ACG CASE REPORTS JOURNAL

CASE REPORT | INFLAMMATORY BOWEL DISEASE

Hermansky-Pudlak Syndrome Complicated by Crohn's Disease and Hidradenitis Suppurativa: A Case of Multisystem Immune Dysregulation

Russell Yanofsky, MD[1], Sarah L. Stein, MD[2], David T. Rubin, MD[1], and Amelia Kellar, MD[1]

[1]*Department of Medicine, Inflammatory Bowel Disease Center, University of Chicago, Chicago, IL*
[2]*Department of Medicine and Pediatrics, Section of Dermatology, University of Chicago, Chicago, IL*

ABSTRACT

Hermansky-Pudlak syndrome (HPS) is a rare autosomal recessive disorder marked by defects in lysosomal function that can manifest with a granulomatous enterocolitis resembling Crohn's disease (CD). We present a 16-year-old adolescent boy with HPS-associated CD and hidradenitis suppurativa (HS), representing one of a few cases of HPS with concurrent CD and HS described in the literature to date. Disease stabilization on combined infliximab and methotrexate highlights potentially shared inflammatory pathways involved in the pathogenesis of HPS-associated CD and HS. Given the rarity and refractory nature of this disease constellation, our case may provide a beneficial treatment strategy for other patients.

KEYWORDS: Hermansky-Pudlak syndrome; Crohn's disease; hidradenitis suppurativa

INTRODUCTION

Hermansky-Pudlak syndrome (HPS) is an autosomal recessive disorder characterized by lysosomal dysfunction, oculocutaneous albinism, and platelet abnormalities.[1] A subgroup of patients develop granulomatous enterocolitis indistinguishable from Crohn's disease (CD); this pathogenesis remains unknown.[1,2] The association between HPS and CD is poorly understood, particularly the prevalence and pathogenesis of extraintestinal manifestations (EIM) of CD in patients with HPS.[3] Hidradenitis suppurativa (HS), an inflammatory condition of the skin, can be an EIM of CD.[4] We present a patient with HPS-associated CD with aggressive HS of the genital and axillary regions.

CASE REPORT

A 16-year-old adolescent boy with HPS (HPS1 gene mutation: c1472+87dup16) presented with ileocolonic and perianal CD. Features included albinism, visual impairment, and platelet dysfunction. In 2013, he was diagnosed with ileocolonic CD and began therapy with 6-mercaptopurine 25 mg daily. He developed perianal fistulizing disease and, in 2014, commenced infliximab 5 mg/kg q8 weeks, with therapeutic levels (34.79 μg/L) recorded in May 2015. Given disease progression, therapy was changed to adalimumab 40 mg weekly with methotrexate 15 mg weekly in August 2015. However, endoscopic disease activity prompted a diverting loop ileostomy in September 2015.

Postoperatively, adalimumab and methotrexate were resumed with partial improvement. In 2017, colonoscopy revealed recurrent colitis. Examination under anesthesia (EUA) demonstrated complex perianal fistulizing disease managed with seton placement. Laparoscopic total colectomy with ileostomy revision was performed, leaving a 20 cm rectosigmoid stump. Adalimumab and methotrexate were restarted postoperatively, though no drug trough levels were documented. Persistent perianal abscesses necessitated repeated incision and drainage (I&D). In 2021, he developed a right groin abscess. Pathology from punch biopsy demonstrated ulceration, foci of leukocytoclastic vasculitis, abscess formation, histiocytic deposition, granulation tissue, and signs of acute

ACG Case Rep J 2025;12:e01647. doi:10.14309/crj.0000000000001647. Published online: March 29, 2025

Correspondence: Amelia Kellar, MD (amelia.kellar@bsd.uchicago.edu).

and chronic inflammation. Pyoderma gangrenosum was suspected, but he failed to respond to systemic corticosteroids, doxycycline, dapsone, clobetasol, tacrolimus, and mupirocin ointments.

In March 2023, he developed abdominal pain and endoscopy revealed areas of mildly friable mucosa with exudate in the rectum. Adalimumab was changed to upadacitinib (8-week 45 mg daily induction, followed by 30 mg daily maintenance). In August 2023, he required I&D, fistulotomy, seton placement, and antibiotics for a recurrent perianal abscess. Persistent symptoms led to switching upadacitinib to ustekinumab in October 2023.

