SM Journal of Gastroenterology & Hepatology

Case Report

Reimagining Old Party Tricks: A Previously Unreported Successful Combination Treatment Regime for a Rare Case of Recalcitrant Gut and Cutaneous Sweet Syndrome

Kalaiyarasi Kaliyaperumal[1*], Hua Yen Ling[1], Rebecca Tian Mei Au[2], Cora Yuk Ping Chau[2], Wee Chian Lim[1] and Charles Kien Fong Vu[1]

[1]Division of Hepatology and Gastroenterology, Tan Tock Seng Hospital, 11 Jln Tan Tock Seng, 308433, Singapore

[2]Division of Pathology, Tan Tock Seng Hospital, 11 Jln Tan Tock Seng, 308433, Singapore

Abstract

Background: We report a rare case of a 50 year old Chinese female with cutaneous Sweet Syndrome (SS) presenting with iron deficiency anaemia who was subsequently found to have small bowel ulcers with a dense neutrophilic infiltrate on histology, with no evidence of Inflammatory Bowel Disease (IBD).

Case presentation: The 50 year old lady underwent an extensive workup including enteroscopy, blood investigations and exclusion of pertinent differentials, she was diagnosed with gut SS. After trying and failing various treatment modalities, she was successfully treated with a combination of subcutaneous adalimumab and oral Methotrexate (MTX). Gut SS is an extremely rare disease with only 2 published cases thus far and both were treated with mainly steroids. To our knowledge, this is the first reported case of this treatment combination of an anti TNF agent and MTX for recalcitrant gut and cutaneous SS.

Conclusion: A diagnosis of gut SS should be considered in the presence of gastrointestinal pathology such as ulcers, especially if histological features of inflammatory bowel disease are absent. In recalcitrant cases anti-TNF (tumor necrosis factor) agents may be an alternative treatment option.

Keywords: Case report; Sweet syndrome; Bleeding gastrointestinal tract; Iron deficiency anemia; Intestinal ulcers.

Introduction

We report a rare case of a patient with cutaneous Sweet Syndrome (SS) presenting with iron deficiency anaemia. On further investigations, she had small bowel ulcers with a dense neutrophilic infiltrate on histology.

Case Presentation

A 50-year-old post-menopausal Chinese female with a 6-year history of cutaneous SS with symptomatic iron deficiency anaemia was referred to the Gastroenterology clinic. The Haemoglobin (Hb) was 8.4 g/dL and ferritin 5 µg/L. Her cutaneous SS was well controlled with colchicine and prednisolone 15mg daily. Her other medications included omeprazole, calcium/vitamin D and iron polymaltose tablets. She did not have any NSAIDs (non steroidal anti inflammatory drugs) usage.

Gastroscopy and colonoscopy revealed presence of superficial clean based Terminal Ileal (TI) ulcers. Histology showed dense neutrophil infiltrates with preserved villi and crypt morphology. There was no histological evidence of Crohn's disease or vasculitis as reported by a pathologist. Infection screen was negative for Cytomegalovirus (CMV) PCR (polymerase chain reaction) and AFB (acid fast bacillus) smear and culture. Video Capsule Endoscopy (VCE) showed presence of more ulcers in the mid ileum as well. Retrograde motorised spiral enteroscopy was performed, which showed deeper ulcers in the mid ileum (Figure 1A) with similar findings on histology (Figures 1B,C) to the previously detected TI ulcers . A full malignancy screen in the form of Computed Tomography (CT) scans and blood works were negative. Bone marrow examination further confirmed iron deficiency with adequate marrow function and stores.

The constellation of the iron deficiency anaemia in known SS and small bowel ulcers without features of IBD raised suspicion for gut SS. She was started on Azathioprine (AZT) 25mg and prednisolone 30mg daily with the former titrated up to a weight-based dose of 100mg. The retrograde motorised spiral enteroscopy was repeated after 6 months of AZT, which showed persistent mid ileal ulcers (Figure 2). The histology again showed acute ulceration with neutrophil predominance. The Hb then was 8.1 g/dL, ferritin 11 µg/L and stool calprotectin was >1000 µg/g.

In view of the absence of mucosal and clinical remission as well as significant abdominal symptoms on AZT, the latter was stopped. She was started on MTX of 10mg/week and continued on oral prednisolone 15mg daily. She presented to Emergency Department 3 weeks later with a 3 day history of melaena and palpitations. The Hb was 9.5 g/dL. VCE showed terminal ileitis with multiple clean based ulcers but there was no active bleeding. She was managed conservatively and continued on the same doses of MTX and prednisolone.

MTX was gradually increased to 25mg/week over 6 months with gradual tapering of prednisolone to 4mg daily. During this time, she also completed a course of isoniazid for latent tuberculosis infection as TB-QuantiFERON (Qiagen,USA) was positive.

