Japanese Journal of Gastroenterology and Hepatology

Case Report ISSN: 2435-1210 | Volume 8

Sweet's Syndrome in A Patient with Myelofibrosis On Ruxolitinib

Haolumei and Yuping Zhong*

Department of Hematology, Qingdao Municipal Hospital, School of Medicine, Qingdao University, Qingdao, China

***Corresponding author:**

Yuping Zhong,
Department of Hematology,
Qingdao Municipal Hospital, School of Medicine,
Qingdao University, Qingdao, China,
E-mail: zhongyp3352@126.com

Received: 04 Mar 2022
Accepted: 19 Mar 2022
Published: 24 Mar 2022
J Short Name: JJGH

Citation:

Yuping Zhong, Sweet's Syndrome in A Patient with Myelofibrosis On Ruxolitinib. J Gstro Hepato.. V8(11): 1-4

Keywords:

Sweet syndrome; Myelofibrosis; Ruxolitinib

1. Abstract

Sweet's syndrome(SS), also known as acute neutrophilic dermatosis, is characterized by fever, tender erythematous skin lesions, neutrophilia, high levels of serum inflammatory markers, and diffuse mature neutrophil in the dermis [1]. It could be associated with malignancy, especially hematologic malignancy [2]. Some drugs used in hematology may also induce SS. We herein report a case of post-et MF developed SS on treatment of ruxolitinib. there seems to be some relationship between ruxolitinib and the SS.

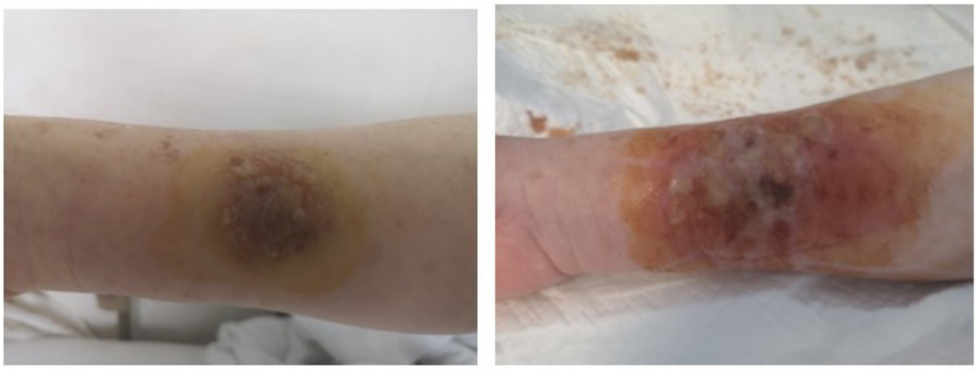
2. Introduction

Sweet's syndrome (SS), is a rare inflammatory condition classically presenting with abrupt onset of high fever and tender erythematous papules, nodules and plaques, with characteristic rapid response to corticosteroid therapy [3]. Ruxolitinib, a Janus kinase inhibitor approved for the treatment of high-risk MF, has been broadly used recently. We herein reported a case of post-ET-MF on ruxolitinib treatment for ten weeks, abruptly developed myalgia in his right lower extremity followed by high fever and tender erythematous plaques on his head and forearm. His clinical condition deteriorated on the treatment with broad spectrum antibiotics. And resolved quickly after withdrawing ruxolitinib and initiating the corticosteroid treatment.

