

Lymphocytic vasculitis on top of Stevens-Johnson syndrome (SJS): Case Report

Abstract

Stevens-Johnson syndrome is a rare, serious disorder of skin and mucous membranes that usually occurs due to any type of medication and other disease (infections). The outer most layer of the skin is affected due to irrational death of the cells. Lymphocytic vasculitis is another severe patho-dermatological condition that causes damages of the blood vessels of on the upper most layer of the skin due to harmful effects of lymphocytes of the blood. Sometimes its effects over shed the other serious conditions of SJS syndrome. Patients at their primary stage may be suspected as SJS syndrome but its severity may leads to get turn over cutaneous vasculities within sometimes. Beside all the serum experiments, histological tests show major outcome in confirming the pathological condition. Signs and symptoms of this particular disease do not affirm that the person is actually suffering from this disorder but histo-pathological sketch contributes major respond in this regard. Medications like oral colchicine 0.5 mg once daily and oral prednisolone 30 mg is said to be used clinically for getting improved result

Background

Stevens-Johnson syndrome (SJS) is a type IV (subtype C) hypersensitivity reaction that typically involves the skin and the mucous membranes. While minor presentations may occur, significant involvement of oral, nasal, eye, vaginal, urethral, gastrointestinal, and lower respiratory tract mucous membranes may develop during the illness. Gastrointestinal and respiratory involvement may progress to necrosis. Stevens-Johnson syndrome is a serious systemic disorder with the potential for severe morbidity and even death. The syndrome was first described in 1922, when the American pediatricians Albert Mason Stevens and Frank Chambliss Johnson reported the cases of 2 boys aged 7 and 8 years with "an extraordinary, generalized eruption with continued fever, inflamed buccal mucosa, and severe purulent conjunctivitis." Both cases had been misdiagnosed by primary care physicians as hemorrhagic measles.^[1]

Case report

32 years old Saudi Female patient presented to ER with fever, chest pain which is relieved by leaning forward and generalized skin rashes. She has no history of drug allergy. The past history is irrelevant.

Physical Examination

On physical examination, the patient is a mildly obese, irritable, in acute distress. She is conscious, alert and oriented. She is feverish, her temperature is

39 38.5° C, her blood pressure is 118/78 mm Hg with a heart rate of 90 beats/min,
40 her respiratory rate is 22 breaths/minute , and her oxygen saturation is 97% .

41 She has itchy erythematous patches in the upper and lower extremities, macular
42 lesions with iris lesions in the center , and bullous lesions in the both palms and
43 forearms and lower extremities with erosions in the both lips and oral mucosa as
44 shown in figures 1 and 2. These lesions developed after infection with herpes
45 simplex in the lips. The remainder of her examination is unremarkable.

46 The patient is diagnosed as Stevens-Johnson syndrome; and is treated by
47 systemic corticosteroid and oral Augmentin 1g bid for 7 days in a private
48 polyclinic, but the lesions are exacerbating, so we stopped systemic
49 corticosteroid.

50 We treated the patient with oral Acyclovir 200 mg 5 times for 5 days, oral
51 cetirizine 10 mg once/day, and topically both betamethasone 0.05% cream and
52 fuscidic acid 2% cream bid.

53 The lesions of Stevens-Johnson syndrome are much improved within one
54 week.

55 The patient is monitored for her heart condition and pericardial effusion in the
56 CCU. After about 8 dyes of admission, there are new developing lesions in the
57 form of tender palpable purpuric lesions which are distributed in the upper and
58 lower extremities and both palms, less in the trunk without any oral lesions as
59 shown in Figures 5, 6 and 7.

60

61 **Work up**

62 **Laboratory Investigations:**

63 The clinically significant results are as follows:

64 White blood cell count (WBC) of 21.56 k/ μ l (High) (n 4 – 10 k/ μ l), with a
65 neutrophilic predominance of 70.70% (n 40-80%) and eosinophilia 10.70% (n
66 1-6%).