However, she remained persistently symptomatic with lethargy, abdominal pain and weight loss despite the MTX and prednisolone. The

Submitted: 12 June, 2024 | **Accepted:** 25 June, 2024 | **Published:** 27 June, 2024

***Corresponding author(s):** Kalaiyarasi Kaliyaperumal, Division of Hepatology and Gastroenterology, Tan Tock Seng Hospital, 11 Jln Tan Tock Seng 308433, Singapore, Tel: +65 91859006

Citation: Kaliyaperumal K, Ling HY, Au RTM, Chau CYP, Lim WC, et al. (2024) Reimagining Old Party Tricks: A Previously Unreported Successful Combination Treatment Regime for a Rare Case of Recalcitrant Gut and Cutaneous Sweet Syndrome. SM J Gastroenterol Hepatol 6: 5.

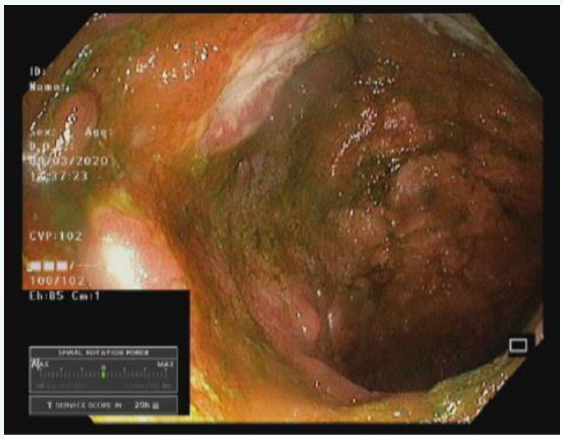

Figure 1A: Index spiral enteroscope showed deep mid ileal ulcers (arrows).

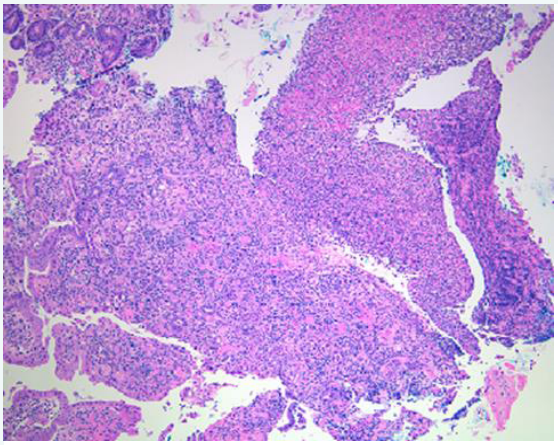

Figure 1B

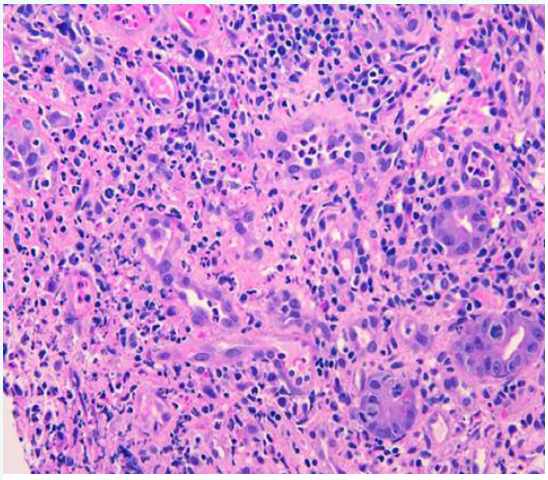

Figure 1C: Histology of the ileal ulcer biopsy showed dense neutrophilic infiltrates: hematoxylin and eosin (H&E) stain 10x magnification (Figure 1B) and 40x magnification (Figure 1C).

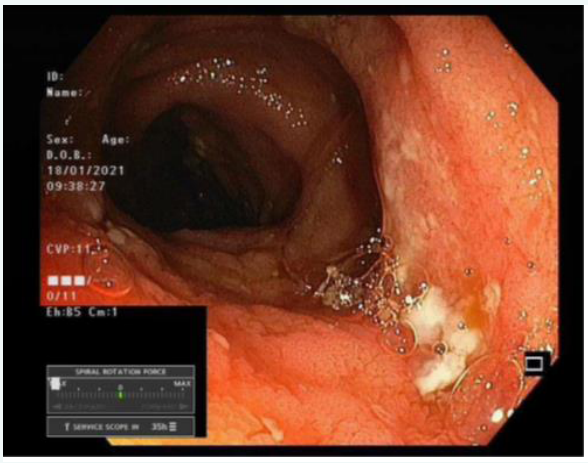

Figure 2: Spiral enteroscopy showed persistence of mid ileal ulcers (arrows) 6 months after AZT therapy.