In December 2023, he presented to our center with worsening groin wounds. EUA revealed healing perianal fistulizing disease, but fibrinopurulent ulceration of the perineum and violaceous nodules in the inguinal creases remained (Figure 1). Per Dermatology, a diagnosis of HS was favored for the groin and perianal lesions. Ustekinumab was stopped, and he underwent reinduction with infliximab 10 mg/kg, followed by maintenance dosing q8 weeks and methotrexate 15 mg weekly. Infliximab trough levels were on target (>25 μg/mL at week 2, >17 μg/mL at week 6). He was tapered off prednisone, which he had been dependent on since the time of diagnosis. Endoscopy, ileoscopy, and EUA in February 2024 revealed a normal neoterminal ileum, a friable rectal stump consistent with diversion colitis (Figure 2), and healing of perianal fistula tracts. HS management, in addition to systemic therapy with infliximab and methotrexate, included topical clobetasol and clindamycin.

In July 2024, he developed a fluctuant, tender left axillary nodule (Figure 3). Ultrasound demonstrated a 5 cm abscess managed with I&D and clindamycin and rifampin. Infliximab levels returned at 3.3 μg/mL, prompting interval shortening to q4 weeks and increasing methotrexate to 20 mg weekly. At follow-up in October 2024, he was in clinical remission from his CD with improved groin HS but active axillary disease (Figure 4).

DISCUSSION

HPS is an autosomal recessive disorder marked by lysosomal dysfunction, with 11 distinct genotypes[1,3] While all patients present with platelet dysfunction and albinism, HPS-1 and HPS-4 are associated with CD-like enterocolitis that is phenotypically indistinguishable from CD.[5,6] However, HPS typically has copious granulomatous disease.[3,7] Enterocolitis is hypothesized to result from impaired microbial clearance and a dysregulated immune response due to the abnormal functioning of an endosomal trafficking protein complex.[6] Other potential mechanisms include impaired platelet dense bodies and tight junctions.[3] Granulomatous disease may result from accumulation of ceroid-like pigment in intestinal macrophages, resulting in rupture, release of lysosomal hydrolases, and resultant tissue damage.[8] This may explain the refractory nature of HPS-associated CD.

Our case highlights a rare presentation of HPS-associated CD complicated by HS, an EIM of CD that has not been well described in the HPS population. In one study, HS was present in only 1 of 37 patients with HPS and CD.[3] HS is a chronic inflammatory condition of hair follicles in the apocrine gland-bearing regions.[9] The etiology is unclear but may involve dysregulated cytokine responses and altered microbiota, similar to CD.[4] This may explain the association between HS and CD.[4] Both HS and CD are characterized by the formation of sinus tracts with HS being more common in the setting of fistulizing CD. The 2 entities share genetic loci associated with immune dysregulation and risk factors including smoking and obesity.[10] Our patient possessed several risk factors of HS, including obesity and fistulizing CD.