67 Red blood cell count (RBC) of 4.49 M/ μ L (n 3.8-4.8 M/ μ l) with a hemoglobin
68 of 12.70 gm/dL.

69 Platelet count of 682 K/ μ L (High) (n 150-410 K/ μ L).

70 ESR is 51 mm (High) (n 0-12 mm).

71 Partial thromboplastin time (PTT) of 30.90 second (n 26- 40 second),
72 prothrombin time (PT) of 14.70 second (slight High) (n 11-14.5 second) and
73 INR of 1.11 (n 0.8-1.2).

74 As regard her chemistry:

75 Her random glucose of 120.20 mg/dL (n 70-140 mg/dL), LDH of 288 μ /L
76 (High) (n 135-214 μ /L), CPK of 27 μ /L (n 24-170 μ /L), ck-MB of 14 μ /L (0-25
77 μ /L), urea of 23.80 mq/dL (n 20-48 mq/dL), creatinine of 0.29 mq/dL (Low) (n
78 0.5-1.1 mq/dL) and calcium of 8.56 mq/dL (Low) (n 8.6-10.20 mq/dL).

79 SGOT (AST) of 42 μ /L (High) (n 0-35 μ /L), SGPT (ALT) of 74 μ /L (n 0-41
80 μ /L), bilirubin (total) of 0.257 mq/dL (0-1.1 mq/dL), low total protein (6.49
81 g/dL) (n 6.6-8.7 g/dL) and albumin of 3.20 g/dL (L) (n 3.97-4.94 g/dL).

82 As regard lipids profile:

83 Cholesterol of 113 mq/dL (n 50-200 mq/dL), triglycerides of 130 mq/dL (n 40-
84 200 mq/dL), HDL of 20.30 mq/dL (L) (n 45-65 mq/dL) and LDL of 62 mq/dL
85 (n 50-100 mq/dL).

86 As regard hormonal profile:

87 Low FT3 (free T3) 2.92 pmol/L (n 3.6-6.9 pmol/L), FT4 of 19.51 pmol/L (n
88 12.36-20.2 pmol/L) and TSH of 1.05 μ U/mL (n 0.27-4.2 μ U/mL).

89 As regard serology results:

90 ANA (anti-nuclear antibody) is -ve, Anti-dsDNA is also -ve, C-reactive protein
91 (CRP) of 9.6 mg/dL (High) (n 0-0.08 mg/dL) and other serology tests as both
92 HBV and HCVAB showed non reactive results, and C3 and C4 are within
93 normal range.

94 Blood culture showed no growth.

95 Urine examination showed proteinuria (11.20 gm/24hours) (n 0-0.2 gm/24h).

96 **Plain chest-x ray and Echocardiogram**

97 As regard the chest pain, plain chest-x ray and Echocardiogram are done. Plain
98 chest-x ray showed pericardial effusion as shown in figure 3 and 4 ;and

99 Echocardiogram showed moderate form of pericardial effusion, systolic atrial
100 collapse and no sign of cardiac tamponade.

101

102



103

104 Figure 1



Figure 2



Figure 3



113

114 Figure 4

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116

117 Figure 5

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120 Figure 6



121

122 Figure 7

123 A punch biopsy was taken from these purpuric lesions.

Histological Findings

Skin with minimal hyperkeratosis and parakeratosis. Papillary dermis showed perivascular edema and moderate inflammatory cellular infiltrate in the form of lymphocytes, esinophilis and histiocytes as well as extravasated red blood cells of small and medium sized vessels. The blood vessels showed endothelial cell swelling and fibrinoid necrosis. No evidence of granuloma. According to these histological criteria the diagnosis is Chronic non specific inflammation and lymphocytic vasculitis as shown in figures 8 and 9.

