

CASE REPORT

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Hermansky-Pudlak syndrome subtype 5 (HPS-5): Safety of cardiac catheterization in patients with a bleeding diathesis

Erik Vincek, Louis Cruz, Stephen Anderson, John Abernathy

ABSTRACT

Introduction: Hermansky-Pudlak syndrome is a rare autosomal recessive form of albinism that leads to defective platelet aggregation and bleeding diathesis. This presents a potential challenge to clinicians involved in the care of these patients. Common manifestations include nystagmus, lighter skin, and hair color than family members, prolonged bleeding after minor procedures, pulmonary fibrosis, colitis, and neutropenia.

Case Report: We present the case of a middle-aged Hispanic patient diagnosed with Hermansky-Pudlak syndrome subtype 5 with prior history of extensive and prolonged bleeding who presented to the emergency department with unstable angina. He eventually required cardiac catheterization which was performed without bleeding complications.

Conclusion: In patients with previously known disease or signs and symptoms of Hermansky-Pudlak syndrome, it is important to acknowledge the hematologic risk of performing even minor procedures on these patients.

Keywords: Chediak-Higashi, Griscelli syndrome, Oculocutaneous albinism, Puerto Rico

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INTRODUCTION

Hermansky-Pudlak syndrome (HPS) is a rare autosomal recessive disease caused by several genetic mutations, including AP3B1, AP3D1, BLOC1S3, BLOC1S6, DTNBP1, HPS1, HPS3, HPS4, HPS5, and HPS6 [1]. It is relatively rare, occurring in up to 1 in 1,000,000 individuals, but occurs in greater frequency in Puerto Rico, particularly in the central and northwest part of the territory [2]. There are eight subtypes of HPS, each of which presents with different manifestations [1]. Common manifestations found in HPS include nystagmus, lighter skin, and hair color than family members, prolonged bleeding after minor procedures, pulmonary fibrosis, colitis, and neutropenia. Subtypes 1, 2, and 4 are those that typically manifest with more severe symptoms and are associated with pulmonary fibrosis; subtypes 1 and 2 are those most commonly associated with colitis [3, 4]. Subtypes 1 and 3 are the most common ones found in patients from Puerto Rico [5]. There is paucity of data regarding prevalence of subtype 5 among HPS patients, including those of Puerto-Rican origin. Subtype 5 manifestations have been described as including oculocutaneous albinism and mild bleeding diathesis [6]. As coagulation cascade is unaffected, activate partial thromboplastin time (aPTT), prothrombin time (PT), and international normalized ratio (INR) are typically normal in these patients, but bleeding time may be affected. The mutations found in HPS cause dysfunction of protein complexes which are necessary for proper lysosomal and lysosomal-related organelles (LROS) function [7]. These cellular components are necessary for the appropriate function of melanosomes, platelets, type 2 pneumocytes, and immune cells such as NK and suppressor T cells, and are likely responsible for the clinical manifestations mentioned above. Diagnosis is obtained based on a combination of clinical presentation and platelet electron microscopy using the “whole mount” technique, which confirms the absence of dense bodies. Diagnosis can be

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confirmed by genetic testing and can clarify subtypes. Hermansky-Pudlak syndrome can easily be confused for other diagnoses, such as Chediak-Higashi and Griscelli syndrome, due to their similar hematologic and cutaneous manifestations.

CASE REPORT

A middle-aged Puerto-Rican-born male presented to the emergency department with acute sharp sternal chest pain radiating to his left shoulder and hand, shortness of breath, palpitations, diaphoresis, and nausea. He reported that he has had minor intermittent chest pain, palpitations, and anxiety in the past week. His past medical history included HPS subtype-5, hypertension, hyperlipidemia, diabetes mellitus, peripheral neuropathy, obstructive sleep apnea, pulmonary embolism, and COVID infection one year prior. The patient reported a past surgical history of a right neck cystic hygroma excision at age 16 which required red blood cell transfusion, wisdom tooth removal which required platelet transfusion, and tonsillectomy which required platelet transfusion. At home, he stated that he is currently on amlodipine, atorvastatin, lisinopril, metoprolol succinate, and apixaban. He was allergic to aspirin and codeine, although he did not have a true aspirin allergy. He was instructed by his previous primary care physicians to avoid aspirin in the setting of HPS.

