

Neutrophilic dermatoses with acute myeloid leukemia associated with an increase of serum colony stimulating factor

Hisashi Uhara MD^a, Toshiaki Saida MD^a, Hideyuki Nakazawa MD^b, Toshiro Ito MD^b

Department of Dermatology^a and Department of Medicine^b, Shinshu University School of Medicine

Corresponding author: Hisashi Uhara MD, PhD

Department of Dermatology, Shinshu University School of Medicine,

3-1-1 Asahi, Matsumoto 390-8621, Nagano, Japan

TEL: +81-263-37-2647, FAX: +81-263-37-2646

E-mail: uhara@hsp.md.shimshu-u.ac.jp

Founding sources: None.

Conflicts of Interest : None.

Prior presentation: None.

Reprints not available from the authors.

Word count: 972, Number of references: 7, Table: 0, Figures: 5

Keyword: neutrophilic dermatoses, acute myeloid leukemia, colony stimulating factor, Sweet's syndrome, neutrophilic panniculitis

ABSTRACT

We report a case of acute myeloid leukemia with folliculitis, Sweet's syndrome, and neutrophilic panniculitis after remission induction chemotherapy for acute myeloid leukemia. The level of endogenous granulocyte colony stimulating factor was closely associated with disease activity.

Neutrophilic dermatoses are a group of disorders that includes Sweet's syndrome, pyoderma gangrenosum, subcorneal pustular dermatosis, erythema elevatum diutinum, and a few other conditions (1). These disorders are characterized by neutrophilic cutaneous infiltration and are frequently associated with systemic disorders such as myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). Although the pathogenesis has not been clarified, recent reports have suggested that some cytokines including granulocyte colony stimulating factor (G-CSF) might play an important role (2). However, G-CSF has not been sequentially examined during the course of disease. We report a case of AML with folliculitis, Sweet's syndrome, and neutrophilic panniculitis. In this patient, monitoring the serum level of G-CSF showed a close association with disease activity.

CASE REPORT

A 64-year-old man with AML (M6) received remission induction chemotherapy with intravenous cytarabine (days 1-7) and idarubicin (days 1-3). On day 6, pruritic follicular papules appeared on the extremities and abdomen (Figure 1). On day 8, he had high fever that persisted until day 22 when he received methylprednisolone intravenously. On day 15, although the follicular papules spontaneously regressed, asymptomatic edematous plaques appeared on the upper eyelids, the right auricular and the chest wall (Figure 2). Simultaneously, subcutaneous indurations with mild erythema appeared on the buttock (Figure 3). A biopsy specimen from the buttock demonstrated a dense predominantly lobular infiltration of normal-looking leukocytes in the subcutaneous tissue (Figure 4). Neither blood and tissue culture nor special staining of the biopsy specimen demonstrated any infectious agents. The serum level of G-CSF was measured by radio immunoassay (SRL, Tokyo, Japan). The clinical course, blood examination data and the serum concentration of G-CSF are shown in Figure 5. The increased concentration of G-CSF was associated with fever, cutaneous condition, and nadir of white blood cell count. Before induction of methylprednisolone, the skin lesions began to regress starting on day 21 and disappeared by day 29. Although leucopenia was present for 2 months after disappearance of the skin lesions, the level of G-CSF never

elevated and the skin lesions did not relapse during a 5-month follow-up after steroid withdrawal. The patient never received G-CSF therapy during hospitalization. HLA phenotype of the patient was not the types usually seen in Behcet's disease.

DISCUSSION

In our patient, skin lesions and increased endogenous G-CSF were simultaneously observed. After the decrease in the G-CSF level, skin lesions improved and have not recurred to date. Previously, some reports have suggested a relationship between exogenous G-CSF and neutrophilic dermatoses such as Sweet's syndrome, pyoderma gangrenosum and eccrine hidradenitis (3-5). In addition, in primary Sweet's disease without MDS or leukemia, the endogenous G-CSF level was significantly higher in patients with active disease than in those in remission (2). However, reports showing an association between endogenous G-CSF and neutrophilic dermatoses with AML or MDS are rare. Hasegawa et al reported that Behcet's disease had developed in the patients with MDS after chemotherapy-induced aplasia and the serum levels of inflammatory cytokines were higher than those in the normal state (6). Reuss-Borst et al reported Sweet's syndrome with MDS in which the serum levels of both interleukin-6 and G-CSF were elevated (7). However, data on the involvement of endogenous G-CSF in skin lesions are still scant; especially, the sequential changes in monitored serum G-CSF have rarely been examined. Therefore, we serially measured serum G-CSF levels during the disease course and found that the G-CSF levels were closely associated with disease activity in our patient. This finding indicates that endogenous G-CSF might have induced the skin lesions, although it could not be denied that other cytokines might be involved in these clinical conditions.

Our patient had 3 different skin lesions: folliculitis, Sweet's syndrome, and neutrophilic panniculitis. Neutrophilic dermatoses is a group of disorders characterized by neutrophilic cutaneous infiltration, proposed by Wallach et al. in 1991, which includes Sweet's syndrome, pyoderma gangrenosum, subcorneal pustular dermatosis, erythema elevatum diutinum and a few other conditions (1). The fact that 3 different

neutrophilic skin conditions were seen in one patient may support Wallach's hypotheses that these conditions represent a continuous spectrum (1).

