shows "Difference between channels", it is important to check the raw results of the machine, prepare a blood smear and review by microscope, and report accurate results.

Key Words: Sysmex XN, Automated hematology analyzer, Spurious count, White blood cells, WNR channel, WDF channel

INTRODUCTION

Automated hematology analyzers (HA) are widely used to obtain complete blood cell counts (CBC). CBC are critical for the accurate assessment of patients' clinical status; thus, the results must be accurate and precise. However, in some cases, spurious CBC can occur, which may require additional action on the part of the clinician to obtain correct results [1, 2]. We report a case of an incorrect white blood cell (WBC) count obtained on a Sysmex XN hematology analyzer (Sysmex Corporation, Kobe, Japan).

CASE REPORT

A 56-year-old man visited our hospital for follow-up of hepatocellular carcinoma with lung metastases. He had started sorafenib (a molecular targeted multi-kinase inhibitor) 3 months before and nivolumab (a humanized monoclonal antibody to the immune checkpoint receptor programmed death 1 [PD-1]) 2 days before his peripheral blood was drawn for laboratory tests, including CBC. The initial WBC count measured on a Sysmex XN hematology analyzer (Sysmex Corporation) was 0.02×10^3/μL; the differential count was not available due to the low WBC count. His he-

Corresponding author: Chan-Jeoung Park, M.D., Ph.D.
https://orcid.org/0000-0003-4396-8348
Department of Laboratory Medicine, University of Ulsan, College of Medicine and Asan Medical Center, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea
Tel: +82-2-3010-4508, Fax: +82-2-478-0884, E-mail: cjpark@amc.seoul.kr

Received: June 2, 2020
Revision received: August 11, 2020
Accepted: August 21, 2020

This article is available from https://www.labmedonline.org

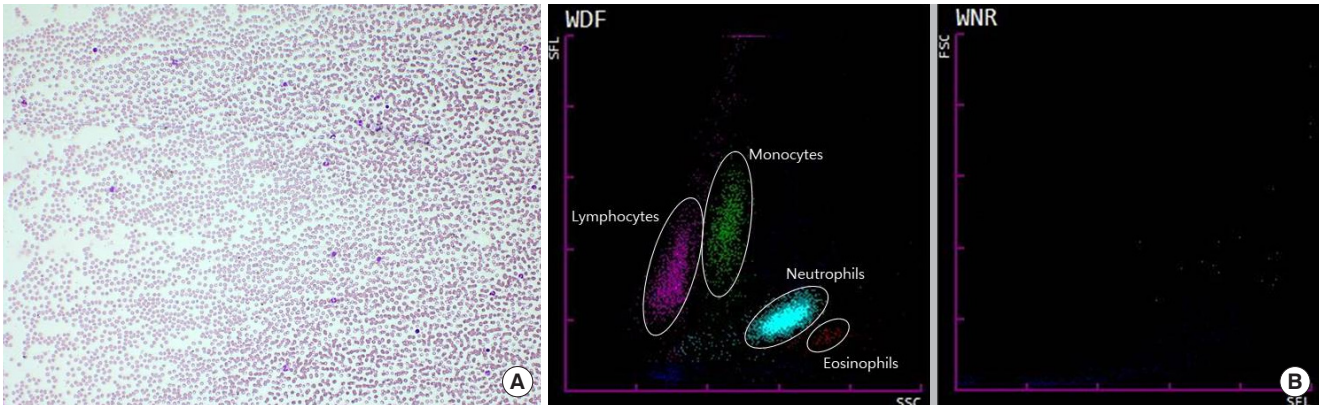

Fig. 1. (A) Peripheral blood smear (100×, Wright stain). (B) Scattergrams from the white cell differential (WDF) (left) and white blood cell and nucleated red blood cells (WNR) (right) channels of the Sysmex XN hematology analyzer.

