Case Report

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Mysterious Leukocytosis in Sickle Cell Disease

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Abstract

Patients with sickle cell disease (SCD) can present with both acute and chronic complications. The diagnosis of these potentially life threatening complications is dependent upon an interdisciplinary team approach and good communication.

We present two patients with SCD both with laboratory evidence of chronic hemolytic anemia. The first is a 39 year old female who presented with generalized fatigue, bilateral leg pain and hypoxia. The second case is a 26 year old female who presented with right leg pain secondary to a sickle cell pain crisis. During both admissions they were found to have unexplained worsening leukocytosis.

When working up hemolytic anemia additional labs to be ordered including LDH, haptoglobin, indirect bilirubin and a review of the peripheral blood smear looking for shistocytes in addition to the basic labs that include a CBC with differential and complete metabolic panel. At our institution CBCs are performed on the Sysmex® XE-5000.

Both of these cases reveal the need to carefully review laboratory data and to communicate with the laboratory when data does not look accurate to find out why.

Keywords: Sickle cell disease, CBC, Differential, nRBC, Sysmex® XE 5000

Introduction

Patients with sickle cell disease (SCD) can present with both acute and chronic complications. Acute complications include acute chest syndrome, multisystem organ failure syndrome, aplastic crisis, splenic sequestration, hyper-hemolysis crisis, thrombotic thrombocytopenic purpura-like syndrome, acute stroke and hepatic sequestration or acute intrahepatic cholestasis [1]. SCD patients often have complications related to vasoocculsive disease including avascular necrosis of the femoral or humeral head, chronic pain and chronic venous ulcers. Chronic hemolytic anemia, pulmonary hypertension and secondary hemochromatosis due to transfusion related iron overload are just some of the chronic manifestations of SCD [2].

When a SCD patient presents a baseline workup is obtained including: CBC with differential, reticulocyte count, complete metabolic panel, blood cultures, ABG, urinalysis with urine culture if indicated, chest X-Ray and a head CT without contrast if cerebral vascular accident (CVA) is in the differential [2]. When working up hemolytic anemia additional labs are ordered including-LDH, haptoglobin, indirect bilirubin and a review of the peripheral blood smear looking for shistocytes. At our institution CBCs are performed on the Sysmex® XE-5000.

The diagnosis of these potentially life threatening complications is dependent upon a team approach and good communication between care givers, support staff, family and the patient.

Case Presentations

We present two patients with SCD both with laboratory evidence of chronic hemolytic anemia. The first case is a 39 year old female who presented with generalized fatigue, bilateral leg pain and hypoxia. There was no radiographic evidence of vaso-occlusive disease. However, on initial lab work it did appear that she had acute worsening of her baseline hemolytic anemia. She was admitted for acute hemolytic crisis. On presentation Hb was 6.4 g/dL, LDH 1447, haptoglobin <15 and nRBC 12. Her baseline Hb was around 7.0 to 7.5 g/dL. She was started on aggressive IV hydration, IV pain control and oxygen. The hemoglobin began to improve, but by day 4 and 5 the WBC was consistently increasing as seen in **Table 1**. The hematology lab was contacted and manually corrected for nRBCs and discovered that the WBC had not

been adjusted for nRBCs either day because the Sysmex® XE-5000 did not flag for nRBCs.

Table 1 Case 1 labs indicating hemolytic anemia with several WBCs reported not corrected for nRBCs. This occurred when the CBC was ordered without the differential

Case 1	Ref. Range	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11
WBC	4-12 10*3/uL				17.4	17.8	12.3	10.0	10.3	11.1	12.6	15.6
Absolute Neutrophil Count	1.96-9.72 10*3/uL	10.39	13.04	12.57								
WBC Corrected	4-12 10*3/uL	15.5	15.9	14.4		13.7						
nRBC		12	9	8		15						
Hb	12-15 g/dL	6.4	6.0	6.8	5.1	7.2	6.8	6.4	7.5	6.9	6.7	7.7
LDH	100-225 U/L	1447	954									
Haptoglobin	15-185 mg/dL	<15										

