ACG CASE REPORTS JOURNAL

CASE REPORT | COLON

Behcet's Disease Presenting as Pancolonic Ulcerations in a Patient With Kikuchi-Fujimoto Disease: A Rare Gastrointestinal Manifestation

Frank Lin, DO[1], Ayah Obeid, MD[1], Harsh Bhalala, MD[1], Nishit Patel, MD[1], Li Ge, MD[1], and Ronak Modi, MD[1]

[1]*Internal Medicine, St. Luke's University Health Network, Bethlehem, PA*

ABSTRACT

Kikuchi-Fujimoto disease (KFD) is a rare and self-limiting disorder characterized by cervical lymphadenopathy and fever. In this report, we present a case of a 24-year-old man with known history of KFD who presented with lower gastrointestinal bleeding and acute blood loss anemia. Further evaluation with colonoscopy showed widespread ulcerations in the colon and terminal ileum with suspicion for Behcet's disease. Biopsy from the colonic mucosa and ileocecal valve demonstrated focal ulcer with cryptitis and lymphoid aggregates that can be seen in Behcet's syndrome; however, it lacks specificity and Behcet's disease is a clinical diagnosis. This case emphasizes the importance of including gastrointestinal bleeding as a potential manifestation due to Behcet's disease in patients diagnosed with KFD.

INTRODUCTION

Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, is an extremely rare enigmatic benign and self-limited disease first described in 1972 characterized by tender regional cervical lymphadenopathy associated with mild fever and night sweats.[1] It is now known to have a worldwide distribution with higher prevalence among Japanese, Vietnamese, and other Asiatic individuals, with young adults (both male and female in 1:1 ratio) younger than 30 years being most affected.[2,3] Generalized lymphadenopathy and mediastinal, axillary, or mesenteric lymphadenopathy has also been described.[4] Nausea, vomiting, diarrhea, and weight loss have also been reported in patients with extranodal disease.[5,6] Laboratory results are usually normal although mild anemia, leukopenia, and leukocytosis with atypical lymphocytes, mild erythrocyte sedimentation rate, and C-reactive protein elevations have been reported.[3]

Etiology currently remains unclear, with the 2 most common hypotheses being viral and autoimmune.[3] Recent case reports suggest association with coronavirus disease 2019 infection and vaccination further supporting possibility of post-viral autoimmune etiology.[7-10] Although pathogenesis is currently unclear, the clinical presentation, course, and histologic changes suggest an intense immune response of histiocytes and T cells to an infectious agent.

Only 1 case report in the literature has highlighted gastrointestinal (GI) bleeding as a manifestation of KFD.[11] In this report, we present a rare, unusual association of KFD with Behcet's disease causing pancolonic ulcerations. Only 1 prior case report shows a possible association between KFD and Behcet's disease.[12] In terms of prior observed rare GI manifestations with this disease, nausea, vomiting, and abdominal pain mimicking acute appendicitis due to mesenteric lymphadenitis has been a common presentation.[13,14] This case highlights the importance of considering Behcet's disease as a differential diagnosis in patients presenting with GI bleeding with preexisting or newly diagnosed KFD.

CASE REPORT

A 24-year-old man with a history of KFD, diagnosed at 13 years of age, and a recent dural venous sinus thrombosis on apixaban presented due to syncope. KFD was diagnosed following the patient's presentation of fever, bilateral cervical lymphadenopathy, and

ACG Case Rep J 2024;11:e01455. doi:10.14309/crj.0000000000001455. Published online: August 30, 2024

Correspondence: Frank Lin, DO (Hanxiong.lin@sluhn.org).

