Case Report

When a Bleeding Hemorrhoid Is a Sign of Something More Sinister

Urgent Message: An expanded list of differential diagnoses can help clinicians identify when isolated bleeding is related to a more serious condition, as was the situation with this case of acute lymphoblastic leukemia.

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Abstract

Introduction

Patients may initially have isolated bleeding, thus leading them to an urgent care setting as their initial site of clinical evaluation. In this case, a life-threatening diagnosis of acute lymphoblastic leukemia (ALL) was made only after the differential was expanded.

Clinical Presentation

A 29-year-old man presented for treatment of symptoms common in an upper respiratory infection (URI) for a 2-3-day duration. He was secondarily concerned about bleeding hemorrhoids and a rash on his abdomen that had started the prior day.

Physical Exam

The patient's rectal exam revealed a macerated and friable thrombosed mass at the 9:00 position. A focused skin examination revealed a non-blanching petechial rash on the abdomen consistent with petechial lesions.

Case Resolution

A complete blood count (CBC) revealed a white blood cell (WBC) count of over 100,000. Further testing at a tertiary center confirmed a diagnosis of acute lymphoblastic leukemia.

Conclusion

Given the varying presentations, a patient with new-onset abnormal bleeding and petechial rash should undergo testing for hematologic pathologies.

Introduction

A patient with multiple complaints including rectal bleeding due to hemorrhoids is typically managed in an outpatient setting. Following is a case with complaints of upper respiratory symptoms, headache, and bleeding hemorrhoids; this life-threatening diagnosis of acute lymphoblastic leukemia (ALL) was made only after the differential was expanded.

Ethics Statement

Patient could not be contacted for follow-up and therefore demographics and some details of the case were changed to protect patient anonymity and confidentiality.

Clinical Presentation

A 29-year-old man presented with a chief complaint of 2-3 days of upper respiratory infection (URI) symptoms which consisted of ear pain, sore throat, nasal congestion, and a rash. He stated he has had body aches and felt stiffness in his back and neck. He had nasal congestion with mild chest congestion, but no productive cough. He was unsure if he had a fever. He was somewhat concerned about meningitis as he did have a headache and a rash

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on his back, arms, and legs the day before. He denied confusion. He also complained of painful bleeding hemorrhoids, which he had also experienced in the past.

The patient's only known medical history was hypothyroidism for which he took levothyroxine. He had no known allergies.

Physical Exam

The patient's vital signs were entirely within normal limits, and he was alert, oriented, and in no distress.

- Neck was supple without rigidity.
- Cardiopulmonary exam revealed regular heart rhythm and sounds and clear lungs bilaterally.
- Abdomen was soft and nontender.
- Rectal exam revealed a thrombosed mass consistent with an external hemorrhoid, with some macerated and friable areas superficially at the 9:00 position.

Evaluation and Medical Decision Making

A summary of this patient's initial presentation would be consistent with an upper respiratory infection with a viral exanthem and an incidental mention of hemorrhoids. Because of the bleeding hemorrhoids, additional questioning explored for other types of bleeding. The patient denied blood in the urine, bruising of the skin and nose bleeds, but curiously mentioned that he lately had been having bleeding of the gums when he brushed his teeth.

Because of the additional information provided in review of symptoms, the treating clinician asked the patient to undress so the rash could be examined. That skin exam revealed a non-blanching rash across the entire abdomen consistent with petechial lesions.

Differential Diagnosis

Petechiae are non-blanching macular skin lesions. Petechiae are < 2 mm in size, distinguishing them from purpura. The differential diagnosis for a petechial rash includes a wide array of etiologies, many of which are life-threatening.[1] Important distinctions can be made that can narrow down differential, with the initial and most critical question being whether the patient is febrile or not.

For patients with petechial rash and fever, important considerations include both infectious and non-infectious etiologies, such as the following:

