Abstract

Neutrophilic spongiosis also known as granulocytic spongiotic papulovesiculosis (GSPV) is an uncommon disorder of uncertain classification. We report the case of a 45-year-old woman suffering from recurrent episodes of itchy, grouped papulovesicles over her body, histologically showing granulocytic spongiosis. The eruptions showed complete response to dapsone.

Key Words: Granulocytic spongiosis, neutrophilic spongiosis, sweet's syndrome

Introduction

Neutrophilic spongiosis was reported for the first time in 1984 by Dr. Sayami and Dr. Tagami who proposed the term “Granulocytic spongiotic papulovesiculosis (GSPV)” for it.[1] It is a disorder of uncertain classification and the etiology has never been fully explained. Literature has only 2 cases on record so far.[1,2] The reported cases showed recurrent outbreaks of small, vesicopustules, predominantly on face, neck, or upper trunk with unique histopathological features of epidermal granulocytic spongiosis, neutrophilic exocytosis without any evidence of vasculitis. This condition is usually steroid resistant and dapsone responsive. Relapses are common after stopping the treatment.

Case Report

A 45-year-old female presented with rapidly progressing grouped red raised, itchy, nontender lesions over lower legs, hands, face, abdomen, and lower back with moderate fever 100-102 degree F for the past 2 weeks. History of similar episodes (for the past 4 years) more in summers was obtained. Successive crops appeared, persisted for 3–4 weeks, and resolved, leaving behind postinflammatory hyperpigmentation. She also had symmetrical, nonmigratory joint pains involving the interphalangeal, wrists, knee, ankle, and metatarsophalangeal joints without any associated swelling and redness for the past 4 years. There was no history of recurrent oral/genital ulcers, raynaud’s phenomenon, photosensitivity, muscle weakness, gastrointestinal complaints, prior drug intake, or history of any topical irrigant or allergen application. Family history was noncontributory. She was receiving tablet amlodipine 5 mg for the last 3 months.

General physical examination was normal. On cutaneous examination, multiple grouped erythematous to vesicopustules of size 0.3 cm × 0.3 cm–0.5 cm × 0.5 cm were present over abdomen, lower trunk, arms, hands, feet, and face [Figures 1 and 2]. Few interspersed erosiculcrusted plaques and koebnerization were evident. Few erythematous to violaceous plaques of size 0.7 cm × 0.7 cm–1 cm × 1 cm were present over the forehead, surface showed fine white
semiadherent scaling [Figure 3]. Examination of scalp, oral mucosa, palms, soles, and nails was within normal limits.

Based on these findings, possibility of contact dermatitis, lupus erythematosus, and neutrophilic dermatosis (sweet’s syndrome) was kept.

Routine hematological and biochemical investigations were normal. Erythrocyte sedimentation rate was raised (34 mm). Antinuclear antibody, rheumatoid factor, perinuclear antineutrophil cytoplasmic antibodies (ANCA), cytoplasmic ANCA, antistreptolysin 0, C-reactive protein, hepatitis B and C antibody were negative. Electrocardiograph did not reveal any abnormal change. Radiographs of bilateral knee joints revealed degenerative changes while that of chest, bilateral hands, feet, and wrist joints were within normal limits.

Histopathological examination of a papule showed mild hyperkeratoses, focal spongiosis, and neutrophilic exocytosis of the epidermis [Figure 4]. It also showed intraepidermal pustule containing neutrophils and few eosinophils [Figure 5]. Dermis showed mild pigment incontinence and perivascular inflammatory infiltrate of neutrophils and few eosinophils till mid-dermis. Dermal capillaries had plump endothelial cell lining but no fibrinoid necrosis. Direct immunofluorescence (DIF) showed no deposition of immunoreactants.

The patient was initially started on oral prednisolone, with only partial improvement and continuous development of new lesions. She was then started on oral dapsone 100 mg daily. The lesions resolved in 4–5 days leaving behind pigmentation. Dapsone was gradually tapered and stopped in 8 weeks. The patient has not developed any new lesion in 4 months of follow-up.

**Discussion**

GSPV is characterized by intermittent outbreaks of myriad, semiconfluent, small papulovesicles, and vesicopustules, predominantly on the face, neck, or upper trunk but sometimes over other sites such as axillae.[3] Only 2 cases have so far been described in literature. The features of these cases are shown in Table 1. Palms, soles, scalp, and nails are usually spared. Predominant flexural and severe mucosal involvement

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of the entire oral, pharyngeal, and vaginal mucous membranes were reported in one patient. Our patient presented with recurrent episodes of rapidly progressing pruritic grouped papulovesicles over face, trunk, and upper limbs. She had no mucosal involvement.

The histopathological findings of GSPV are unique showing epidermal granulocytic spongiosis, neutrophilic exocytosis with vesicles containing neutrophils and eosinophils, and not fulfilling the features of vasculitis. These features are similar to the findings in our patient.