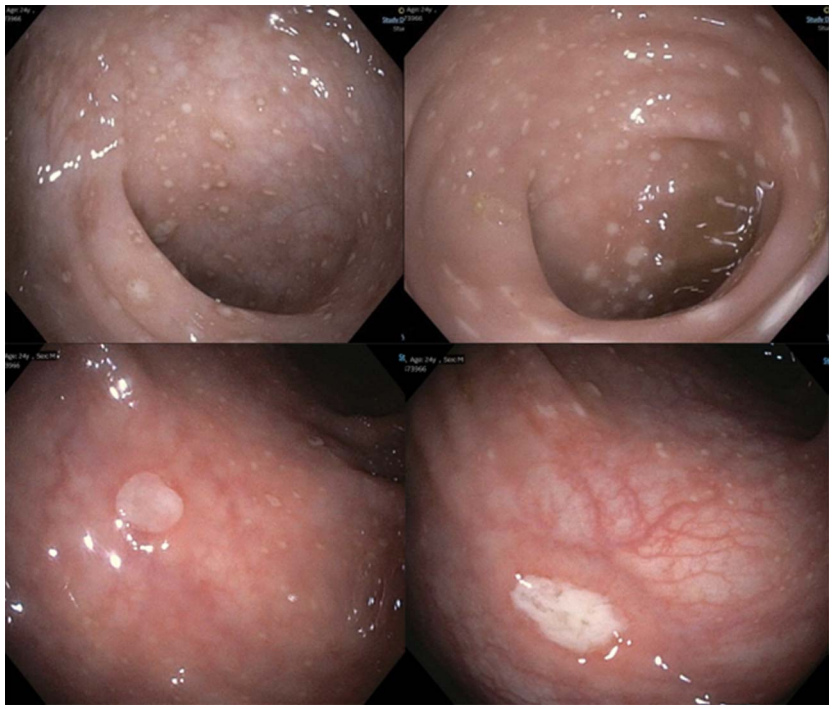

Figure 1. Numerous, discrete, small to large round ulcers throughout the colon and terminal ileum with no signs of bleeding.

leukopenia. An excisional biopsy of the right cervical lymph node, which is the gold standard for diagnosis, revealed necrotizing lymphadenitis with overall features compatible with histiocytic necrotizing lymphadenitis and no immunophenotypic evidence of a clonal B or T-cell population. The patient reported nonbloody vomiting, diarrhea, and blood in stools for 1 week, associated with mild lower abdominal pain and loss of appetite. He also reported recurrent oral ulcers. Physical examination revealed fever, tachycardia, and tenderness in the lower abdominal quadrant. Initial laboratory workup showed a hemoglobin level of 5.7 g/dL, platelets at 334,000/μL, and a white blood cell count of 19,000/μL with elevated bands. Elevated international normalized ratio and mildly increased aspartate aminotransferase and alanine aminotransferase were noted. Abdominal and pelvic computed tomography scan revealed multifocal high-density areas throughout the small and large bowel, suggesting acute hemorrhage and an incidental 3.7 cm lesion in the liver. Despite receiving 2 units of blood, the patient did not respond and hemoglobin further dropped to 4.8 g/dL. Consequently, the patient was admitted to the critical care unit, and an urgent consultation with the gastroenterology team was initiated. He received another 2 units of blood and underwent an urgent colonoscopy with flexible sigmoidoscopy and esophagogastroduodenoscopy with enteroscopy. Esophagogastroduodenoscopy showed no signs of bleeding and was only remarkable for a clean ulcer on the tongue. Colonoscopy showed numerous, discrete, small to large ulcers throughout the colon and terminal ileum with no signs of bleeding (Figure 1). Biopsy of terminal ileum showed no significant findings. Biopsy from the ileocecal valve and colon showed focal ulcer, cryptitis, and lymphoid aggregates with no granulomas (Figure 2). The pathology report noted that ulcers such as this one may be indicative of Behcet's disease. The liver lesion was evaluated by magnetic resonance cholangiopancreatography and was consistent with focal nodular hyperplasia. The patient was started on broad-spectrum antibiotics due to fever and elevated band count for concerns of bacteremia resulting from GI translocation associated with diffuse colonic ulcers and ganciclovir for concerns of hepatitis C virus or cytomegalovirus given its broader antiviral spectrum than acyclovir. Given oral and colonic ulcers, comprehensive workup for rheumatologic and infectious causes was performed. Infectious laboratory tests including herpes simplex virus, cytomegalovirus, HIV, cryptococcus, syphilis, and histoplasma were all negative. Antinuclear antibodies and rheumatoid factor were negative. The patient was restarted on apixaban and discharged with a stable hemoglobin to follow with rheumatology for further workup and was instructed to repeat magnetic resonance imaging in 6–12 months for the liver lesion.