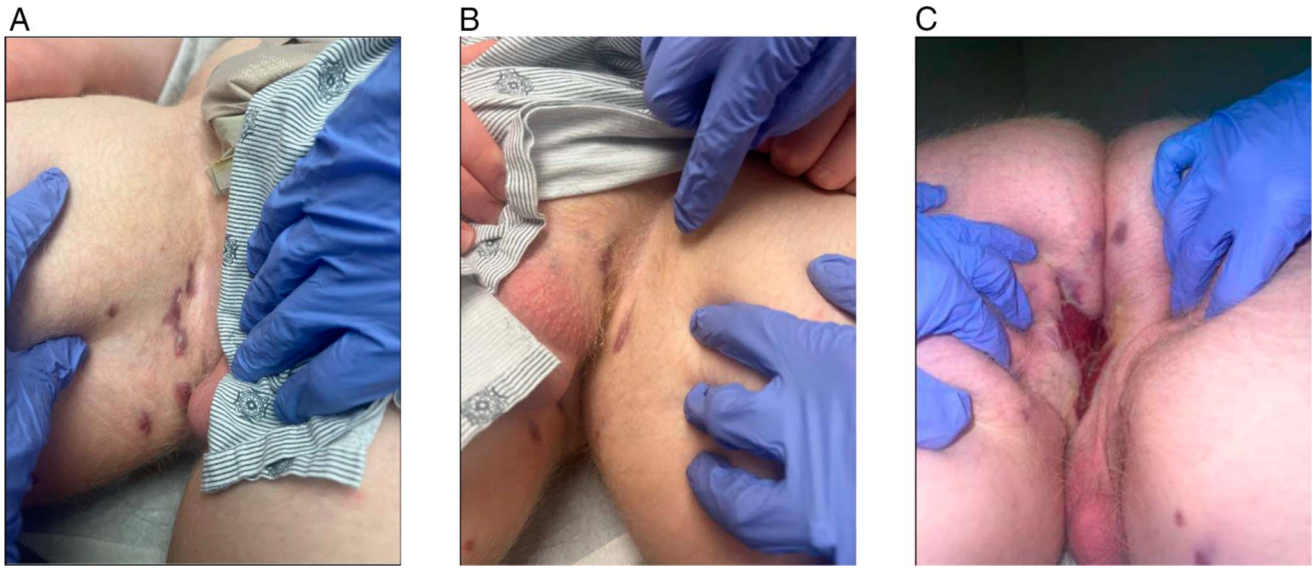

Figure 1. EUA December 2023 demonstrating healing of perianal fistulizing disease, but fibropurulent ulceration on the perineum and violaceous nodules in the inguinal creases. A. Right groin. B. Left groin, C. Gluteal cleft.

Figure 2. Ileoscopy and flexible sigmoidoscopy performed February 2024 demonstrating a normal neo-terminal ileum and friable mucosa in the rectum consistent with diversion colitis.

Antitumor necrosis factor (TNF) therapy is effective for both CD and HS.[11,12] While no evidence-based treatment recommendations for HPS enterocolitis exist, case reports suggest variable success with traditional CD therapies.[3] Our patient achieved clinical and endoscopic remission from his CD and improved perianal HS, demonstrating its efficacy in managing CD and HS. Multiomics analysis of patients with HPS-1 revealed increased levels of TNFα compared with healthy controls.[6] While its exact role remains unknown, we suspect that TNFα acts as a proinflammatory cytokine in HPS, similar to its functioning in inflammatory bowel disease, and therefore, increased TNFα may underlie the benefit of anti-TNF therapy for HPS-associated CD.[6,13] A retrospective study found that 7 of 13 patients with HPS-associated CD had a prolonged response to anti-TNF therapy, though details regarding drug levels were not provided.[3] Despite this, several case reports have noted improved outcomes with the use of anti-TNF therapy.[6–8,14–19] Optimal therapeutic drug level of anti-TNF therapy in HPS-associated enterocolitis remains unknown, highlighting the need for further studies.[20]

This case presents the intersection of HPS, CD, and HS, highlighting potentially shared inflammatory pathways. The prospect of parallel pathophysiological processes underlying these conditions may facilitate more targeted therapy and help guide recommendations in these refractory cases.

DISCLOSURES

Author contributions: R. Yanofsky drafted the manuscript. A. Kellar was the treating inflammatory bowel disease specialist for

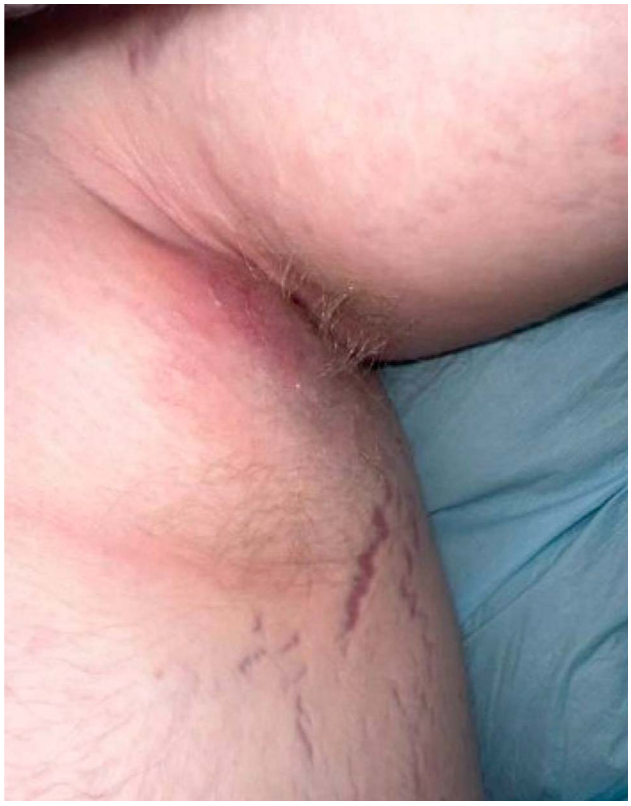

Figure 3. July 2024 Image of the left axilla, following which ultrasound demostrated 5cm abscess.