Table 1. CBC data from the WDF and WNR channels of the Sysmex XN hematology analyzer

	WDF channel	WNR channel
WBCs	7.16×10^3/μL	0.02×10^3/μL
Neutrophils	70.1% (5.02×10^3/μL)	Not available
Lymphocytes	18.4% (1.32×10^3/μL)	
Monocytes	10.5% (0.75×10^3/μL)	
Eosinophils	1.0% (0.07×10^3/μL)	
Basophils	0.0% (0.00×10^3/μL)	
Nucleated RBCs	None	None

Abbreviations: CBC, complete blood cell count; WDF, white cell differential; WNR, white blood cell and nucleated red blood cells; WBC, white blood cell; RBC, red blood cell.

moglobin concentration was 8.5 g/dL and his platelet count was 230×10^3/μL. After a thorough washout, the repeated analysis showed the same results as initially obtained. The sample was also re-examined in the "low-WBC" mode, which gave a WBC count of 7.16×10^3/μL. A peripheral blood smear (PBS) was automatically prepared and reviewed according to the laboratory protocol. The WBC count in the PBS was closer to the 7.16×10^3/μL count obtained in the "low-WBC" mode. WBC aggregation was not observed. A few hypersegmented neutrophils were seen and the monocytes were slightly activated.

Under suspicion of falsely decreased WBC count, the raw data from the hematology analyzer were reviewed. The analyzer displayed the following error message: "Difference between WNR and WDF. Check the results." The reported WBC count (0.02×10^3/μL) was obtained from the WBC and nucleated red blood cells (WNR) channel, while the WBC result from the white cell differential (WDF) channel was 7.16×10^3/μL, the same as the result obtained in 'low-WBC' mode, and for which the differential count was available (Table 1). The scattergrams of the two channels were also reviewed (Fig. 1). The scattergram from the WDF channel was more compatible with the PBS findings than the scattergram from the WNR channel. Additional tests were performed to determine the cause of this falsely decreased WBC count. The blood viscosity and neutrophil respiratory burst activity were both within normal limits.

DISCUSSION

The XN, a fully automated hematology analyzer introduced in 2011, has several new channels compared to the previous model, the Sysmex XE (Sysmex Corporation). Among these, the WNR channel is designed to automatically measure nucleated red blood cells (RBC) at the same time as the CBC is measured. The result from this channel is reported as the default WBC count. The differential WBC count is measured separately through the white cell differential (WDF) channel; however, the WBC count from this channel is not automatically reported. According to the manufacturer, in the WNR channel, samples are treated with a more acidic reagent (pH 2.95–3.05; Lysercell WNR) than that used in the WDF channel (Lysercell WDF). Theoretically, the WBC count from both channels should be the same [3]. However, in the present case, the two channels did not give the same results. Two similar cases have been reported [4, 5].

Zandecki et al. [1] reviewed factors that can result in inaccurate WBC counts. First, aggregation of polymorphonuclear neutrophils or lymphocytes in blood collected in ethylenediaminetetraacetic acid (EDTA) may result in low WBC counts. Certain anti-

https://doi.org/10.47429/lmo.2021.11.3.191

coagulants, particularly tripotassium (K3)-EDTA, can also cause spurious WBC counts. In our case, no aggregation of leukocytes was seen in the PBS and the sample was collected in dipotassium (K2)-EDTA. It has also been hypothesized that WBCs that are fragile due to cytotoxic agents such as chemotherapy are more prone to lysing, potentially resulting in low WBC counts. However, another report found that chemotherapy did not cause a difference in WBC counts between the WNR and WDF channels [3]. There was also no evidence of WBC lysis in our case. Finally, hyaluronic acid has been reported as a possible cause of WBC aggregation in the presence of the acidic WNR reagent, leading to inaccurate counts [6]. This could be an issue in paraneoplastic syndromes with hypersecretion of hyaluronic acid or hyaluronidase. Unfortunately, we did not measure hyaluronate or hyaluronidase levels to evaluate this possibility.