DISCUSSION

Although the typical presentation of KFD involves fever, tender regional cervical lymphadenopathy, involvement of other lymph nodes, and night sweats, it can involve other systems, with the GI tract more rarely affected.[1,11] There has only been 1 other case of KFD manifesting as GI bleeding reported by Akgol Gur et al.[11] In contrast to the typical GI manifestations of KFD, our patient presented with severely ulcerated mucosa in the terminal ileum and throughout the colon with suspicion for Behcet's disease based on biopsy findings. In the setting of the patient's history of recurrent oral ulcers, suggestive biopsy

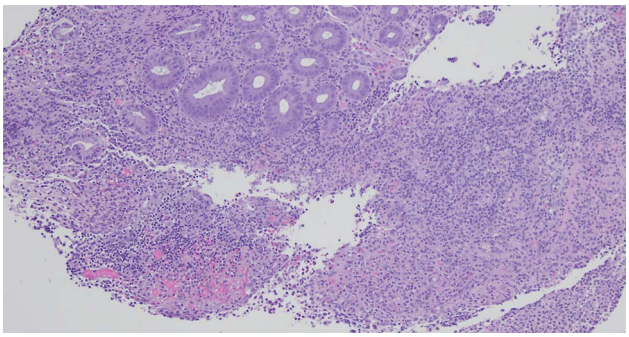

Figure 2. Ileocecal valve biopsy shows colonic mucosa with ulcer, granulation tissue, cryptitis, lamina propria expansion by mixed inflammation, and preserved crypt architecture. Magnification: 100×.

findings from the ileocecal valve, and venous thrombosis in the form of a dural venous sinus thrombosis, the diagnosis of Behcet's disease was made over alternative etiologies such as Crohn's disease.

With the patient's known history of KFD, autoimmune triggers, particularly Behcet's disease, were considered based on the biopsy results from the terminal ileum, ileocecal valve, and colon. The common autoimmune triggers can include systemic lupus erythematosus, rheumatoid arthritis, Still disease, Sjögren syndrome, and granulomatosis with polyangiitis.[15] Behcet's disease is a clinical diagnosis, and the typical presentation is recurrent tender ulcerations involving the oral mucosa and genitalia.[5] A prominent feature of Behcet's disease is an increased risk of venous thrombosis, with lower extremity venous thrombosis being the most frequent manifestation, followed by other vascular complications including vena cava thrombosis, abdominal aortic aneurysms, pulmonary artery aneurysms, peripheral artery aneurysms, Budd-Chiari syndrome, and dural venous sinus thrombosis.[16] Involvement of the ileocecal valve is classically seen with Behcet's disease; however, any part of the GI tract can be afflicted with mucosal inflammation and ulcer formation, a form of intestinal Behcet's disease known as neutrophilic phlebitis.[17] Distinguishing intestinal Behcet's disease from Crohn's disease can often be difficult, but a supportive finding for Behcet's disease in our patient was the presence of round-shaped and often focal ulcers on colonoscopy as opposed to longitudinal ulcers, which are more suggestive of Crohn's disease.[18]

The etiology of KFD remains unknown and multifaceted. Our patient's diffuse ulcerations throughout the colon may be explained by an autoimmune process such as vasculitis of the GI tract due to Behcet's disease.[17] Autoantibody positivity is not a diagnostic criterion seen in patients with Behcet's disease, with 1 study showing no difference in the rate of antinuclear antibody positivity between the control group and the Behcet's disease group.[19] Other possible triggers include environmental factors, particularly viruses, considered in our patient with unremarkable findings.

Treatment of the GI symptoms of Behcet's disease with active KFD may require high-dose corticosteroid therapy with immunomodulatory agents. The use of nonsteroidal anti-inflammatory medications is recommended for the alleviation of lymph node tenderness and fever of KFD, and most symptoms improve within a few months. Possibility of effectiveness of chloroquine and hydroxychloroquine in treating recurrent disease has been demonstrated in seldom case reports.[20,21] Our patient did not require these interventions as KFD was in its inactive stage.

DISCLOSURES

Author contributions: F. Lin, A. Obeid, H.J. Bhalala, N. Patel, and R. Modi: concept and design, acquisition, analysis, or interpretation of data, drafting of the manuscript, critical review of the manuscript for important intellectual content. L. Ge: pathology slide and description. F. Lin is the article guarantor.

Financial disclosure: None to report.

Informed consent was obtained for this case report.