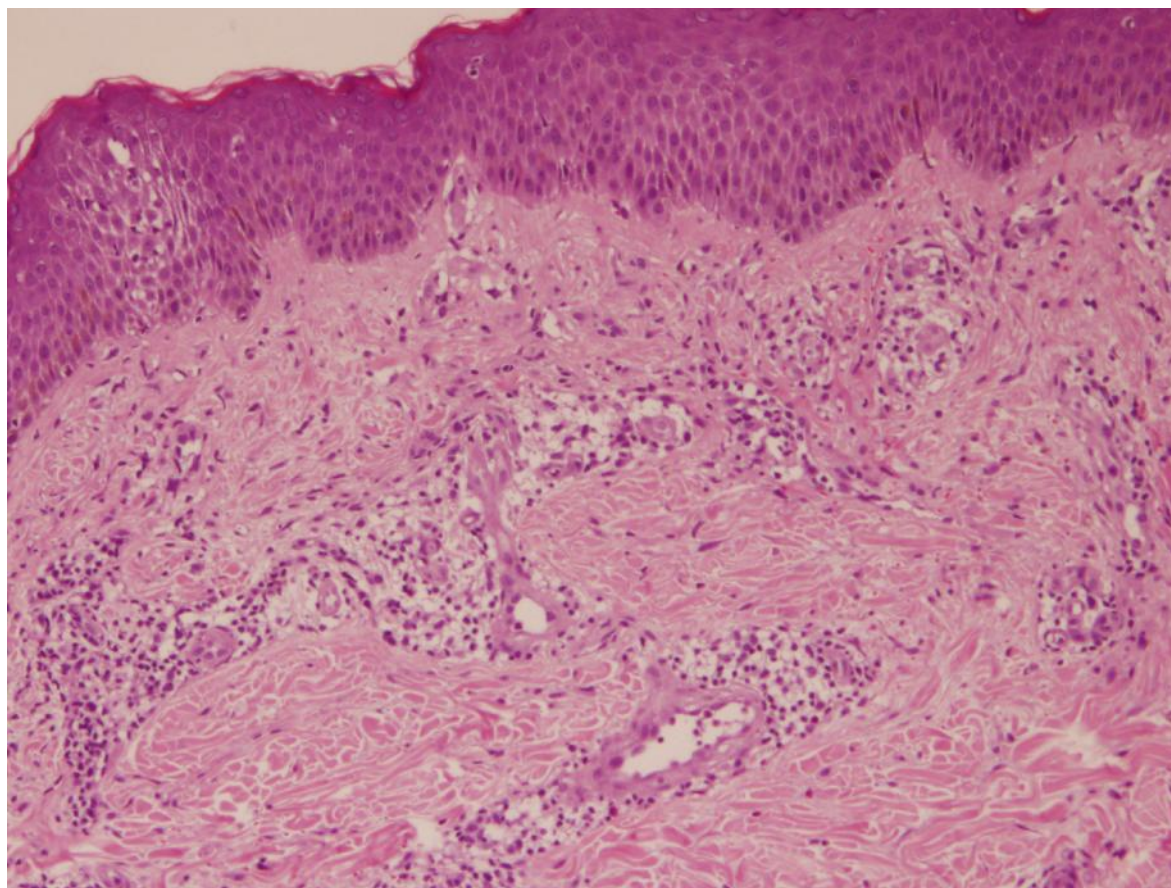


Figure 8

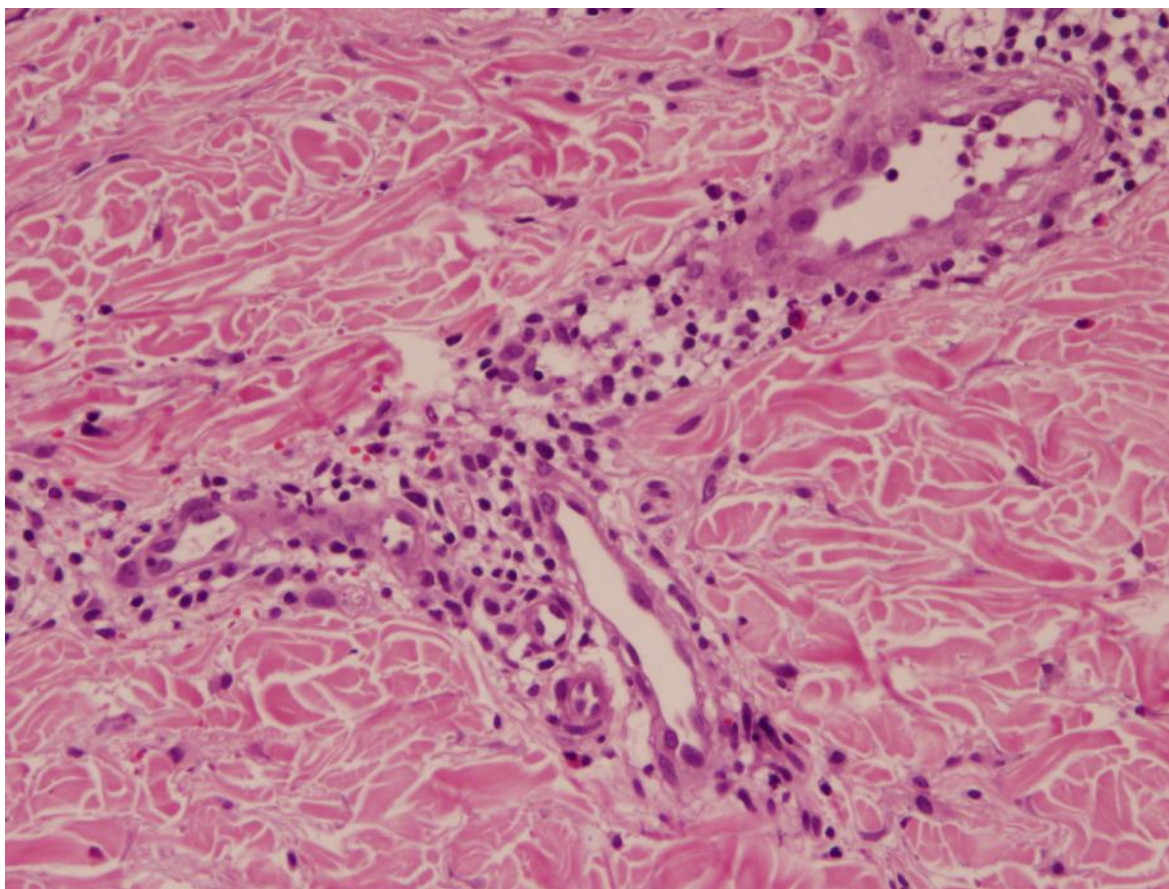


Figure 9

Discussion

Diagnosis of Churg-Strauss syndrome (allergic granulomatosis and angiitis) was suspected firstly due to high eosinophilia (10.70%), purpuric rash, proteinuria and pericardial effusion. The full diagnosis of this syndrome needs 4 criteria of 6 according to American college of Rheumatology. These criteria are Asthma, eosinophilia 10%, mononeuropathy or polyneuropathy, pulmonary infiltrates, Sinus problems, extravascular eosinophils in histological findings. ^[2]

Allergic granulomatosis and angiitis takes many years to the full clinical picture to be completed.

148 Differential diagnosis

- 149 1- Lymphocytic vasculitis.
- 150 2- Churg-Strauss syndrome (allergic granulomatosis and angiitis).
- 151 3- Cutaneous vasculitis due to amoxicillin in Augmentin.
- 152 4- Hypersensitivity vasculitis with idiopathic etiology.

153 **Lymphocytic Vasculitis**

154 In lymphocytic vasculitis, white blood cells (lymphocytes) cause damage
155 to blood vessels in the skin. This condition is thought to be caused by a number
156 of factors, but the exact cause of most cases is not known. This disease can
157 present with a variety of symptoms, depending on the size, location, and
158 severity of the affected area. In a minority of patients, cutaneous vasculitis can
159 be part of a more severe vasculitis affecting other organs in the body - this is
160 known as systemic vasculitis.^[3,4]

161 Lymphocytic vasculitis is thought to be caused by a number of different factors,
162 such as infection, trauma, drug reaction, or an underlying condition such
163 as arthritis.^[4]

