A Case of Sweet Syndrome Associated With Human Granulocytic Anaplasmosis

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Background: Acute febrile neutrophilic dermatosis, or Sweet syndrome (SS), is a condition that is presumed to be triggered by infectious disease agents. We report a case of SS associated with human granulocytic anaplasmosis (HGA), which is of interest because *Anaplasma phagocytophilum* infects, multiplies in, and disrupts the function of neutrophils, the key infiltrating cell in SS.

Observations: A patient with initial dermatologic manifestations of SS who did not respond to standard SS treatment was suspected to have concurrent HGA with the demonstration of leukopenia, thrombocytopenia, and elevated hepatic transaminase levels. The HGA diagnosis was established when morulae in neutrophils were observed on a peripheral blood smear, a finding confirmed by both serologic examination and polymerase chain reaction on the skin biopsy specimen used to establish the SS diagnosis.

Conclusion: The significant involvement of neutrophils with both SS and HGA warrants a broader search for additional cases that may further define whether pathogenetic linkages could exist.

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The Anaplasmataceae family consists of obligate intraacellular, gram-negative bacteria that are causes of tick-borne zoonoses. In 1994, human granulocytotropic ehrlichiosis was described. The causative organism was subsequently determined to be the same as *Ehrlichia equi* and *Ehrlichia phagocytophila*, and all were classified as a single species, *A phagocytophilum*, in 2001.

Confirmation of the diagnosis of HGA in a patient with clinically compatible illness requires 1 or more of the following: (1) 4-fold change in antibody titer by indirect fluorescent antibody test, (2) a positive result on polymerase chain reaction targeting *A phagocytophilum* DNA, (3) visualization of morulae in neutrophils and a single positive serum antibody titer by indirect fluorescent antibody, (4) immunohistochemical analysis of antigen in a skin biopsy specimen or tissue sample, or (5) isolation and culture from a clinical specimen. The case presented herein fulfills 3 separate HGA diagnostic criteria.

In general, descriptions of cutaneous eruptions in adults with HGA are infrequent and brief, and along with human monocytic ehrlichiosis, it has been referred to as "spotless" Rocky Mountain spotted fever. Although Wallace et al mentioned rash in 10 (16%) of 62 patients, local tick bite reactions were included, and only 2 patients had "erythematous" rashes. Similarly, in a large study by Bakken et al, only 1 patient (2%) was found to have a rash.

The case described herein raises the possibility that an additional cutaneous reaction, SS, may also be a mani-
festation of *Ehrlichia* or *Anaplasma* infections. The positive polymerase chain reaction result during the earliest phases of SS supports the hypothesis that neutrophils may have been activated by a small number of *A phagocytophilum* organisms.

Some superficial similarities exist between SS and HGA, including their self-limiting nature, seasonal occurrences, and responses to doxycycline. However, the broader geographic distribution of SS suggests that any connection between these entities may be as a result of activation and recruitment of neutrophils by cytokines and chemokines. Increasing evidence suggests that SS results from local or even systemic cytokine and chemokine recruitment and activation of neutrophils. Likewise, the pathogenesis of HGA is increasingly linked to aberrant neutrophil activation and deactivation by virtue of the intracellular infection, including local and systemic inflammation. Whether such pathogenetic linkages between HGA or other infectious agents and neutrophilic dermatoses such as SS exist will require more study.

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