3. Case Report

A 78-year-old man with a 5-year history of ET was admitted in our hospital. He complained ongoing fatigue and weakness, poor appetite and night sweats. Physical examination revealed pallor and splenomegaly. a complete blood count showed heavy anemia (HGB 45g/L), slightly thrombocytosis ,leukocyte was in normal range. Leukocyte differentiation showed blast 1%; myelocyte7 %; metamyelocyte 9%; and nucleated red blood cell 2%/100 white blood cells. bone marrow biopsy showed myelofibrosis with MF-grade 2. Jak-2V617F mutation was positive. An abdominal ultrasound revealed the splenomegaly which was 17cm in the longest dimension. He was diagnosed with post-et MF with high-risk according to the International Prognostic Scoring System (IPSS 4) [4], and dynamic IPSS plus 4 [5]. He was treated with ruxolitinib on a dose of 15mg twice daily for his splenomegaly and constitutional symptoms. His spleen reduced 2cm in the longest diameter after 6 weeks on ruxolitinib treatment. His appetite and night sweats also improved. But he was still dependent on red blood cell transfusion about 2u per month. Ten weeks after initiating RUX he suddenly suffered a pain in the posterior of his right lower extremity. Physical examination found nothing except for a local tenderness in gastrocnemius. Ultrasonography of blood vessels in both lower extremities was normal. Loxonin was given to release his pain. Two days later he experienced a fever of 38.3℃ accompanied with Swelling of the right lower extremity. The myalgia progressed gradually with hyper myotonia and heavy tenderness。Repeated ultrasonography showed gastrocnemius intermuscular vein thrombosis in the right lower extremity. The blood test showed WBC $5.2*10^9$/l, HGB78g/l, PLT$327*10^9$/l. Leukocyte differentiation showed blast 3-4%; C-reactive protein (CRP) was 62.98mg/l (normal range:0-5 mg/l) and procalcitonin (PCT) was normal. Considering the potent susceptibility to infection in patients with myelofibrosis itself and with treatment on ruxolitinib, Ceftazidime sulbactam and vancomycin was given. In the next two days He developed several tender erythematous plaques and nodules with blisters and pustules on his head and right forearm with high fever. Myalgia and swelling in the right lower extremity continued to progress. The MRI scan of the right lower extremity showed edema of the right posterior calf muscles group and subcutaneous soft tissues. His CRP was 152.53mg/l with

PCT still in normal range. The tissue fluid and blood culture were negative. The CT-scan of the chest showed bilateral ground-glass opacities in the lower lobes and interstitial thickening. Considering that the sepsis emboli can't be completely excluded, we upgraded the antibiotics with meropenem**,** linezolid and daptomycin. Ruxolitinib was tapered down to 10mg twice daily but not stopped to avoid its withdrawal symptoms [6]. Unfortunately, his condition continued to deteriorate despite of broad-spectrum antibiotic treatment. The highest temperature was up to 39.8℃ and the painful skin lesions on his head and right forearm extended quickly with ulcerations. His CRP rise up to 269.13mg/l. He experienced cough and dyspnea and weakness. The repeated pulmonary CT-scan showed bilateral pleural effusion and bilateral ground-glass opacities and interstitial thickening. We consulted again with the dermatologist for the quickly progressed skin lesions three days later, and a diagnosis of sweet syndrome was suspected. A skin biopsy was performed by the dermatologist. At the same time, we initiated 30mg/d prednisolone. his fever and skin lesions were controlled in the next two days along with the CRP down to 94.63mg/l. within that time his sputum culture showed candida tropocalis. we initiated voriconazole to cover fungal infection. After two dose of voriconazole, he was febrile to 39.7℃ with the skin lesions deteriorated again, CRP rose up again to 228.66mg/l. And besides the pain in his right lower extremity, he suffered same pain in his left lower extremity. Bedside ultrasonography showed same change as the right lower extremity. The skin biopsy showed edema of the dermal papillae with diffuse mature neutrophil infiltration within the dermis and subcutaneous adipose tissue. The diagnosis of sweet syndrome was confirmed. With a doubt of ruxolitinib inducing the SS, we withdrew ruxolitinib totally, and gave him prednisolone at a dose of 30mg twice daily. which resulted in rapid resolution of fever and pain of the both lower extremities. The tender skin lesions improved quickly along with local debridement and dressing change. His CRP level decreased to near normal range within the next 3 days, and he experienced rapid improvement in his pulmonary symptoms too. We soon withdrew all the antibiotics except voriconazole along with the prednisolone tapered down gradually. Follow-up two months after discharge demonstrated complete resolution of the skin lesions and stable condition with transfusion of RBC about 2u per month alone.



Photograph of the right forearm: A. erythematous plaques with blisters and pustules on his right forearm. B. The skin lesion progressed three days later.