The histological features of neutrophilic spongiosis can be seen in several conditions as enumerated in Table 2. Sweet’s syndrome has certain diagnostic criteria which are not fulfilled by our patient. The lesions in our patient were nontender unlike in sweet’s syndrome. The histology of sweet’s syndrome shows dense, predominantly neutrophilic, infiltrate located in the superficial dermis in a band-like pattern, and prominent papillary dermal edema which may occasionally lead to subepidermal vesiculation. Lymphocytes, eosinophils, and “histiocytes” may be present. Neutrophil karyorrhexis (fragmented neutrophil nuclei; nuclear dust) is a common finding. Furthermore, sweet’s syndrome responds dramatically to steroids, which was not seen in our patient. Thus, the clinical and laboratory data along with dramatic response to dapsone in our patient preclude the possibility of sweet’s syndrome and other disorders as mentioned in Table 2. Subcorneal pustular dermatoses present with chronic, recurrent vesiculopustular eruptions. However, papules or papulovesicles are rarely seen, unlike in GSPV. The lesions coalesce into annular, circinate or serpinginous patterns, preferring the trunk and intertriginous areas, including the axillae, groin, and submammary regions. Histopathologically, the hallmark of subcorneal pustular dermatosis is a strictly subcorneal pustule filled with polymorphonuclear leukocytes. The underlying epidermis is generally spared and spongiosis is usually absent which help in differentiating it from GSPV. Hence, the diagnosis of GSPV was made.

DIF in GSPV is usually negative, but a positive DIF with IgA deposition at the dermoepidermal junction was noted in a single patient. Our patient had a negative DIF.

Our patient had certain distinct features such as association with multiple joint pains (attributed to systemic inflammation), fever, itching, and increased frequency of lesions in summers. Another interesting feature in our patient was koebnerization, which has not been reported so far in this disease.

Treatment with rifampicin, gentamicin, erythromycin, antihistamines, corticosteroids, azathioprine, methotrexate, and colchicine is usually ineffective. GSPV responds dramatically to dapsone in 48–72 h. Clofazimine was tried in a patient intolerant to dapsone, which showed therapeutic response similar to that with dapsone. Relapses are quite common after stopping the drugs. Our

### Table 1: Features of cases reported in literature

| Case authors, year and sex of patient | Age (years) and sex of patient | Clinical presentation | Special features | Histopath | DIF | Response to |
|--------------------------------------|--------------------------------|----------------------|-----------------|-----------|-----|------------|
| Sayami and Tagami, 1984[1]           | 15 and male                    | Pruritic papulovesicles on upper trunk, neck | Relapse after stopping dapsone | Granulocytic spongiosis in epidermis, few eosinophils | Negative | Dapsone |
| Batista et al. ANC, 1986[2]          | 22 and female                  | Nonpruritic grouped vesicopustules over face, neck, axilla, umbilicus, and abdomen | Oral, pharyngeal, vaginal mucosal involvement, Multiple relapses | Epidermal neutrophilic spongiosis | Initially negative, later IgA at dermoepidermal junction | Dapsone and clofazimine |
| Our case                             | 45 and female                  | Pruritic papulovesicles and vesicopustules over face, arms, abdomen | Koebnerization, multiple relapses | Intraepidermal neutrophilic spongiosis with few eosinophils | Negative | Dapsone |

DIF: Direct immunofluorescence

![Figure 5: Intraepidermal pustule containing neutrophils and few eosinophils (H and E, ×40)](image-url)
patient showed poor response to steroids, and hence, dapsone was started with response seen in 3–4 days.

We report this case for its rarity. Since this condition has several close differentials, it can be easily missed out and misinterpreted. Hence, GSPV can be suggested as a diagnosis although uncommon, especially where neutrophilic spongiosis is encountered as the predominant feature on histopathology.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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**Table 2: Differential diagnosis of neutrophilic spongiotic vesiculopustular dermatoses**

| Disease                                | Clinical                                                                 | Histological                                                                 | DIF                          |
|----------------------------------------|--------------------------------------------------------------------------|------------------------------------------------------------------------------|------------------------------|
| Contact dermatitis<sup>[1]</sup>       | Papulovesicles at site of contact with allergen                           | Parakeratoses                                                                | Negative                     |
| Pemphigus with neutrophilic spongiosis<sup>[4]</sup> | Early stages of pemphigus, resembling dermatitis herpetiformis           | Diffuse infiltration of epidermis with eosinophils and neutrophils. Acantholysis may be absent in early stages | Intepidermal IgG              |
| Dermatitis herpetiformis<sup>[5]</sup> | Papulovesicles over extensors. Severely itchy                            | Subepidermal microabscess of neutrophils and eosinophils                     | Negative                     |
| Pustular psoriasis<sup>[3]</sup>       | Sterile pustules on an erythematous background                            | Parakeratoses, spongiform pustule of Kogoj                                   | Negative                     |
| Subcorneal pustular dermatoses<sup>[5]</sup> | Sterile pustules in an arcuate or annular morphology, mostly over flexures | Subcorneal pustule of neutrophils and eosinophils, but no or minimal spongiosis | Usually negative             |
| Acute generalized exanthematous pustulosis<sup>[6]</sup> | Nonfollicular pustules over flexures, within 24-48 h of drug intake or viral infection | Neutrophilic spongiotic pustules, with apoptotic keratinocytes                 | Negative                     |

DIF: Direct immunofluorescence

**What is new?**

GSPV is a rare entity with several close differentials. Dermatologists should consider this possibility in any patient presenting with recurrent episodes of papulovesicles showing neutrophilic spongiosis on histopathology. It can show koebnerization and rapid response to dapsone.

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