Hb was 7.0g/dL, ferritin 11 µg/L and stool calprotectin of 190 µg/g. Repeat Retrograde double balloon enteroscopy revealed persistent deep and superficial ulcers at the mid ileum. Biopsies of all these lesions again showed acute inflammation without features of chronicity.

As she was not responding to corticosteroids and immunomodulators, we decided to start her on a combination of Anti- Tumour Necrosis Factor (TNF) agent with MTX.

An induction dose of 80mg adalimumab was given followed by 40mg every 2 weeks. MTX was continued at 10mg/week to reduce formation of anti-TNF antibodies. She tolerated adalimumab well. The MTX and oral prednisolone was gradually reduced to 10mg weekly and 5mg daily respectively. 6 weeks after treatment, the Hb increased to 12.8 g/dL, ferritin to 26 µg/L and stool calprotectin was 53 µg/g.

The repeat double balloon enteroscopy five months after adalimumab/MTX/prednisolone combination therapy showed complete healing of the mid and terminal ileal ulcers with occasional reactive lymphoid follicles and pseudopolyps seen (Figure 3A). Biopsies revealed non-specific regenerative changes on histology, with much reduced neutrophil infiltrate compared to previously (Figures 3B,C). Clinically, she was in remission with no abdominal pain, improved appetite with weight gain and less fatigue. The cutaneous lesions were also quiescent.

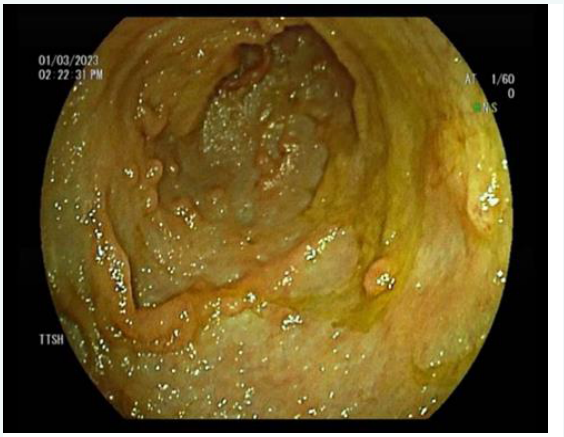

Figure 3A: Double balloon enteroscopy showed complete healing of the ileal ulcers with occasional reactive lymphoid follicles and pseudopolyps seen (6 months after adalimumab/MTX combination treatment).

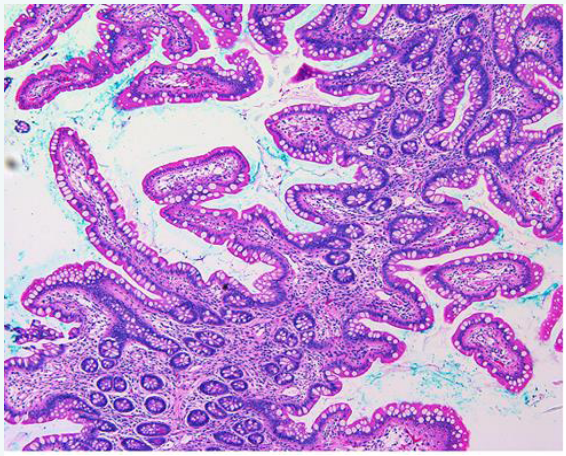

Figure 3B:

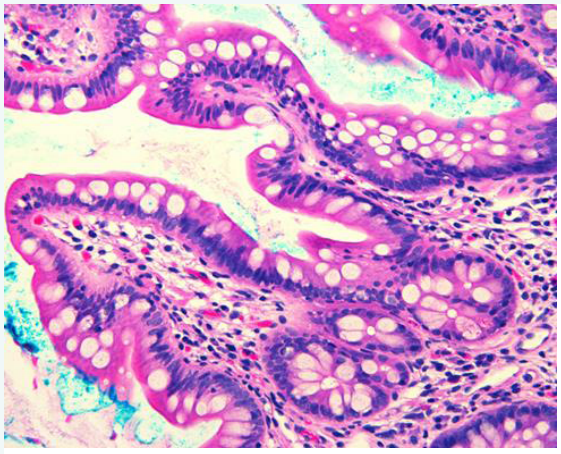

Figure 3C: Mid ileal biopsies showed non-specific regenerative changes with much reduced neutrophil infiltrates, hematoxylin and eosin (H&E) stain at 10x magnification (Figure 3B) and 40x magnification (Figure 3C).