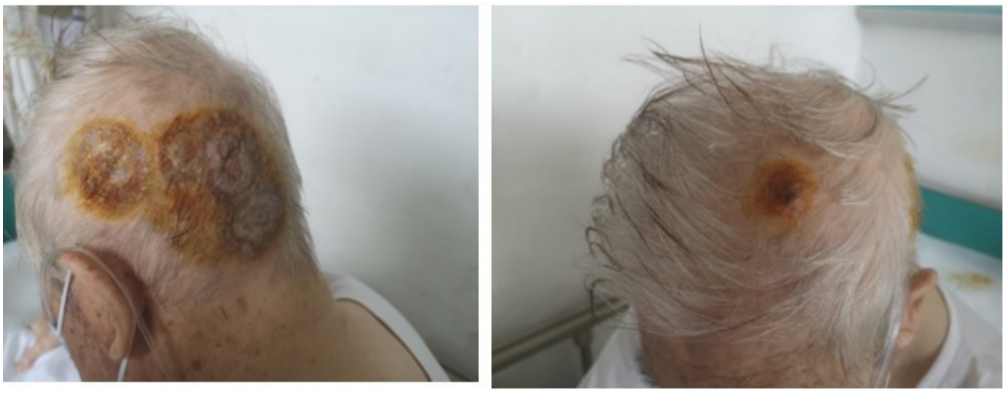
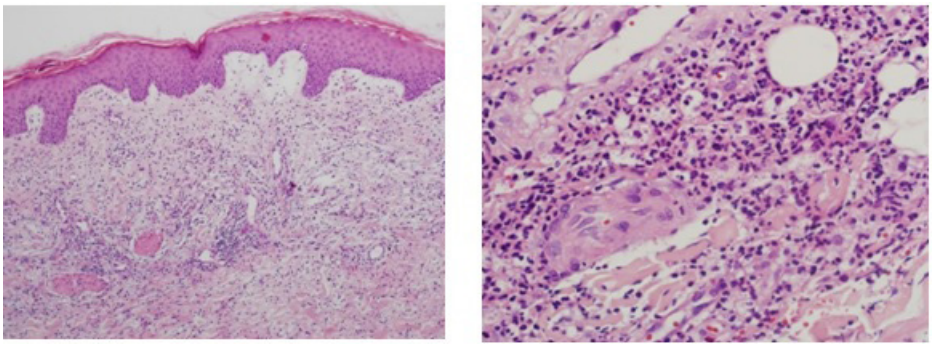


Figure C, D: Erythematous plaques and nodules on his head.



Figures E, F: Skin biopsy showed edema of the dermal papillae with diffuse mature neutrophil infiltration within the dermis and subcutaneous adipose tissue.

4. Discussion

Sweet's syndrome (SS), is a rare inflammatory condition classically presenting with abrupt onset of tender erythematous papules, nodules and plaques often with a pseudovesicular or psuedopustular appearance, with characteristic rapid response to corticosteroid therapy [1]. The tender skin lesions mostly occur on the face, neck, trunk and upper extremities [7]. Besides skin lesions, many extracutaneous manifestations have been reported including involvement with the eyes, neuro-muscular system, internal organs and musculoskeletal system. Myositis, fasciitis, and myalgias are seen in 50% of cases [1]. In our case, the patient suffered a local myalgia with edema in the right lower extremity at the beginning, which progressed gradually during the whole clinical courses and resolved dramatically after initiating oral corticosteroids treatment in the end. That led us to believe the myalgia an extracutaneous manifestation of SS in this patient. Pulmonary involvement in SS have also been reported. Dyspnea and dry cough are common symptoms of pulmonary involving SS, which typically present concomitantly with cutaneous lesions. Chest CT often shows diffuse unilateral or bilateral interstitial infiltrates with pulmonary ground glass opacities and pleural effusions [8]. In our case, the pulmonary CT scan showed bilateral pleural effusion and bilateral ground-glass opacities and interstitial thickening with little improvement on broad-spectrum antibiotic management, but resolved quickly after initiating corticosteroids. Although pulmonary infections can't be completely ruled out, pulmonary involvement of Sweet's syndrome should be considered in differential diagnosis. The most common laboratory abnormalities in patients with SS are neutrophilic leukocytosis and elevated erythrocyte sedimentation rate and C-reactive protein [1]. However, without neutrophilia can't be ruled out SS especially in patient with hematologic malignances [9], just like the case in our report. We also found c-reactive protein a sensitive laboratory index paralleled well to the progression of SS. SS can be clinically divided into three subtypes: classical, malignancy-associated and drug-induced [10]. About 85% of cases of malignancy-associated Sweet's had underlying hemopoietic neoplasia, most commonly acute myeloblastic leukemia, myelodysplastic syndrome and myeloproliferative neoplasmas [1]. In our case, considering the increasing of blasts in the blood smear at the moment of the SS onsetting, the possibility that SS was caused by the post-et MF itself could not be ruled out, although ruxolitinib had improved the patient's clinical status already. However, the use of ruxolitinib also seemed to be connected with SS. Sakoda T et.al reported a case of post-et mf developed recurrent of SSD after treatment with ruxolitnib for 7 weeks, and speculated that JAK1/2 inhibition could cause a dynamic change in the intricate cytokine network which may have some relationship with the pathogenesis of SS [11]. Chatterjee B et.al also reported a case of MF developed with SS after stopping ruxolitinib for two weeks due to loss of response [12]. In our case, since we initiating 30mg prednisolone per day for suspecting SS, the patient's fever and skin lesions had been ever controlled for two days. then his condition worsened again after voriconazole being added to control fungal infection. Voriconazole as a strong CYP3A4 inhibitor coadministration with ruxolitinib may increase the serum level of the ruxolitinib when coadministration with ruxolitinib. and this may explain the above recurrence episode. After stopping ruxolitinib and increasing prednisolone to 60 mg per day his all symptoms soon got resolved and with no recurrence during more than two 2 months 's follow up till now. Based on this we thought that ruxolitinib may have a role in the onset of SS.

