Impairment of Some Granulocyte Functions in Sweet’s Syndrome

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Chemotaxis, phagocytic and intracellular killing activities of polymorphonuclear leukocytes (PMNL) were investigated in vitro in 7 patients suffering from the acute phase of Sweet’s syndrome. A moderate but consistent impairment of neutrophilic chemotactic activity (NCA) was revealed in all patients. Intracellular killing of blastospores of Candida albicans was diminished in 5/7 patients. Phagocytosis and oxidase activities were within normal levels. These results point to an alteration of some PMNL functions in the acute phase of Sweet’s syndrome. Key words: Chemotaxis.

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Acute febrile neutrophilic dermatosis, so-called Sweet’s syndrome (SS), named after Robert D. Sweet, who in 1964 first described this entity based on observations of 8 female patients (1), is characterized by the sudden onset of painful erythematous plaques accompanied by fever and leukocytosis, with neutrophilia and elevated ESR as typical laboratory parameters.

Histologically, infiltration of the upper corium, predominantly by neutrophils but without evidence of vasculitis, is characteristic. Middle-aged female patients are mostly affected, often after an infection of the upper respiratory tract 1–3 weeks previously. Association with inflammatory disorders like Crohn’s disease (2), Colitis ulcerosa (1) and others has also been frequently reported. Paraneoplastic appearance, especially with hemoproliferative diseases, represents the third group of SS (3). Conflicting results as regards neutrophil functions have been reported in the past (4–10). Since these cells are intimately associated with the progress of the disease because of their local and systemic recruitment, the aim of the present prospective study was to determine some PMNL functions during the acute phase of SS.

MATERIAL AND METHODS

The study involved 7 patients (4 females, 3 males, mean age 53 years), who were diagnosed at our Department suffering from Sweet’s syndrome. Diagnosis depended on the standard criteria (2). Both major and more than two of the minor criteria were fulfilled in all cases. None of the patients received steroidal or other anti-inflammatory drugs within 4 weeks of admission. The onset of the disease ranged from 2 days up to 3 months. Five patients had the idiopathic/postinfectious type of the disease, Crohn’s disease and chronic rheumatoid polyarthritis were associated in 2 female patients.

Venepuncture was done immediately after admission during the generalization phase of skin lesions. All patients reported general malaise and had fever. White blood cell counts ranged between 9,700 and 14,000 (average 11,800) with 55–90% (mean 70%) polymorphonuclear neutrophils and 2–21% (mean 7.3%) stab cells.

Serum IgA was determined by laser nephelometry with commercially available reagents (Behring, Marburg, FRG).

PMNL separation was performed using the sedimentation method as described elsewhere (11). Chemotaxis was tested by means of the “in filter count” technique, by a modification of Boyden’s method (11). Autologous and blood group A/B pooled serum with or without musel glycerol served as chemoattractants. Additional chemotaxis experiments were performed with sera from 4/7 patients and granulocytes of a healthy volunteer using the same assay. The volunteer’s own and A/B pooled serum served as controls.

Intracellular killing activity, phagocytosis of viable and heat-inactivated Candida albicans (Ca) blastospores were assessed after 1 and 2 h by applying Lehrer’s method (12) and the NADH-dependent oxidase activity using the nitroblue-tetrazolium test (NBT) ad modum Preisig & Hitzg (13). Normal ranges as outlined in Fig. 1 were based on investigations of 100 healthy individuals examined in the same way.

RESULTS

Compared with the findings in 100 healthy volunteers, a marked and consistent disturbance of chemotactic activity was observed for all patients with SS (Table 1, Fig. 1). This decrease was obtained when using patient’s own as well as AB pooled serum. No clear-cut correlation of this phenomenon to the serum IgA level was demonstrable (Table 1). Using granulocytes from a healthy individual, chemotactic activity with sera from 4/7 SS patients ranged between 12 and 15 cells/microscopic field, whereas volunteers’ own serum and A/B pooled serum revealed 15–17 cells/microscopic field in three independent experiments. Intracellular killing of Ca blastospores was reduced in 5/7 patients (Table 1, Fig. 1) after 1 and 2 h. Phagocytic activities were within normal ranges and with the NBT test more than 95% of the PMNL stained positive for all patients.

