Neutrophilic Dermatosis (Pustular Vasculitis) of the Dorsal Hands

A Report of 7 Cases and Review of the Literature

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Background: Neutrophilic dermatosis (pustular vasculitis) of the dorsal hands is a recently described disorder, which may clinically resemble a localized variant of Sweet syndrome.

Objectives: To describe the clinical and histopathologic characteristics of this rare disorder; to compare and contrast these features with those of Sweet syndrome; and to investigate possible associations with systemic diseases.

Observations: Seven women were referred for pustular or ulcerative plaques and nodules on the dorsal hands. In most patients, the initial diagnosis was cutaneous infection, but antibiotic therapy was ineffective. Skin biopsy specimens showed dense dermal neutrophilic infiltrates with leukocytoclasis and fibrinoid vascular necrosis. Cutaneous cultures yielded negative findings in all cases. Prednisone and dapsone appeared to be helpful, but recurrences were common. Minocycline hydrochloride was of uncertain benefit. Among the 7 patients, possible systemic associations included bowel disorders and a urinary tract infection.

Conclusions: Neutrophilic dermatosis of the dorsal hands may be closely related to Sweet syndrome but frequently shows the histologic pattern of leukocytoclastic vasculitis. Recognition of this disorder is important, because it may be misdiagnosed as a localized cutaneous infection. Additional studies are needed to investigate further the possible associations with internal diseases, especially bowel disorders.

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RESULTS

CLINICAL AND LABORATORY DATA

Clinical and laboratory data are summarized in the Table. All patients were women, who ranged in age from 44 to 82 years; the mean age was 64 years. Three patients had a history of minor trauma to the hands preceding the eruption. Cutaneous infections were suspected in most of the patients, and they had been treated unsuccessfully with systemic antibiotics before evaluation in our department. All patients presented with severely painful purulent nodules and plaques, frequently accompanied by ulceration, involving predominantly the dorsal hands (Figure 1). Areas of involvement on the dorsal hands variably included the radial aspect, the ulnae, and the interscapular region.
PATIENTS AND METHODS

From June 1, 1990, through August 31, 2000, 7 patients were referred to the Department of Dermatology, Mayo Clinic Scottsdale, Scottsdale, Ariz, for a similar pustular eruption on the dorsal hands. In each case, punch biopsies were performed or previous biopsy specimens were reviewed. Fungal and acid-fast staining procedures were performed on paraffin sections from biopsy specimens. Cutaneous culture specimens were collected by means of swabbing the ulcerative lesions (4 cases) or from punch biopsy specimens (3 cases). The specimens were collected for the following cultures: bacterial culture in all 7 cases, fungal culture in 6 cases, mycobacterial culture in 5 cases, and viral culture in 1 case. An additional biopsy specimen from the dorsal hand of patient 2 was submitted for direct immunofluorescence.

Follow-up information was obtained during patients’ subsequent visits in the department. When needed, additional information was obtained by means of questionnaires, which were sent to the patients or to the physicians who had previously referred the patients.