5. Conclusion

Although SS is a rare condition, it could be associated with hematologic malignancies and some certain target drugs. It is important for hematologists to suspect a diagnosis of SS especially in cases with skin lesions and high fever with little response to sufficient antibiotic treatment.

References

1. Paydas S. Sweet's syndrome: A revisit for hematologists and oncologists. Critical Reviews in Oncology/Hematology. 2013; 85-95.
2. Rochet NM, Chavan RN , Cappel MA. Sweet syndrome: Clinical presentation, associations, and response to treatment in 77 patients . J Am Acad Dermatol 2013; 69: 557 - 64 .
3. Raza S, Kirkland RS, Patel AA. Insight into sweet's syndrome and associated-malignancy: a review of the current literature. Int J Oncol. 2013; 42: 1516-22.
4. Cervantes F, Dupriez B, Pereira A. New prognostic scoring system for

primary myelofibrosis based on a study of the International Working Group for Myelofibrosis Research and Treatment. Blood 113: 2895-2901, . 2009.

5. Gangat N, Caramazza D, Vaidya R. DIPSS plus: a refined Dynamic International Prognostic Scoring System for primary myelofibrosis that incorporates prognostic information from karyotype, platelet count, and transfusion status. J Clin Oncol. 2011; 29: 392- 397.
6. Tefferi A, Pardanani A. Serious adverse events during ruxolitinib treatment discontinuation in patients with myelofibrosis. Mayo Clin Proc. 2011; 86: 1188-1191.
7. Herbert-Cohen D, Jour G, Saul T. Sweet's syndrome. J Emerg Med. 2015; 49(3): e95-7.
8. Mehrtens SH, Hasan ZU, Halpern SM. McLornan DP. Sweet's syndrome with pulmonary involvement. BMJ Case Rep. 2019;12: e229997.
9. Paudel A, Dhital R , Areoye G. Sweet's syndrome in a granulocytopenic patient with acute myeloid leukemia on FLT3 inhibitor Journal of Community Hospital Internal Medicine Perspectives. 2020; 275-278.
10. Nelson CA, Stephen S, Ashchyan HJet al. Neutrophilic dermatoses: pathogenesis, sweet syndrome, neutrophilic eccrine hidradenitis, and behcet disease. J Am Acad Dermatol. 2018; 79: 987-1006.
11. Sakoda T, Kanamitsu Y, Mori Y. Recurrent subcutaneous sweet's disease in a myelofibrosis patient treated with ruxolitinib before allogeneic stem cell transplantation. Intern Med. 2017; 56: 2481-5.
12. Chatterjee B, Rqieh U, Greaves P. Sweet syndrome as terminal event in ruxolitinib-treated myelofibrosis. Br J Haematol. 2015; 169: 307.