164
165 Lymphocytic vasculitis is thought, by some, to be an end-stage finding of a
166 neutrophilic-mediated vasculitis and there is some controversy as regard
167 acceptance of the concept of lymphocytic vasculitis. There is a spectrum of
168 histopathologic presentation, from a classic fully developed vasculitis with
169 fibrinoid necrosis and lymphocytes, to endothelialitis or
170 endovasculitis.^[5] Lesions with endothelialitis or endovasculitis may take much
171 longer to manifest clinically, as compared to acute lesions of neutrophilic
172 vasculitis. Skin biopsies demonstrating lymphocytic vasculitis can be classified
173 by the vessels involved and by the morphologic changes associated with the
174 vasculitis as the following: lymphocytic endovasculitis, lymphocytic lichenoid
175 vasculitis and angiocentric/angiodestructive lymphocytic vasculitis.^[6]
176

177 **Eosinophilic granulomatosis with polyangiitis (EGPA)**

178 Eosinophilic granulomatosis with polyangiitis (EGPA) (alternatively termed
179 Churg-Strauss syndrome or allergic granulomatosis and angiitis) is a rare
180 disorder characterized by a small- and medium-sized vessel vasculitis with
181 severe asthma and tissue eosinophilia.^[7] The combination of allergic
182 granulomatosis and angiitis associated with asthma, typically of adult onset,
183 and allergic rhinitis^[8] was first described by Churg and Strauss in 1951, when

they reviewed 13 autopsy cases that were previously classified as polyarteritis nodosa. These cases were atypical in that asthma and eosinophilia preceded the systemic vasculitis. They named the syndrome "allergic angiitis and allergic granulomatosis," which came to be known as Churg-Strauss syndrome (CSS) and is now EGPA.^[9] Since the identification of antineutrophil cytoplasmic antibodies (ANCA) in the early nineties, EGPA is part of a group of diseases known as the ANCA-associated vasculitides (AAV) that includes granulomatosis with polyangiitis (previously known as Wegener granulomatosis) and microscopic polyangiitis.^[10]

Cutaneous vasculitis due to antibiotics

Antibiotics are the most common drugs to cause hypersensitivity vasculitis, particularly beta-lactams. Nonsteroidal anti-inflammatory drugs and diuretics also frequently cause vasculitis. However, almost all drugs and drug additives are potential causes.^[11, 12] Hydralazine, minocycline, propylthiouracil, and levamisole-adulterated cocaine use should be considered in patients with ANCA-associated vasculitis.^[13]

Various infections may be associated with vasculitis. Upper respiratory tract infections (particularly beta-hemolytic streptococcal infection) and viral hepatitis (particularly hepatitis C) are most often implicated. Hepatitis C is a commonly recognized cause of vasculitis, likely secondary to the presence of cryoglobulins. However, when 1614 patients with hepatitis C were studied, vasculitis occurred in only 12 patients (9 with cryoglobulinemia, 3 without). Interestingly, cryoglobulins were present in roughly 40% of those tested; many patients with cryoglobulins (98%) did not have vasculitis despite an abnormal circulating paraprotein. Hepatitis B has been implicated in some cases of vasculitis in the past. HIV infection may also be associated with some cases of cutaneous vasculitis. Foods or food additives may also cause vasculitis. Collagen-vascular diseases account for 10-15% of cases of cutaneous vasculitis. In particular, rheumatoid arthritis, Sjögren syndrome, and lupus erythematosus may have an associated hypersensitivity vasculitis. The presence of vasculitis often denotes active disease and possibly a poorer prognosis. Inflammatory bowel disease, ulcerative colitis, or Crohn colitis may be associated with cutaneous vasculitis. Malignancy accounts for 1-5% of cases of cutaneous hypersensitivity vasculitis. Lymphoproliferative diseases are more common (particularly hairy cell leukemia); however, any type of tumor at any site may be related to cutaneous vasculitis. Effective management of malignancy can lead to resolution of the hypersensitivity vasculitis.^[14]

Final diagnosis

Lymphocytic vasculitis.

Treatment

The patient is improved in her clinical pictures as regard vasculitis in the skin, pericardial effusion, and proteinuria by oral colchicine 0.5 mg once daily and oral prednisolone 30 mg once daily for 2 weeks.

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