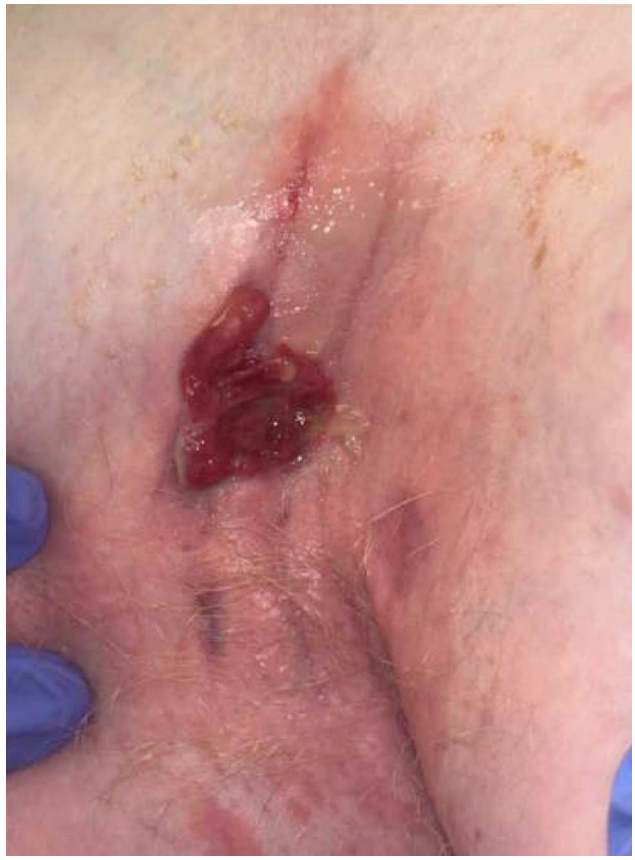

Figure 4. October 2024 Image of the left axilla following incision and drainage of 5cm abscess. Topical therapy ongoing with clobetasol ointment for treatment of granulation tissue and topical clindamycin lotion applied to surrounding skin surface.

the patient and provided final manuscript revisions. D.T. Rubin was an advisor on the management for the patient and provided final manuscript revisions. S.L. Stein was the treating dermatologist for the patient, provided the images used in the manuscript, and provided final manuscript revisions. A. Kellar is the article guarantor.

Financial disclosure: D.T. Rubin has received grant support from Takeda and has served as a consultant for Abbvie, Altrubio, Abivax SA, Altrubio, Avalo Therapeutics, Bausch Health, Bristol-Myers Squibb, Buhlmann Diagnostics Corp, ClostraBio, Connect BioPharma, Douglas Pharmaceuticals, Eli Lilly & Co., Genentech Inc., InDex Pharmaceuticals, Iterative Health, Janssen Pharmaceuticals, Odyssey Therapeutics, Pfizer, Sanofi, and Takeda Pharmaceuticals. He serves on the Board of Trustees for the Crohn's & Colitis Foundation and is on the Board of Directors for Cornerstones Health.

Informed consent was obtained for this case report.