This patient was confirmed to have HPS subtype 5 at age 16, after bleeding complications secondary to his neck surgery. Manifestations of his condition additionally include prolonged bleeding with flossing, recurrent epistaxis with prolonged bleeding, recurrent hospital admissions for hemarthrosis in the left hip between the ages of 8 and 15, and hematuria with rough intercourse. As a teenager, he had blonde hair and had the lightest skin of any of his family members. He has been legally blind since the age of 18 and has had horizontal nystagmus since a child. He reported having a cousin with HPS.

In the emergency department, his vitals were remarkable for tachycardia to 113 bpm, and he was hypertensive to 137/87 mmHg. His laboratory results were remarkable for negative troponins (<0.01), PT 10.5 s, aPTT of 29.0 s, an INR of 1.0, hemoglobin of 16.1 g/dL, and platelets of 275,000/mL. Electrocardiogram (EKG) showed sinus rhythm and no evidence of acute ischemic changes, and his chest X-ray was unremarkable. He was admitted for unstable angina and managed per hospital protocol. Due to continued substernal chest pain despite nitro paste, cardiology recommended cardiac catheterization. The patient was informed of the risks and benefits of the procedure in the setting of bleeding diathesis secondary to HPS. The patient understood the risks and benefits of the procedure and consented.

Cardiac catheterization duration was 19 minutes from sedation to application of hemostatic gauze. Access was via the right radial artery. A 6F × 10 cm Glidesheath Slender 591914 sheath was advanced into the vessel, followed by

5F CATH RAIAL TIGER 4.0 catheter placement. Contrast was injected into the right and left coronary arteries, and images were obtained using multiple projections (Figures 1 and 2). Right radial hemostasis was achieved using a 27 cm VascBand hemostat long-776223 device.

The cardiac catheterization was performed without complications. Before the catheterization, the patient's platelets were at 247,000. Interventional cardiology reported 10% stenosis in the left anterior descending artery, and he did not require stenting. There was negligible blood loss and hemostatic gauze and compression were applied to the right radial artery through which the guidewire was inserted. His laboratory results remained stable throughout the hospital course and he was discharged the following day.

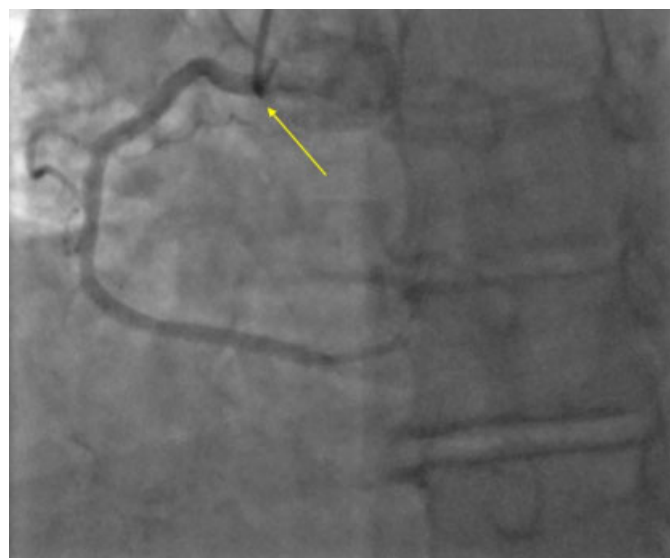


Figure 1: Image of right coronary catheterization. Dye is being injected into the right main coronary artery (yellow arrow).