Received May 14, 2024; Accepted June 28, 2024

REFERENCES

1. Bosch X, Guilabert A. Kikuchi-Fujimoto disease. *Orphanet J Rare Dis.* 2006;1:18.
2. Bosch X, Guilabert A, Miquel R, Campo E. Enigmatic Kikuchi-Fujimoto disease: A comprehensive review. *Am J Clin Pathol.* 2004;122(1):141–52.
3. Perry AM, Choi SM. Kikuchi-Fujimoto disease: A review. *Arch Pathol Lab Med.* 2018;142(11):1341–6.
4. Joean O, Thiele T, Raap M, Schmidt RE, Stoll M. Take a second look: It's Kikuchi's disease! A case report and review of literature. *Clin Pract.* 2018;8(4):1095.
5. Alpsoy E, Zouboulis CC, Ehrlich GE. Mucocutaneous lesions of Behcet's disease. *Yonsei Med J.* 2007;48(4):573–85.
6. Kuo TT. Cutaneous manifestation of Kikuchi's histiocytic necrotizing lymphadenitis. *Am J Surg Pathol.* 1990;14(9):872–6.
7. Al-Roubaie A, Uthuman A, Aldujaili T, Asadi K, Alabbood M. Kikuchi's disease diagnosed by an excisional biopsy in a patient with COVID-19. *Cureus.* 2023;15(2):e35251.
8. Lencastre Monteiro R, Cabaço S, Soares L, Inácio H, Nazário Leão R. Kikuchi-Fujimoto disease: A case of SARS-CoV-2 infection triggering the rare disease. *Cureus.* 2023;15(3):e35858.
9. Hamamoto Y, Kawamura M, Mori H, et al. Kikuchi disease after SARS-CoV-2 vaccination: A case report with immunohistochemical analyses. *Int J Surg Pathol.* 2023:10668969231212428.
10. Craig JW, Farinha P, Jiang A, Lytle A, Skinnider B, Slack GW. Kikuchi-Fujimoto disease following COVID-19 vaccination: Experience at a population-based referral center. *Am J Clin Pathol.* 2023;160(2):114–8.
11. Akgol Gur ST, Tahiroğlu AL, Kocak AO. Mortal complication of Kikuchi–Fujimoto disease; lower gastrointestinal bleeding, case presentation and literature review. *J Emerg Med Case Rep.* 2023;14(1):16–7.
12. Kim JH, Yoon MY, Kim W, Young An J. Kikuchi-Fujimoto disease associated with neuro-Behçet's disease. *Clin Neurol Neurosurg.* 2021;202:106541.
13. Hua CZ, Chen YK, Chen SZ, Gu WZ, Shu Q. Histiocytic necrotizing lymphadenitis mimicking acute appendicitis in a child: A case report. *Front Pediatr.* 2021;9:682738.
14. Shrestha A, Newton K, Benbow E, Kushwaha R. Kikuchi-Fujimoto disease of mesenteric lymph nodes mimicking acute appendicitis. *JNMA J Nepal Med Assoc.* 2013;52:627–30.

15. Al-Allaf A-W, Yahia YM. Kikuchi-Fujimoto disease associated with Sjögren's syndrome: A case report. *Eur J Case Rep Intern Med.* 2018;5(5): 000856.
16. Seyahi E, Yurdakul S. Behçet's syndrome and thrombosis. *Mediterr J Hematol Infect Dis.* 2011;3(1):e2011026.
17. Hokama A, Kishimoto K, Ihama Y, et al. Endoscopic and radiographic features of gastrointestinal involvement in vasculitis. *World J Gastrointest Endosc.* 2012;4(3):50–6.
18. Lee S, Kim BK, Kim TI, Kim WH. Differential diagnosis of intestinal Behçet's disease and Crohn's disease by colonoscopic findings. *Endoscopy.* 2009;41(1):9–16.
19. Ilhan F, Aksoy R, Tutkak H. Are the specific and nonspecific ANA staining patterns of Behçet's disease patients important? *Reumatol Clin (Engl Ed).* 2022;18(3):147–9.
20. Honda F, Tsuboi H, Toko H, et al. Recurrent Kikuchi-Fujimoto disease successfully treated by the concomitant use of hydroxychloroquine and corticosteroids. *Intern Med.* 2017;56(24):3373–7.
21. Hyun M, So IT, Kim HA, Jung H, Ryu SY. Recurrent Kikuchi's disease treated by hydroxychloroquine. *Infect Chemother.* 2016;48(2):127–31.