Received October 24, 2024; Accepted February 18, 2025

REFERENCES

1. El-Chemaly S, Young LR. Hermansky-Pudlak syndrome. *Clin Chest Med.* 2016;37(3):505–11.
2. Miranda C, Javaheri N, Carlson A, Aijaz A, Nallapeta N. Hermansky-Pudlak syndrome associated inflammatory bowel disease: A systematic review on clinical manifestations and investigations into optimal management. *Inflamm Bowel Dis.* 2024;30(Supplement_1):S26–7.
3. O'Brien KJ, Parisi X, Shelman NR, et al. Inflammatory bowel disease in Hermansky-Pudlak syndrome: A retrospective single-centre cohort study. *J Intern Med.* 2021;290(1):129–40.
4. Chen W-T, Chi C-C. Association of hidradenitis suppurativa with inflammatory bowel disease: A systematic review and meta-analysis. *JAMA Dermatol.* 2019;155(9):1022–7.
5. Sofia MA, Sakuraba A, Rubin DT. Two complex cases of Hermansky-Pudlak syndrome highlight a potential biologic explanation for an associated Crohn's disease phenotype. *ACG Case Rep J.* 2017;4:e14.
6. Cavounidis A, Pandey S, Capitani M, et al. Hermansky-Pudlak syndrome type 1 causes impaired anti-microbial immunity and inflammation due to dysregulated immunometabolism. *Mucosal Immunol.* 2022;15(6):1431–46.
7. Hussain N, Quezado M, Huizing M, et al. Intestinal disease in Hermansky-Pudlak syndrome: Occurrence of colitis and relation to genotype. *Clin Gastroenterol Hepatol.* 2006;4(1):73–80.
8. Kouklakis G, Efremidou EI, Papageorgiou MS, Pavlidou E, Manolas KJ, Liratzopoulos N. Complicated Crohn's-like colitis, associated with Hermansky-Pudlak syndrome, treated with infliximab: A case report and brief review of the literature. *J Med Case Rep.* 2007;1:176.
9. Diaz MJ, Aflatooni S, Abdi P, et al. Hidradenitis suppurativa: Molecular etiology, pathophysiology, and management-A systematic review. *Curr Issues Mol Biol.* 2023;45(5):4400–15.
10. Tandon P, Govardhanam V, Gallinger Z, Weizman AV. Risk factors for developing hidradenitis suppurativa in patients with inflammatory bowel disease: A retrospective case-control study. *J Can Assoc Gastroenterol.* 2021;4(4):165–72.
11. Stidham RW, Lee TC, Higgins PD, et al. Systematic review with network meta-analysis: The efficacy of anti-TNF agents for the treatment of Crohn's disease. *Aliment Pharmacol Ther.* 2014;39(12):1349–62.
12. Savage KT, Flood KS, Porter ML, Kimball AB. TNF-α inhibitors in the treatment of hidradenitis suppurativa. *Ther Adv Chronic Dis.* 2019;10:2040622319851640.
13. Scharl M. Pathophysiological role of TNF in inflammatory bowel disease: TNF and its effect on innate immune defense. In: Rogler G, Hibi T, Herfarth H, et al, eds. *Anti-Tumor Necrosis Factor Therapy in Inflammatory Bowel Disease*. S.Karger AG; 2015:49–55.
14. Girot P, Le Berre C, De Maissin A, Freyssinet M, Trang-Poisson C, Bourreille A. Crohn's-like acute severe colitis associated with Hermansky-Pudlak syndrome: A case report. *World J Gastroenterol.* 2019;25(8):1031–6.
15. de Leusse A, Dupuy E, Huizing M, et al. Ileal Crohn's disease in a woman with Hermansky-Pudlak syndrome. *Gastroenterol Clin Biol.* 2006;30(4):621–4.
16. Erzin Y, Cosgun S, Dobrucali A, Tasyurekli M, Erdamar S, Tuncer M. Complicated granulomatous colitis in a patient with Hermansky-Pudlak syndrome, successfully treated with infliximab. *Acta Gastroenterol Belg.* 2006;69(2):213–6.
17. Yoshiyama S, Miki C, Araki T, Morimoto Y, Okita Y, Kusunoki M. Complicated granulomatous colitis in a Japanese patient with Hermansky-Pudlak syndrome, successfully treated with infliximab. *Clin J Gastroenterol.* 2009;2(1):51–4.
18. Felipez LM, Gokhale R, Guandalini S. Hermansky-Pudlak syndrome: Severe colitis and good response to infliximab. *J Pediatr Gastroenterol Nutr.* 2010;51(5):665–7.
19. Kani HT, Tezcan N, Aydin Y, Banzragch M, Akin H, Imeryuz N. Hermansky Pudlak syndrome with granulomatous colitis complicated by an abscess formation. *Eur J Intern Med.* 2013;24:e80–1.
20. Papamichael K, Afif W, Drobne D, et al. Therapeutic drug monitoring of biologics in inflammatory bowel disease: Unmet needs and future perspectives. *Lancet Gastroenterol Hepatol.* 2022;7(2):171–85.