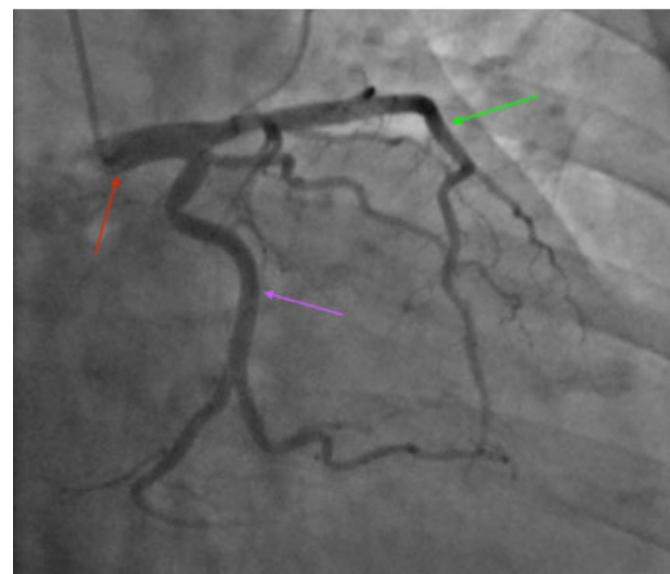


Figure 2: Image of left coronary catheterization. Dye is being injected into the left main coronary artery (red arrow). Left anterior descending coronary artery (purple arrow) and left circumflex coronary artery (green arrow) both well visualized.

DISCUSSION

It is important to recognize the potential for catastrophic bleeding in patients with bleeding diathesis. Clinical manifestations of HPS include albinism, visual impairment, lung fibrosis, colitis, and platelet dysfunction. Manifestations of platelet dysfunction can include easy bruising, bleeding gums, epistaxis, heavy menstruation, and prolonged bleeding after injuries and surgeries. As HPS is a rare condition in most parts of the world, it can easily go unnoticed, and many clinicians may be unaware of the bleeding diathesis among patients with HPS. The cutaneous manifestations may also be misinterpreted as a solitary entity and dismiss the need for further workup. Like with this patient, other HPS patients have suffered from bleeding complications after relatively minor surgical procedures, including tooth extractions, septoplasty, and mammoplasties, and have required red blood cell transfusion, platelet transfusion, or administration of fresh frozen plasma [8, 9]. Successful use of DDAVP has been described in previous cases, along with use of hemostatic packing and gel foam [9]. Hermansky-Pudlak syndrome is not an absolute contraindication to surgery. Major surgeries, including bilateral lung transplantations, have been successfully performed with careful administration of platelet transfusions and intraoperative desmopressin [10, 11]. The risks of bleeding complications during cardiac catheterization in a patient with HPS has never been independently investigated to our knowledge and was the impetus for this report.

Cardiac catheterization remains one of the most common procedures performed in the United States, with bleeding complications that may include hematomas and retroperitoneal bleeding [12]. Although incidence of retroperitoneal bleeding during cardiac catheterization remains very rare (0.18%), HPS patients may potentially be at higher risk of complications, although this has not been investigated [13]. This case report of an uncomplicated cardiac catheterization through a peripheral vein site in an HPS patient can be used to guide clinicians who are weighing the risks and benefits of such interventions in patients with HPS. All surgical procedures should be carefully considered, and providers should be prepared to respond to severe bleeding complications. This patient was able to receive a cardiac catheterization without complications. The patient was discharged 24 hours after cardiac catheterization and has not been re-admitted to the hospital at 4-month follow-up. This does not guarantee that other patients with HPS will respond without complications, as there are several subtypes of HPS, and each may have higher or lower bleeding tendencies. Other reports of HPS subtype-5 have presented with albinism and mild bleeding diathesis, which align with the findings in our patient and classical description of the subtype-5 phenotype [6]. We believe that cardiac catheterization is a safe procedure for patients with HPS subtype-5 but physicians should be aware of potential complications

and be prepared to respond to complications should they arise. As with other disorders of platelet dysfunction, HPS may theoretically confer a protective effect in regard to risk of coronary disease, stroke, and other forms of cardiovascular disease. This protective effect is the basis of the use of aspirin and other anti-platelet agents in patients with coronary artery disease worldwide. Further studies need to be done to show whether patients with HPS share this cardioprotective benefit.

CONCLUSION

Minor procedures, such as cardiac catheterizations, should thus be performed with caution, and achievement of hemostasis should be highly prioritized in patients with HPS. The diagnosis of HPS should be on a diagnostician's radar for any patient of Puerto Rican descent with bleeding diathesis. Other clues a clinician can use to diagnose HPS are albinism, nystagmus, pulmonary fibrosis, and colitis, and suspicions can be confirmed by genetic testing. The authors recommend that suspicion for HPS should warrant genetic confirmation so that patients may be aware of their subtype and relative risks of bleeding and other long-term complications.

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Author Contributions

Erik Vincek – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Louis Cruz – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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