Granulocyte Colony Stimulating Factor Induced Sweet's Syndrome Following Autologous Transplantation in a Child with Relapsed Acute Myeloblastic Leukemia

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Abstract Sweet's syndrome is characterized by the triad of fever, erythematous skin lesions and neutrophilia. The etiologic factors are quite variable, and granulocyte colony-stimulating factor (G-CSF) use is an extremely rare cause in children with Sweet's syndrome. We report a G-CSF induced Sweet's syndrome following autologous transplantation in a child with relapsed acute myeloblastic leukemia.

Keywords Sweet's syndrome · G-CSF · Leukemia · Transplantation

Introduction

Sweet's syndrome, also known as acute febrile neutrophilic dermatosis, is characterized by fever, tender or painful erythematous skin plaques or nodules, and leukocytosis with neutrophilia that typically show neutrophilic dermal infiltrations in histopathology [1]. This syndrome often occurs in association with malignancies, inflammatory diseases or drugs but an idiopathic (classical) form also exists, usually in adult women [1, 2]. Granulocyte colony-stimulating factor (G-CSF) induced Sweet's syndrome has been reported to date in only two children, one with glycogen storage disease type Ib and the other with aplastic

anemia [3, 4]. Herein we report a G-CSF induced Sweet's syndrome following autologous stem cell transplantation (SCT) in a 15 years old boy with relapsed acute myeloblastic leukemia (AML).

Case Report

The case underwent autologous SCT with G-CSF mobilization (15 µg/kg/day) that yielded a maximum CD34+ count of 1.5×10^6 cells/kg. On day +10, he developed fever and severe neutropenia not responding to broad-spectrum antibiotics and G-CSF therapy. Time to neutrophil and platelet engraftment were 14 and 25 days, respectively. The white blood cell count (WBC) increased to $1,500/\text{mm}^3$, absolute neutrophil count to $1,300/\text{mm}^3$, and erythrocyte sedimentation rate to 40 mm/h prior to the onset of the skin eruption. The results of viral screen blood, urine, throat and catheter cultures were all negative. Papular skin lesions appeared on head, neck and trunk on day 16 of G-CSF treatment (Fig. 1a). Skin biopsy revealed mature neutrophilic infiltrate consistent with Sweet's syndrome. Bone marrow aspiration on day 21 revealed a reactive regenerative phase. On day 24, methylprednisolone (2 mg/kg/day) was commenced as he met the criteria of Sweet's syndrome including fever, typical skin lesions and histopathologic findings (Fig. 1b). G-CSF was stopped on day 21. Fever and skin findings gradually resolved over 6 weeks of steroid therapy and cessation of G-CSF. He has been well without any signs of recurrence for 24 months follow up period after SCT.

Discussion

In a comprehensive review of Sweet's syndrome in children and adolescents by Hospach et al. [5] in 37

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Fig. 1 **a** Papular skin lesions on head, neck and trunk in patient. **b** Dense infiltrate of mature neutrophils in the *upper half* of the dermis (HE, $\times 200$)

malignancies and drugs account for 58 and 8 % of reported cases, respectively. Because AML and G-CSF are both common causes of Sweet's syndrome, it can be difficult to distinguish which one is responsible for Sweet's syndrome. Our patient was in complete remission and symptoms of Sweet's syndrome emerged during G-CSF administration following SCT. Literature review revealed only one case of Sweet's syndrome after SCT in a child with AML. This patient developed systemic inflammatory response syndrome associated with Sweet's syndrome ~6 months after autologous transplantation and responded well to steroid therapy [6]. As this reported patient had recurrent Sweet's syndrome and was diagnosed to have myelodysplastic syndrome, the authors think that Sweet's syndrome may be attributed to some degree of malignancy activity rather than G-CSF use. Although recurrence of skin lesions is more common and the course is usually more serious in AML, it was not seen in our patient during a 2-year follow-up period [7].

