

A Non-classical Presentation of Parvovirus B19 in a Known Sickle Cell Patient

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Abstract

Parvovirus B19 is a well-studied complication in sickle cell patients. The classic presentation is a patient with a lacey, reticular type rash, small joint pain, signs of infection, and a low reticulocyte count. It is possible however, for a patient without the classic rash to have parvovirus infection, and a reticulocyte count should be ordered, even if clinical suspicion is low. Here, we present a case of a patient with known Sickle cell disease who presented with an unusual type of arthralgia and no rash. It is important to take a thorough history and consider Parvovirus infection in any Sickle cell patient who presents with signs of infection.

Keywords: Parvovirus B19; Sickle cell disease; Hydroxyurea

Introduction

Sickle cell disease (SCD) is a hereditary disorder caused by a point mutation in the beta globin gene which results in hemoglobin molecules that are prone to sickling in times of oxidative stress [1]. This can lead to occlusion of micro vascular beds and cause precarious complications, notably strokes, acute chest syndrome, and splenic and myocardial infarctions [2]. Infections, both bacterial and viral, are also an important cause of disease exacerbation.

SCD patients are susceptible to bacterial infections, especially with encapsulated organisms, due to their functional hyposplenism from repetitive vaso-occlusive crises in their spleen. This is a well-documented phenomena [3-5]. SCD patients are also at increased risk for viral infections and exacerbations of infections than healthy individuals, but this mechanism is less clear. Studies point to their increased RBC sickling due to stress and enhanced inflammatory response as possible causes [6,7]. One study concluded that influenza causes excess morbidity in SCD patients [6].

Parvovirus B19 is another pathogen that can lead to severe and lethal complications. Parvovirus B19 infections classically present with a malar rash and arthralgias [8-10]. Joint pain is more common in adults and women, and rarer in children and

men [8]. Parvovirus usually presents with acute, symmetric joint manifestations that preferentially affect small joints such as the wrists and feet [8]. An overwhelming 75% of patients with arthralgias as a presenting symptom have a concomitant rash [8]. Due to the near universality of the rash and the nonspecific nature of 'arthralgia' as a presenting symptom, clinicians often fail to include Parvovirus in their differential diagnosis when it is absent.

Here, we discuss an interesting case of Parvovirus infection in a known sickle cell patient that presented with non-classical migratory large joint arthralgia and without the telltale malar rash.

Case Report

An 18-year-old African American male with a past medical history of Sickle Cell disease with multiple crises presented to the emergency department with a chief complaint of chest and back pain. The pain began 2 days prior, and was initially described as neck stiffness. The pain is described as sharp, non-radiating and graded as 10/10; it was not made better with over the counter Tylenol. The patient reported the pain as typical of his past sickle cell crises; his last episode was 4 months prior to this presentation. He also reports nasal congestion, denies fevers, chills, nausea, vomiting, cough, abdominal pain. Current medications include hydroxyurea and folic acid. He reported no allergies or recent illnesses and is otherwise healthy.

On exam, the patient was afebrile and vital signs were stable. Other than diffuse tenderness to palpation of the ribs and lumbar paraspinal tenderness, physical exam showed no abnormal findings, including no rash or exanthems. A chest x ray was obtained which demonstrated no acute processes. CBC showed a WBC of 12.7 ($5.2-12.4 \times 10^3/\mu\text{L}$), Hgb of 8.3 (12-18 g/dl), Hct 26.3 (42-52%), and reticulocyte percentage of 6.9 (normal 0.5-1.5%).

The patient was subsequently admitted for management of Sickle cell crisis and treated with fluids and pain control. The patient developed a fever of 102.2 F on the day of admission; the remainder of the exam remained unchanged. Infectious disease was consulted at this time along with hematology. Blood cultures, urine cultures and viral titers were ordered. The patient continued to have intermittent fevers ranging from

102-103.7 F. The fevers were managed with Tylenol. Ceftriaxone 2 gram IV daily, Azithromycin 500 mg IV daily was administered empirically.