Discussion

SS was first described by Dr Robert Douglas Sweet in 1964; a syndrome consisting of acute onset of fever, leucocytosis and painful oedematous plaques in middle-aged women for which histology showed dermal neutrophilic infiltrates [1]. Since then, there has been a diagnostic criteria proposed by Su and Liu in 1986 which included major criteria of cutaneous plaque and histopathology consistent with SS; minor criteria of leucocytosis, fever and constitutional symptoms, association with malignancy, inflammatory disorders and excellent response to systemic corticosteroids [1].

Over the years, as our understanding of SS expanded considerably, various clinical and histological subtypes of SS have emerged. Clinically, it can be categorised into inflammatory (idiopathic), malignancy associated, and drug- induced [2]. The association of SS with IBD, especially Crohn's disease has been reported and it is the 3rd most common association after malignancies and infections [3]. SS can manifest prior, concurrently or following the diagnosis of IBD [3].

Thus far there have been only 2 published case reports in literature on adult gut SS in the form of oesophageal, duodenal, and colon ulcers occurring with cutaneous SS, that did not fulfil diagnostic criteria for IBD [4,5]. One patient responded well to a 10-day course of prednisolone while the other, required prednisolone, dapsone and sulfasalazine therapy.

This previously unreported treatment regime that we started our patient on, is based on extrapolation of data from previously published case reports of recalcitrant cutaneous SS as well as cutaneous SS and IBD, that were successfully treated with anti-TNF agents, namely infliximab and adalimumab [6-8]. Also drawing from our experience in treating IBD patients, MTX was included in this regime to reduce immunogenicity [9].We were then successful at achieving both clinical and endoscopic remission and reducing steroid dependence. To our knowledge, this is the first reported case of such a combination therapeutic regime for gut and cutaneous SS.

Conclusion

This case presents both a diagnostic and therapeutic challenge in the management of a very rare condition, in which conventional immunosuppressive agents were unsuccessful. Endoscopy including small bowel evaluation should be offered to all patients with iron deficiency anaemia in known cutaneous SS, both for exclusion of gastrointestinal malignancies as well as exclusion of IBD. A diagnosis of gut SS should be considered in the presence of gastrointestinal pathology such as ulcers, especially if histological features of IBD are absent. In recalcitrant cases anti-TNF agents may be an alternative treatment option.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Acknowledgement

Our patient.

Competing Interests

The authors declare that they have no competing interests.

Funding

None to declare.

Author's Contributions

K.K: Conceptualization, Investigation, Methodology, Resources, Visualization, Writing – original draft.

H.Y.L: Writing – original draft.

R.T.M.A: Investigation, Resources.

C.Y.P.C: Investigation, Resources.

W.C.L: Resources, Writing – review & editing.

C.K.F.V: Investigation, Methodology, Resources, Writing – review & editing.

References

1. Weiss EH, Ko CJ, Leung TH, Micheletti RG, Mostaghimi A, Ramachandran SM, et al. Neutrophilic dermatoses: A clinical update. Curr Dermatol Rep. 2022; 11: 89-102.
2. Cohen PR. Sweet's syndrome-a comprehensive review of an acute febrile neutrophilic dermatosis. Orphanet J Rare Dis. 2007; 2: 34.
3. Joshi TP, Friske SK, Hsiou DA, Duvic M. New practical aspects of sweet syndrome. Am J Clin Dermatol. 2022; 23: 301-318.
4. Evans AV, Sabroe RA, Setterfield J, Greaves MW. Erythema elevatum diutinum/sweet's syndrome overlap with gastrointestinal and oral involvement. Br J Dermatol. 1999; 141: 766-767.
5. Yuchi H, Yamaga J, Ishikawa N, Aoki T, Sakata J, Eto T. Endoscopic appearance of the GI lesions associated with Sweet's syndrome. Gastrointest Endosc. 2000; 52: 287-289.
6. Agarwal A, Barrow W, Selim MA, Nicholas MW. Refractory subcutaneous sweet syndrome treated with adalimumab. JAMA Dermatol. 2016; 152: 842-844.
7. Calabrese L, Caldarola G, Peris K, De Simone C. Recalcitrant sweet syndrome successfully treated with adalimumab. J Dtsch Dermatol Ges. 2021; 19: 122-124.
8. Knöpfel N, Theiler M, Luchsinger I, Hafner B, Brunner C, Kolm I, et al. Infliximab for the treatment of recalcitrant bullous sweet syndrome in a 10-year-old girl. Pediatr Dermatol. 2020; 37: 1183-1184.
9. Jani M, Barton A, Warren RB, Griffiths CE, Chinoy H. The role of DMARDs in reducing the immunogenicity of TNF inhibitors in chronic inflammatory diseases. Rheumatology (Oxford). 2014; 53: 213-222.