The clinical picture was also different in our case; unlike an isolated large erythematous painful plaque on leg in a reported case, our patient had multiple erythematous

papular lesions scattered on the head, neck and trunk which is a rare presentation of Sweet's syndrome [8].

The minor diagnostic criteria for classical Sweet's syndrome are leukocytosis ($>8,000/\text{mm}^3$) and neutrophilia ($>70\%$) [1, 2]. However, Sweet's syndrome reported in a few cases of AML during leukopenic and/or neutropenic period following chemotherapy [9]. Similarly, Sweet's syndrome developed during the leukopenic/neutropenic period shortly after the transplantation-conditioning regimen. Sequestration of neutrophils at skin regardless of peripheral white blood counts may be attributed to the primary effect of the disease or to the treatment [10–12]. Therefore, we believe that G-CSF use was responsible for Sweet's syndrome in our case.

Sweet's syndrome usually shows dramatic response to steroid therapy as in our case, though there are occasional unresponsive or unremitting cases. The appropriate diagnosis and identification of cause in cases with acute leukemia are of great clinical importance because G-CSF induced Sweet's syndrome is reversible with cessation of the drug and administration of steroid.

Conflict of interest The authors declare no conflict of interest, financial or otherwise.

References

1. Von den Driesch P (1994) Sweet's syndrome (acute febrile neutrophilic dermatosis). *J Am Acad Dermatol* 31(4):535–556
2. Cohen PR (2007) Sweet's syndrome—a comprehensive review of an acute febrile neutrophilic dermatosis. *Orphanet J Rare Dis* 2:34
3. Garty BZ, Levy I, Nitzan M, Barak Y (1996) Sweet syndrome associated with G-CSF treatment in a child with glycogen storage disease type Ib. *Pediatrics* 97(3):401–403
4. Shimizu T, Yoshida I, Eguchi H, Takahashi K, Inada H, Kato H (1996) Sweet syndrome in a child with aplastic anemia receiving recombinant granulocyte colony stimulating factor. *J Pediatr Hematol Oncol* 18(3):282–284
5. Hospach T, von den Driesch P, Dannaecker GE (2009) Acute febrile neutrophilic dermatosis (Sweet's syndrome) in childhood and adolescence: two new patients and review of the literature on associated diseases. *Eur J Pediatr* 168(1):1–9
6. Otheo E, Ros P, Vázquez JL, Carrillo R, Moreno R, Maldonado S, Martos I (2002) Systemic inflammatory response syndrome associated with SS. *Pediatr Crit Care Med* 3(2):190–193
7. Cohen PR, Kurzrock R (1987) Sweet's syndrome and malignancy. *Am J Med* 82(6):1220–1226
8. Hassouna L, Nabulsi-Khalil M, Mroueh SM, Zaynoun ST, Kibbi AG (1996) Multiple erythematous tender papules and nodules in an 11 month old boy: Sweet's Syndrome (acute febrile neutrophilic dermatosis). *Arch Dermatol* 132(12):1507–1510
9. Probert C, Ehmann WC, al-Mondhiri H, Ballard J, Helm KF (1996) Sweet's syndrome without granulocytosis. *Int J Dermatol* 37(2):108–112
10. Piette WW, Trapp JF, O'Donnell MJ, Argenyi Z, Talbot EA, Burns CP (1994) Acute neutrophilic dermatosis with

- myeloblastic infiltrate in a leukemia patient receiving all-trans retinoic acid therapy. *J Am Acad Dermatol* 30(2):293–297
11. de Lacerda JF, do Carmo JA, Guerra ML, de Almeida LS, Fernandes A, de Lacerda JM (1994) Leukemia cutis in acute lymphoblastic leukemia. *J Am Acad Dermatol* 30(6):1041–1043
 12. Rubin CM, Arthur DC, Meyers G, McClain KL, Kim TH, Woods WG (1985) Leukemia cutis treated with total skin irradiation. *Cancer* 55(11):2649–2652