The second case is a 26 year old female who presented with right leg pain secondary to a sickle cell pain crisis. Initial labs revealed a Hb of 7.7 g/dL, nRBC of 23 and corrected WBC of 11.6. The hemoglobin began to decrease a couple days into the admission to 7.1 g/dL, an LDH and peripheral smear were ordered. LDH was elevated at 365 and the peripheral smear revealed a microcytic anemia with anisocytosis, sickle cells, target cells, nRBCs and shistocytes. On the fourth day of admission the patients WBC dramatically increased from 14.1-28.3 **(Table 2)**. The ANC from the prior day was 8.18, within normal limits (WNL), and the patient denied any signs or symptoms of underlying infection. The next day the WBC was 13.7. Then on day 6 the WBC was again elevated at 19.3. Based on the patient's labs there appeared to be a hemolytic anemia, but more investigation was needed to explain the leukocytosis.

Table 2 Case 2 labs with two markedly elevated WBCs reported because they were not corrected for nRBCs. This occurred when the CBC was ordered without the differential

Case 2	Ref. Range	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
WBC	4-12 10*3/uL				28.3		19.3		
Absolute Neutrophil Count	1.96-9.72 10*3/uL	5.92	9.31	8.18					
WBC corrected	4-12 10*3/uL	11.6	19.4	14.1		13.7		9.9	11.9
nRBC		23	45	110				85	82
Hb	12-15 g/dL	7.7	7.1	7.1	7.3	6.4	5.8	7.7	8.8
LDH	100-225 U/L			365		510			447

Discussion

Both patients presented had marked increases in their WBC on multiple occasions; all occurring when the CBC was ordered without a differential. Our institution uses a Sysmex® XE-5000 to analyze all CBCs, differentials, reticulocyte counts and nRBCs. The Sysmex® will only flag for nRBCs when a CBC with diff is ordered as it flags via the diff channel3. The Sysmex® will not flag for nRBCs if a CBC without diff or reticulocyte count is ordered. At our institution when the Sysmex® flags for nRBCs, the CBC is then manually corrected for nRBCs. The Sysmex® XE-5000 can be used for automated reporting of nRBCs and is known to be accurate and reliable such use [4,5].

So why during these patients' admissions did they initially have CBCs with differentials followed by CBCs without differentials? This is likely because at our institution there is an on-going quality improvement (QI) project investigating the necessity of drawing daily CBCs and residents have become cost-conscious regarding the cost-difference between a CBC with and without a differential. In fact, both of these patients and several other SCD patients on subsequent admissions had the majority of CBCs ordered without differentials. It is important to remember that when one is suspicious of the presence of nRBCs the only way for a Sysmex® machine to flag nRBCs is by ordering a CBC with a differential as it is programmed to use the differential channel [6]. Our residents were not aware of this. It is an issue that needs to be discussed further with information technology to develop a solution.

The discovery behind the cause of the elevated WBC came to fruition by communicating with care providers, patients and the hematology lab. The patients provided key information to assess the need for additional work-up based on signs and symptoms. As care providers we were able to rule out infection as the cause of the leukocytosis based on the patients' signs, symptoms and physical exam. Discussing our findings with the hematology lab was the key, who then spoke with the technicians at Sysmex®. They were able to provide the answer to our mysterious leukocytosis: Sysmex® will not flag for nRBCs unless the diff channel is used. This was an example of open communication between care providers, patients and support staff. It is one of the principles of interdisciplinary rounds (IDR) that has shown to decrease readmission rates and improve patient satisfaction [7,8]. SCD patients are complex patients that would benefit from IDR.

The idea of interdisciplinary rounds (IDR) was first developed in the critical care setting. Teams involving the critical care attending, residents, medical students, RNs, dieticians, pharmacists and family discuss a patient's case and develop a comprehensive plan together. The initial goals to this approach of rounding were to improve patient safety and decrease the risk of adverse events. IDR was thought to help be able to provide better communication and increase both staff and patient/family satisfaction [6]. IDR is now widely used throughout health care and several studies have shown improved patient outcomes, including reduced re-admission rates and improved patient satisfaction [7,8]. The use of communication tools like the situation background assessment recommendation (SBAR) combined with IDR allowed for open communication and ensured that the care team was updated on the plan of care8.

Conclusion

SCD patients are complex patients that would benefit from IDR. It is important to have open communication so that all care givers, patients and family are aware of the plan of care. To avoid erroneous or potentially dangerous errors it is critical to communicate with the laboratory when data does not look accurate to find out why.

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