Clinical and Laboratory Data

<table>
<thead>
<tr>
<th>Patient No./Age, y</th>
<th>Duration</th>
<th>No. of Previous Similar Episodes</th>
<th>Review of Systems</th>
<th>Medical History</th>
<th>Medications</th>
<th>Treatment Before Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/78</td>
<td>1 mo</td>
<td>0</td>
<td>Fever</td>
<td>Chronic idiopathic renal failure, with hemodialysis; seizure disorder; cardiomyopathy</td>
<td>Digoxin, phenytoin sodium, lisinopril, epoetin alfa</td>
<td>None</td>
</tr>
<tr>
<td>2/69</td>
<td>1 y</td>
<td>0</td>
<td>Fever, rectal bleeding; recent possible thorn injury to hands</td>
<td>Rheumatic fever during childhood; mastectomy for precancerous changes of breast</td>
<td>Digoxin, furosemide, triazolam</td>
<td>Oral and intravenous cephalosporins</td>
</tr>
<tr>
<td>3/82</td>
<td>1 mo</td>
<td>0</td>
<td>Red patch on the right gingiva</td>
<td>Diabetes mellitus, renal artery stenosis, sigmoid resection for diverticulitis, small bowel obstruction, possible diabetic gastroparesis, hypertension</td>
<td>Furosemide, clonidine hydrochloride, nadolol, losartan potassium</td>
<td>None</td>
</tr>
<tr>
<td>4/55</td>
<td>2 mo</td>
<td>21 Episodes in 4 y</td>
<td>Fever and elbow pain during flares of hand lesions</td>
<td>Myocardial infarction, hypertension, pyelonephritis</td>
<td>Dapsone, dilazem hydrochloride, metoprolol tartrate, aspirin, doxepin hydrochloride, alprazolam</td>
<td>Oral prednisone, dapsone, ciprofloxacin hydrochloride, penicillin V potassium, intramuscular ceftriaxone sodium</td>
</tr>
<tr>
<td>5/73</td>
<td>2 wk</td>
<td>1</td>
<td>Acute burn injury to the involved finger</td>
<td>Hypertension</td>
<td>Estrogen, combination of hydrochlorothiazide and triamterene, acetaminophen, clonazepam</td>
<td>Oral erythromycin</td>
</tr>
<tr>
<td>6/44</td>
<td>7 mo</td>
<td>0</td>
<td>Negative</td>
<td>Pneumonia, hepatitis</td>
<td>Combination of propoxyphene hydrochloride and acetaminophen</td>
<td>Oral antibiotics</td>
</tr>
<tr>
<td>7/46</td>
<td>3 wk</td>
<td>1</td>
<td>Negative</td>
<td>Traumatic back pain, hypertension, pneumonia</td>
<td>Carisoprodol, aspirin, combination of propoxyphene hydrochloride and acetaminophen, combination of hydrocodone bitartrate and acetaminophen, diazepam, estrogen, medroxyprogesterone acetate</td>
<td>Ciprofloxacin, valacyclovir hydrochloride</td>
</tr>
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</table>

*CBC indicates complete blood cell count; ANA, antinuclear antibody; and RF, rheumatoid factor (reference range, 1-39).*
Direct immunofluorescence, which was performed on the hand specimen from patient 2, revealed no vascular deposits of immunoglobulin, complement, or fibrinogen.

TREATMENT AND CLINICAL COURSE

Follow-up ranged from 1 month to 4 years; median follow-up was 1 year. Cutaneous lesions resolved in 6 of 7 patients, during a period of 1 to 9 weeks. Those 6 patients had been treated with prednisone, dapsone, or minocycline hydrochloride. No hematologic disorder developed in any patient. One patient died of chronic renal failure shortly after the evaluation of her hand lesions.

Sweet described acute febrile neutrophilic dermatosis in 1964. Most patients with this rare disorder are women, who present with tender erythematous or violaceous plaques and nodules, predominantly on the face, upper trunk, and extremities. Skin biopsy specimens show dense dermal neutrophilic infiltrates with leukocytoclasis. Associated findings may include fever, peripheral blood neutrophilia, and an elevated erythrocyte sedimentation rate.

Diagnostic criteria for Sweet syndrome were proposed by Su and Liu in 1986, and were modified by subsequent authors. Although the absence of vasculitis has been considered a diagnostic criterion, some reports describe focal fibrinoid necrosis of superficial vessels in a minority of cases with Sweet syndrome.

In 1995, Strutton et al described 6 women with lesions resembling Sweet syndrome, but with a distribution limited almost entirely to the dorsal hands. In contrast to most cases of Sweet syndrome, those 6 cases showed definite leukocytoclastic vasculitis. The term pustular vasculitis of the hands was used to describe this eruption. In all cases, the hands were the predominant site of involvement, although lip ulceration was present in 1 patient. Similar dorsal hand lesions showing fibrinoid vascular necrosis were subsequently reported in 3 patients, including 2 men.

Galaria et al recently described 3 additional patients with hand lesions that clinically resembled the previous cases of pustular vasculitis. In their 3 cases, however, dense dermal neutrophilic infiltrates were present without diagnostic features of vasculitis. They therefore proposed that the entity be renamed neutrophilic dermatosis of the dorsal hands and suggested that it was a subset of Sweet syndrome.

