INCREASED INCIDENCE OF MENSTRUATION-ASSOCIATED BACTERICIDAL DEFECTS IN NEUTROPHILS FROM WOMEN WHO HAVE RECOVERED FROM TOXIC SHOCK SYNDROME

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Abstract—There is a growing suspicion that a host abnormality may contribute to the pathogenesis of toxic shock syndrome (TSS). We found that females (5 of 5) who had recovered from TSS had transient, menstruation-associated decreases (≥ 9%) in the ability of their neutrophils to kill Staphylococcus aureus, 502A in vitro more often (P = 0.040 by Fisher's exact test) than non-TSS-affected control subjects (5 of 12). In addition, the average decrease in bactericidal activity in neutrophils obtained during menstruation from recovered TSS patients was 30 ± 9% compared to 7 ± 7% for neutrophils from non-TSS-affected control subjects. The results are consistent with the possibility that transient menstruation-associated decreases in neutrophil bactericidal function may indicate susceptibility and/or contribute to the development of TSS.

INTRODUCTION

Toxic shock syndrome (TSS) is a rare illness which is primarily seen in young, otherwise healthy, menstruating females (1–3). The pathophysiology of TSS is unknown but appears to involve toxins made by certain strains of Staphylococcus aureus (4–8). In addition, several observations have suggested that a host defense defect might contribute to the pathogenesis of TSS. First, the incidence of TSS is remarkably low (1, 9) considering that so many menstruating females are colonized with appropriate staphylococcal strains (10, 11). Second, the re-
occurrence rate of TSS in menstruating females was initially very high (approaching 30%), suggesting some additional host-related factors were involved (1, 12). The latter is emphasized by a recent description of a young woman with three recurrences of TSS during successive menstrual periods (12).

Faced with the possibility of a host abnormality, we wondered if neutrophil dysfunction might contribute to the development of TSS. This suspicion was based on a number of findings. First, the ability of neutrophils to kill bacteria, especially staphylococcal bacteria, is a well-appreciated, necessary component of efficient host defense. Individuals with insufficient numbers of neutrophils or neutrophils with genetic defects in bactericidal function (chronic granulomatous disease or Chediak-Higashi syndrome) often have frequent and/or severe bacterial infections with staphylococcal organisms (13–16). Second, acquired conditions, such as thermal injury (17), viral infection (18), uncontrolled diabetes mellitus (19), or malnutrition (20), which appear to predispose certain individuals to staphylococcal and other bacterial infections, are often associated with temporary reductions in neutrophil bactericidal activity (17–20). Third, cases of TSS which are not related to menstruation occur after surgery (21), another situation which is associated with acquired, transient decreases in neutrophil bactericidal function (22, 23). Fourth, S. aureus infections can be associated with transient reductions in neutrophil bactericidal activity in vitro (24–26). Finally, during menstruation, some females have neutrophils which develop transient, in vitro reductions in bactericidal activity (27).

Based on these observations, we hypothesized that temporary neutrophil bactericidal defects during menstruation might partially explain why some otherwise healthy women appear to be more susceptible to TSS. Our results supported this premise. We found that menstruation-associated decreases in in vitro neutrophil bactericidal activity occurred more frequently and with a greater average severity in females who had recovered from TSS than in non-TSS-affected control subjects.

MATERIALS AND METHODS

Patient Selection. Investigation was approved by Human Volunteers Committees of the Universities of Colorado and Utah. The study population consisted of 12 females, aged 20–46 with no previous histories of TSS or other repeated and/or serious infections (non-TSS-affected control subjects) and five females, aged 17–46 with proven histories of menstruation-associated TSS (recovered TSS patients). Recovered TSS patients and non-TSS-affected control subjects were all completely healthy and not pregnant at the time of study. All individuals who were taking oral contraceptives, antibiotics, or aspirin and/or who had acute infections were excluded. TSS was documented in each individual using criteria established by the Center for Disease Control. These criteria included fever, rash with subsequent desquamation, hypotension, disorientation, thrombocytopenia, and gastrointestinal, mucous membrane, hepatic, and/or renal alterations (28). A pathogenic strain of Staphylococcus aureus was cultured from an appropriate localized focus in