On hospital day 2, the reticulocyte count had dropped to 2.1%, WBC was 18, Hgb was 7.1, Hct 21.2. On hospital day 3, viral serology showed a positive IgM for Parvovirus with negative IgG. These findings are consistent with an acute infection with Parvovirus B19 and were postulated to be the cause of his intermittent fevers and red cell aplasia. A non-contrast CT scan of the abdomen and pelvis was performed as part of the workup of aplastic anemia which demonstrated bibasilar atelectatic changes and a heavily calcified spleen consistent with infarction.

The patient did not meet criteria to receive IgG for the active Parvovirus infection. The remainder of the course was complicated by a Hgb of 6.3 which required a transfusion of 1 unit of packed red blood cells on hospital day 5. Otherwise the patient responded well to supportive care and his reticulocyte count improved to 8.3 by hospital day 10. The patient was stable for discharge home on hospital day 17 with instructions to follow up at the outpatient clinic.

Discussion

Parvovirus B19 is a single stranded, un-encapsulated DNA virus that preferentially infects and destroys erythroid progenitor cells [9]. It can cause a variety of syndromes in both healthy and immuno compromised patients, including erythema infectiosum ("Fifth disease"), hydrops fetalis, red cell aplasia and aplastic crises [2,7]. A typical infective course begins approximately a week after exposure and lasts about five days. Presentation can range from asymptomatic or a nonspecific flu-like illness to severe anemia, depending on the host's susceptibility [2,7,9,10]. Healthy individuals tend to have milder symptoms, because reticulocyte destruction is not as much of an issue since their RBCs have adequate lifespans of around 120 days. However, patients with preexisting hematologic abnormalities that shorten this life span, such as SCD, thalassemias, hereditary spherocytosis, etc., are at risk for severe anemia and aplastic crises [2,10]. It is important to find and treat the precipitating cause of the crisis in a SCD patient to fully stabilize the patient and prevent long term sequelae. SCD patients can abruptly worsen and it imperative to incorporate the use of packed red blood cells (PRBC) and IVIG as needed. Some guidelines suggest transfusing adult patients with SCD at a hemoglobin concentration of <6 g/dl [10-13]. IVIG can also be used to inhibit leukocyte binding to the endothelium, thus improving blood flow.

Diagnosis

Guidelines vary for patients with and without immunosuppression, but in general, any patient with the classical erythema infectiosum, acute arthralgia, aplastic crises and chronic reticulocytopenic anemia should raise suspicion. High suspicion should be raised when an individual presents, like this patient eventually did, with severe anemia and a paradoxically low reticulocyte count. An uncommon pattern of

arthralgia, such as this patient's large joint migratory pain, and lack of rash should not deter from the diagnosis. This brings up an important point to note: a majority of sickle cell patients are African American, and a light red rash may be masked by their darker complexion, especially on a cursory glance in a busy emergency room. Classical physical exam findings are important, but lab tests should not be ignored.

The diagnosis can be clinched with serologic testing for antigens and antibodies as was done in this case. IgM antibody assays tend to be the gold standard, but have sensitivity rates of between 70%-100%, depending on the study [11,12].

Other, newer options include nucleic acid amplification testing which is gaining popularity due to increased sensitivity [13], however, this test was not available at our institution (and not necessary based on high clinical suspicion).

Treatment

The severity of a Parvovirus often depends on the patient's immune status and can subsequently range from benign to life threatening [5-7,10]. A major complication is transient aplastic crisis. In such crises, the host will experience a suspension of erythropoiesis resulting in severe anemia. In our patient, this was further exacerbated by preexisting Sickle cell disease. An aplastic crisis is typically managed with transfusions of PRBC to replete the total red blood cell count until the patient is able to mount an immune response to clear the infection (9). IVIG is another treatment modality reserved for severe or refractory disease. Our institution recommended administering IVIG if the reticulocyte count dropped below 0.05%. Patients typically have positive outcomes with IVIG regimens of 400 mg/kg for 5 or 10 days or 1000 mg/kg for 3 days.

Conclusion

Astute clinicians should always keep infection with Parvovirus on their differential when a known sickle cell patient presents with generalized symptoms and a low reticulocyte count, regardless of rash or other more classical symptoms. Although potentially lethal, Parvovirus is a very treatable pathogen and should be managed supportively, allowing the patient's immune system to combat the virus. Fluids, pain control and PRBC transfusions remain the standard, with IVIG only necessary for severe infections.

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