<table>
<thead>
<tr>
<th>Hand Lesions</th>
<th>Other Sites</th>
<th>Laboratory Findings</th>
<th>Treatment</th>
<th>Clinical Course</th>
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<tbody>
<tr>
<td>Hemorrhagic nodules on dorsal hands</td>
<td>Papule on lip; pustular nodule on left ulnar forearm</td>
<td>Negative yields of blood cultures</td>
<td>Intravenous vancomycin hydrochloride and gentamicin sulfate</td>
<td>Dorsal hand lesions persisted; after 5 wk, while culture results were pending, patient decided to discontinue hemodialysis and died 5 d later, due to renal failure</td>
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<tr>
<td>Pustular nodules, 1-2 cm, on the dorsal hands</td>
<td>Erythematous macules on the back and petechiae on ankles; pink nodule on left knee</td>
<td>Bacteriuria and elevated urine white blood cells; normal CBC and serum protein electrophoresis findings; ANA, 1:40; RF, 40</td>
<td>Oral prednisone, 40 mg/d, dosage subsequently tapered; oral antibiotic for urinary tract infection</td>
<td>All cutaneous lesions resolved in 6 wk; colonoscopy revealed possible sigmoid diverticulitis or colitis and tubulovillous adenoma; no recurrence of hand lesions after 4 y; subsequent peptic ulcer disease Hand lesion healed in 1 wk; 2 new sites of involvement arose on the dorsal fingers during the subsequent year due to minocycline therapy</td>
</tr>
<tr>
<td>Ulcerated yellow plaque, 2 cm, on left dorsal hand</td>
<td>Diffuse, bright erythema of right upper gingivae</td>
<td>Serum protein electrophoresis findings; ANA, 1:40, RF, 40</td>
<td>Oral minocycline hydrochloride, 100 mg twice daily</td>
<td></td>
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<tr>
<td>Boggy red plaques and papules on both dorsal hands, 0.6-2.0 cm</td>
<td>Two scars, each 0.6 cm, on right ankle</td>
<td>Normal findings on chest x-ray film</td>
<td>Continue oral dapsone</td>
<td>Lesions were resolving at time of evaluation; 2 recurrences were reported by the patient during the following 2 y</td>
</tr>
<tr>
<td>Ulcer on dorsal right second finger; edematous and vesicular red nodule on left second finger</td>
<td>None</td>
<td>Neutrophilia, thrombocytosis; negative findings for ANA and RF, normal findings of serum protein electrophoresis; colon x-ray film showed diverticulosis</td>
<td>Prednisone, 40 mg/d, dosage subsequently tapered</td>
<td>Ulcers resolved in 1 mo; had no recurrence in &gt;2 y</td>
</tr>
<tr>
<td>Atrophic scars on dorsal left second finger and right fifth finger</td>
<td>Atrophic scar on the left forearm</td>
<td>Hypogammaglobulinemia; normal findings of ANA and RF</td>
<td>Minocycline hydrochloride, 100 mg twice daily</td>
<td>Ulcers had nearly resolved with oral prednisone given before her evaluation, but recurred with the withdrawal of corticosteroid therapy; minocycline was added; the patient reported multiple recurrences in the subsequent 4 mo</td>
</tr>
<tr>
<td>Ulcerated, purulent, hemorrhagic plaques on dorsal hands and dorsal fingers</td>
<td>Pustular nodule on left wrist; transient papule on cheek</td>
<td>Normal findings on chest x-ray film</td>
<td>Oral dicloxacillin sodium; oral prednisone, 20 mg twice daily, dosage subsequently tapered</td>
<td>Ulcers healed in 1 mo, with a course of oral prednisone</td>
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</table>

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Further links to Sweet syndrome were evident in patient 2 of the present series. The biopsy specimen from her hand showed a neutrophilic dermal infiltrate with fibrinoid vascular necrosis, whereas the biopsy specimen from a papule on her back showed a neutrophilic infiltrate without vasculitis. Five of our patients also had lesions at sites other than the hands. These areas of involvement were typically minimal and, in some cases, had not been noticed by the patients. However, the clinical and histopathologic features of the hand lesions were very similar to those described in previous cases of NDDH. Additional features resembling Sweet syndrome in these 7 patients included female sex (7 cases), pathergy (3 cases), fever (3 cases), and peripheral blood neutrophilia (2 cases). At the time of laboratory testing, 1 of the 2 patients with neutrophilia was already receiving treatment with oral prednisone, which may have caused the neutrophilia.