- Rocky Mountain spotted fever (*Rickettsia rickettsii*) is a bacterial infection spread by tick bites. Infection will usually be accompanied by headaches and fevers along with the rash.[2]
- Bacterial meningitis (most commonly from *S. pneumoniae)* can cause a petechial rash in severe cases by causing platelet consumption via blood vessel damage, although associated symptoms would also include nuchal rigidity, fevers, and oftentimes altered mental status. *N. meningitis* infection can cause petechiae with or without meningitis, as is the case with meningococcemia.[3]
- Disseminated gonococcal infection can also lead to petechiae, although it will usually be accompanied by other inflammatory signs and symptoms such as migrating arthritis.[4]
- Parasites, such as *Babesia microti*, can cause a petechial rash due to platelet destruction from intracellular multiplication.[5]
- Henoch Schoenlein Purpura (HSP) (IgA vasculitis) can lead to petechiae and accompanying fevers are also common. It will be preceded by a viral illness and will often be accompanied by hematuria.[6]
- Thrombotic thrombocytopenic purpura (TTP), in which a defective coding for the enzyme ADAMTS13 leads to unrestrained propagation of microthrombi.[7] TTP is associated with a classic pentad of symptoms, although patients will commonly present without one or more of these symptoms:[8]
  - Thrombocytopenia
  - Microangiopathic hemolytic anemia
  - Neurologic abnormalities
  - Renal impairment
  - Fever
- Many self-limited viral infections, such as parvovirus B19, rhinovirus, adenovirus, enterovirus, and Epstein-Barr virus (EBV), can cause petechiae (with and without significant thrombocytopenia) via as a consequence of the patient's immune response.[9]

Among patients with petechial rash who present without fever, the differential includes:

- Disseminated intravascular coagulation (DIC) can lead to petechiae via widespread consumption of platelets, typically caused by severe systemic illness or injury. Patient's coagulation studies will often show thrombocytopenia as well as abnormal coagulation studies (eg, prothrombin time (PT) and decreased fibrinogen).[10]
- Autoimmune conditions that can cause vasculitis, such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), can cause petechiae via autoimmune destruction of platelets as well as direct microvascular inflammation.[11]
- Immune thrombocytopenic purpura (ITP) is a diagnosis of exclusion. This can lead to severe thrombocytopenia and petechiae via autoimmune destruction of platelets. Patients will frequently be well appearing otherwise.[11]
- Heparin induced thrombocytopenia (HIT) that oc-

curs due to antibody formation against platelet factor-4 (PF4) after exposure to a heparin product.[12]

- Antiphospholipid syndrome (APLS) is an autoimmune disorder that can lead to a petechial rash. This condition can result in platelet destruction and thrombocytopenia.[13]
- In a younger patient, such as this, with new onset symptoms, ALL as well as other hematologic malignancies should be suspected. ALL typically presents with symptoms of abnormal bleeding, fatigue, and can also present with relapsing fever.[14]

While it is important to consider the above diagnoses in patients with petechiae, it is also worth noting that petechiae are more often benign in otherwise well-appearing, afebrile, ambulatory patients. Localized petechiae and petechiae isolated to above the nipple line, particularly in the face and neck, are generally reassuring patterns and may occur after localized pressure to the skin or Valsalva related to coughing or vomiting in the absence of underlying systemic illness.[15,16]

Case Resolution

The patient had a CBC drawn that revealed a WBC count of over 100,000. He was evaluated at a tertiary care center and found to have acute lymphoblastic leukemia.

Discussion

Acute lymphoblastic leukemia is the most common cancer in pediatric populations with approximately 3,000 cases diagnosed annually in the United States. The peak incidence of ALL occurs between the ages of 3 and 5 years with higher rates seen in boys when compared to girls and also in White/Hispanic populations.[17] ALL is also the most frequent cause of death from cancer in patients under the age of 20.

ALL is caused when DNA mutations result in marrow proliferation and production of abnormal lymphocytes. Normal lymphocytes are important for immune function; the immature lymphocytes seen in ALL are unable to ward off infections effectively, resulting in functional immunodeficiency. These abnormal lymphocytes will continue to divide and replace normal cells leading to anemia and thrombocytopenia, which accounts for the myriad associated symptoms such as fatigue, shortness of breath, easy bruising, and bleeding seen in patients with ALL.[4] The diagnostic work-up for ALL includes a CBC, bone marrow aspirate, cytogenetic analysis, and/or immunophenotyping.[4] With current therapies for ALL, including chemotherapy, immunotherapy, and bone marrow transplantation, there is now a 90% overall survival rate for those less than 21 years of age.[17]

Conclusion

- Causes of petechiae are wide-ranging, and most well-appearing patients have no serious underlying diagnosis, especially if petechiae are localized and involve only the face and/or neck.
- Presence of fever, general appearance, associated symptoms, and distribution of rash can help to narrow the differential. Ill appearing patients should be referred immediately to an emergency department.
- A CBC has excellent utility in the initial screening work-up of patients with petechiae.
- Clinical manifestations of ALL can be vague and nonspecific, and patients may not have constitutional symptoms. ■

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