References

1. Wallach D, Vignon-Pennamen MD. From acute febrile neutrophilic dermatosis to neutrophilic disease: forty years of clinical research. *J Am Acad Dermatol.* 2006 Dec;55 (6):1066-71.
2. Kawakami T, Ohashi S, Kawa Y, Takahama H, Ito M, Soma Y, et al. Elevated serum granulocyte colony-stimulating factor levels in patients with active phase of sweet syndrome and patients with active Behcet disease: implication in neutrophil apoptosis dysfunction. *Arch Dermatol.* 2004 May; 140(5):570-4.
3. Reuss-Borst MA, Muller CA, Waller HD. The possible role of G-CSF in the pathogenesis of Sweet's syndrome. *Leuk Lymphoma.* 1994 Oct; 15(3-4):261-4.
4. Lewerin C, Mobacken H, Nilsson-Ehle H, Swolin B. Bullous pyoderma gangrenosum in a patient with myelodysplastic syndrome during granulocyte colony-stimulating factor therapy. *Leuk Lymphoma.* 1997 Aug;26(5-6):629-32.
5. Bachmeyer C, Chaibi P, Aractingi S. Neutrophilic eccrine hidradenitis induced by granulocyte colony-stimulating factor. *Br J Dermatol.* 1998 Aug; 139(2): 354-5.
6. Hasegawa H, Iwamasa K, Hatta N, Fujita S. Behcet's disease associated with myelodysplastic syndrome with elevated levels of inflammatory cytokines. *Mod Rheumatol* 2003; 13: 350-355
7. Reuss-Borst MA, Pawelec G, Saal JG, Horny HP, Muller CA, Waller HD. Sweet's syndrome associated with myelodysplasia: possible role of cytokines in the pathogenesis of the disease. *Br J Haematol.* 1993 Jun; 84 (2): 356-8.

Legends

Figure 1: follicular papules on the abdomen.

Figure 2: Edematous erythemas in the chest wall.

Figure 3: Subcutaneous indurations with dark-reddish erythema on the buttock

Figure 4: A biopsy specimen of the lesion in figure 2. Dense leukocytic infiltration was seen in the subcutaneous tissue (A). Higher magnification (B).

Figure 5: The clinical course, blood examination data, and the serum concentration of G-CSF



Figure 1



Figure 2



Figure 3

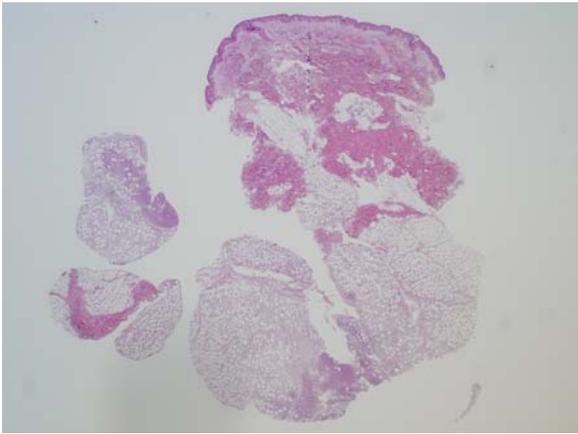


Figure 4(A)

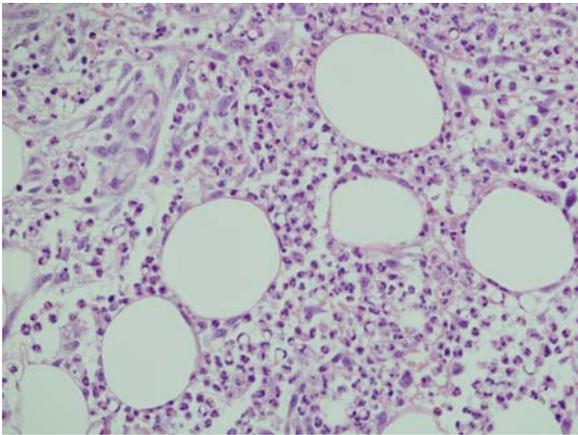


Figure 4(B)

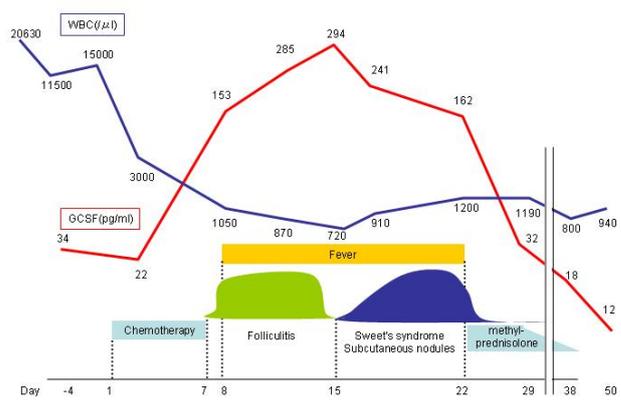


Figure 5