The original description of acute febrile neutrophilic dermatosis noted the association with a preceding upper respiratory tract infection. Subsequent reports have linked Sweet syndrome to myeloproliferative disorders, myelocytic leukemia, visceral malignancies, inflammatory bowel disease, connective tissue diseases, pregnancy, infections, drug reactions, and other disorders. Because relatively few reported cases of NDDH exist, the possible systemic associations in these patients are less clear. In previous reports, associations of uncertain significance have included a history of breast carcinoma in 2 patients, preceding pharyngitis, metastatic renal adenocarcinoma, and Raynaud disease with arthritis.

Three patients in the present series had concurrent bowel disorders at the onset of their cutaneous lesions. These active problems included diverticulosis, diverticulitis, acute proctitis (with a sigmoidoscopic appearance suggestive of diverticulitis or segmental colitis), a tubulovillous adenoma, and possible diabetic gastropathy. In addition, 1 of the 3 patients had a history of small-bowel obstruction. It is not clear whether these bowel disorders are related to the cutaneous eruption. Another neutrophilic dermatosis, bowel-associated dermatosis-arthritis syndrome, has been reported in patients with previous bowel bypass procedures and other bowel disorders. The syndrome may be related to bacterial antigens and immune complexes that occur in the setting of bacterial overgrowth in the bowel. In contrast to NDDH, bowel-associated dermatosis-arthritis syndrome typically has a widespread distribution on the upper extremities and trunk. Another neutrophil-rich cutaneous disorder, pyoderma gangrenosum, is commonly associated with inflammatory bowel disease.

In patient 2, an additional possible association included a concurrent urinary tract infection. Resolution of her hand lesions occurred after antibiotic therapy for the urinary tract infection and simultaneous treatment with oral prednisone. Thus, it is difficult to know which action may have contributed to her improvement.

Sweet syndrome may sometimes occur as a drug reaction. In typical cases, the initiation of the medication therapy and the onset of the eruption are closely associated in time. None of the medication therapy described...
in the Table had a clear temporal relationship with eruption in these 7 patients.

Neutrophilic dermatosis of the dorsal hands may respond to treatments that are commonly used for Sweet syndrome. The usefulness of oral corticosteroids1-4 and dapsone4 has been described previously. Minocycline16,17 may be helpful for pyoderma gangrenosum, but its use has not previously been reported in NDDH. In the present study, both patients who were treated with minocycline initially improved, then experienced subsequent recurrences during minocycline therapy. In addition, minocycline has been reported as a possible cause of drug-induced Sweet syndrome.18,19

Appropriate treatment of NDDH may be delayed because of misdiagnosis. Six of the 7 patients in the present report were originally believed to have cutaneous infection. Systemic antibiotics were given without benefit. Histologic findings, such as neutrophilic infiltrates and pseudoepitheliomatous hyperplasia, may also mimic infection.

CONCLUSIONS

Neutrophilic dermatosis of the dorsal hands is a neutrophil-rich cutaneous disorder, which may be a subset of or closely related to Sweet syndrome. Associated clinical features include pathergy, fever, and peripheral neutrophilia in some cases. The localized distribution, clinical appearance, and histopathologic findings often lead to misdiagnosis as a cutaneous infection. Oral prednisone and dapsone may be effective treatments, whereas minocycline is of uncertain benefit. With all treatments, recurrences are common. Bowel disorders, such as diverticulitis, may be associated with NDDH. Additional studies are needed to investigate further the systemic diseases that may be associated with this rare disorder.

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REFERENCES