![Fig. 1. Reduced chemotactic activity (left) of PMNL demonstrated by using autologous and blood group A/B pooled serum and musel glycerol as chemoattractant in 7 patients with Sweet’s syndrome. Diminished intracellular killing activity (right) of PMNL to Candida albicans blastospores after 1 and 2 h in the same patients.](attachment:image)
DISCUSSION

Reports about neutrophil functions in SS are rare and controversial. In 1981, Nunzi et al. reported reduced chemotaxis and slightly reduced killing of Staph. aureus, but normal phagocytosis for a 68-year-old female patient with postinfectious SS (8). Schröder et al. also found reduced neutrophil chemotactic activity (NCA) in a 46-year-old female patient in their series of 33 patients with diverse neutrophilic dermatoses (6). Additionally, diminished NCA but normal superoxide production were the results of PMN function studies performed by Altmare et al. in a 55-year-old male subject with SS (9). Leibovici et al. considered their NCA results for 2 patients to be normal, though they reported a reduction of about 10% for both (10).

In contrast to these results, Oseroff et al. (5) and Arum (4) found increased NCA in isolated cases. Oseroff et al. additionally reported reduced killing and oxidase activity for the same patient, but found normal function values in another unpublished case (cited according to Storer et al., ref. 14). Kaplan et al. reported elevated chemotactic activity measured in 89 cases when following up a male 56-year-old patient with concomitant cysto- nodular acne for 4 years (7). Additionally, a heat-stable, non-lipid chemotactant was consistently demonstrable in the serum of this patient.

Thus, present knowledge about granulocytic functions in SS depends on sporadic observations. The controversial results may therefore be due in part to problems with the standardization of the functional assays. Another explanation could be the existence of possible SS subtypes, though the data presented here do not support this view. Our results are based on well established and at our laboratory routinely performed methods and clearly support the findings of Nunzi et al., Altmare et al., and Schröder et al. The latter considered the diminished NCA to be due to the elevated serum concentrations of IgA, since influence of IgA levels on chemotaxis is well established (6). We cannot confirm a clear-cut correlation between diminished NCA and elevated serum IgA, because reduced NCA was found for the 3 patients with normal serum IgA as well (Table 1).

Since sera from 4 patients showed normal or slightly reduced chemotactic activity for granulocytes of a healthy donor, we cannot confirm the results presented by Kaplan et al. about a stable chemotactic serum factor being demonstrable, especially during the acute phases of SS.

Activation and local recruitment of neutrophils are essential in SS. A chemotactic gradient towards the skin is hence probable. The reduced NCA in vitro may therefore be an epiphenomenon due to the maximum stimulation that occurred in vivo during the acute phase of the disease. This view is supported by the observations of Schröder and Christophers who recently reported a temporary non-response of PMNL to chemotactic stimulation with C5a during the acute phase of various diseases, including bacterial infections, acne conglobata and severe psoriasis (15). Thus, we believe it likely that the results of our study demonstrate a temporary phenomenon.

On the other hand, reduced neutrophil functions may be more intimately associated with the pathogenesis of SS. Disturbed NCA and killing may for example lead to uncontrolled release of pro-inflammatory mediators in an inadequate attempt to restore the immunological balance.

Alteration of some granulocytic functions has also been reported for pyoderma gangrenosum representing a neutrophil disease probably with some pathogenetic similarities, since the possibility of coincidence with SS is well known. In fact, one of the patients investigated in this study had a sterile pyoderma gangrenosum-like ulceration on his right hand, again demonstrating this relationship (2). Longitudinal studies are now required to determine whether the alteration of PMNL functions is temporary or long-lasting.

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