All clinical laboratories operating automated hematology analyzers should be aware of this phenomenon. When the instrument displays the error message "Difference between WNR and WDF. Check the results", the raw data from the hematology analyzer and PBS should be carefully reviewed.

요 약

대부분의 임상검사실은 전혈구검사(complete blood count, CBC)를 위한 자동혈구분석기를 운용한다. 백혈구수를 비롯한 전혈구검사는 임상의가 환자의 상태를 파악하기 위해 중요하므로, 그 값은 정확하게 보고되어야 한다. 우리는 최근 자동혈구분석기인 Sysmex XN hematology analyzer (Sysmex Corporation, Japan)에서 부정확하게 감소된 백혈구수가 측정되는 증례를 경험하였다. 이 환자는 폐전이가 있는 간암을 진단받고 본원에서 추적관찰 중인 56세 남성으로, 2018년 10월 추적 관찰을 위해 본원을 방문하였다. XN (Sysmex Corporation)에서 측정된 초기 백혈구수는 0.02×10^3/μL이었으며, 백혈구의 감별계산은 불가능했다. 검사실 원칙에 따라 자동으로 말초혈액도말 슬라이드를 제작했고, 판독 결과 슬라이드 상으로 관찰되는 백혈구수는 기기에서 측정된 값보다 월등히 높아 정상으로 여겨졌으며, 백혈구의 응집 현상은 관찰되지 않았다. 또한 기기에서 직접 원측정값을 확인하였고, 그 결과 기기 내부의 두 채널(WNR과 WDF 채널)에서 측정된 백혈구수 결과에 큰 차이가 있었다. WNR 채널에서는 백혈구수가 아주 낮게 측정되었지만, WDF 채널에서는 백혈구수가 7.16×10^3/μL로 측정되어 말초혈액도말 슬라이드와 상응하는 소견을 보였다. 혈액 점성 검사와 호중구 호흡 폭발 검사(neutrophil respiratory burst activity test)의 결과는 정상 범위 내에 해당하였다. 결론적으로, 자동혈구분석기를 도입한 모든 임상 검사실에서는 "Difference between channels"라는 경고 문구가 도출되었을 때, 기기에서 직접 원데이터를 확인하고 말초혈액도말 슬라이드를 제작 및 검경하여 잘못된 측정값을 수정하고 필요한 조치를 취함으로써 정확한 결과를 보고해야 한다.

Conflicts of Interest

None declared.

REFERENCES

1. Zandecki M, Genevieve F, Gerard J, Godon A. Spurious counts and spurious results on haematology analysers: a review. Part II: white blood cells, red blood cells, haemoglobin, red cell indices and reticulocytes. Int J Lab Hematol 2007;29:21-41.
2. Zandecki M, Genevieve F, Gerard J, Godon A. Spurious counts and spurious results on haematology analysers: a review. Part I: platelets. Int J Lab Hematol 2007;29:4-20.
3. Kim H, Hur M, Choi SG, Oh KM, Moon HW, Yun YM. Comparison of white blood cell counts by WNR, WDF, and WPC channels in Sysmex XN hematology analyzer. Int J Lab Hematol 2015;37:869-75.
4. Nguyen VT, Gobin D, Li R, Cantinieaux B. Spurious decrease in the WBC count measured by the WNR channel of XN haematology analyser (Sysmex) could be associated with metastatic adenocarcinoma. Int J Lab Hematol 2015;37:e129-32.
5. Tantanate C. Spurious white blood cell count from a new automated Sysmex XN hematology analyzer. Int J Lab Hematol 2014;36:e86-7.
6. de Jonge R, Brouwer R, Smit M, de Frankrijker-Merkestijn M, Dolhain RJ, Hazes JM, et al. Automated counting of white blood cells in synovial fluid. Rheumatology (Oxford) 2004;43:170-3.