Lymhocytic 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 irrational death of the cells. Lymhocytic 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.

Key words: Lymhocytic vasculitis. Stevens-Johnson syndrome.

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]
So this case report demonstrated the lymhocytic vasculitis on top of Stevens-Johnson.

Case report

Thirty two years old Saudi Female patient presented to emergancy room with fever, chest pain which was relieved by leaning forward and generalized skin rashes. She had no history of drug allergy. There was no history of cardiac disease. The past history was irrelevant.

Physical Examination

On physical examination, the patient was a mildly obese, irritable , in acute distress. She was conscious, alert and oriented. She was feverish, her temperature was 38.5° C, her blood pressure was 118/78 mm Hg with a heart rate of 90 beats/min, her respiratory rate is 22 breaths/minute , and her oxygen saturation was 97% .

She had itchy erythematous patches in the upper and lower extremities, macular lesions with iris lesions in the center , and tense bullous lesions in the both palms and forearms and lower extremities, less in the trunk with erosions in the both lips and oral mucosa as shown in Plates 1 and 2. These lesions developed after infection with herpes simplex in the lips which was recurrent since many years. The remainder of her examination was unremarkable.

The patient was diagnosed as Stevens-Johonson syndrome; and was treated by systemic corticosteroid and oral Augmentin 1g bid for 7 days in a private polyclinic, but the lesions were exacerbating, so we stopped systemic corticosteroid.

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

The lesions of Stevens-Johonson syndrome were much improved within one week.

The patient was monitored for her heart condition and pericardial effusion in the CCU. After about 8 days of admission, there were new developing lesions in the form of tender palpable purpuric lesions which were distributed in the upper and lower extremities and both palms, less in the trunk without any oral lesions as shown in Plates 5, 6 and 7.

Work up

Laboratory Investigations:

The clinically significant results were as follows:

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

Red blood cell count (RBC) of 4.49 M/µL (n 3.8-4.8 M/µl) with a hemoglobin of 12.70 gm/dL.

Platelet count of 682 K/µL (High) (n 150-410 K/µL).

Erythrocyte Sedmentation Rate (ESR) was 51 mm (High) (n 0-12 mm).

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

As regard her chemistry:

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

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

As regard lipids profile:

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

As regard hormonal profile:

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

As regard serology results:

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

Blood culture showed no growth.

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

Plain chest-x ray and Echocardiogram

As regard the chest pain, plain chest-x ray and Echocardiogram were done. Plain chest-x ray showed pericardial effusion as shown in plate 3 and 4 ;and Echocardiogram showed moderate form of pericardial effusion, systolic atrial collapse and no sign of cardiac tamponade.

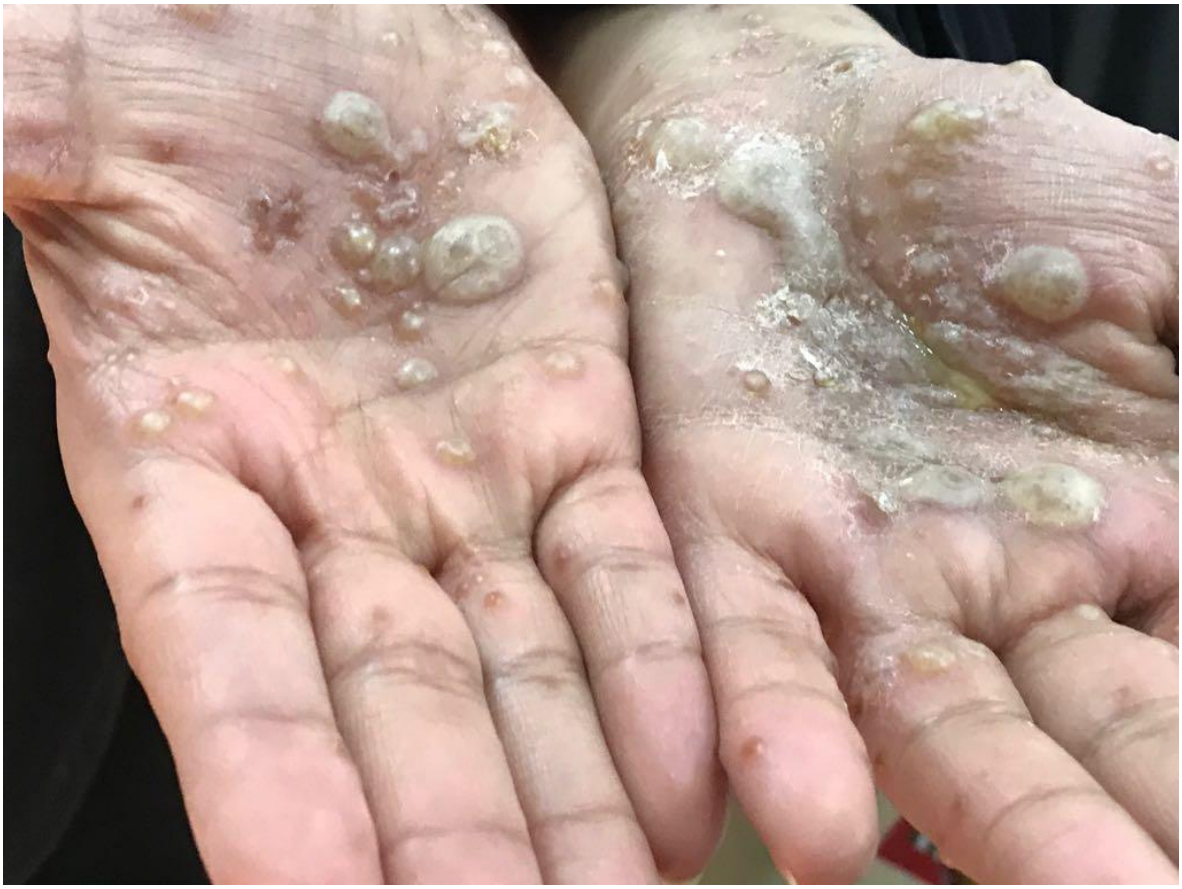

Plate 1:showed active and dried tens blisters of Stevens-Johnson syndrome, some of them showed iris lesions as in right palm.

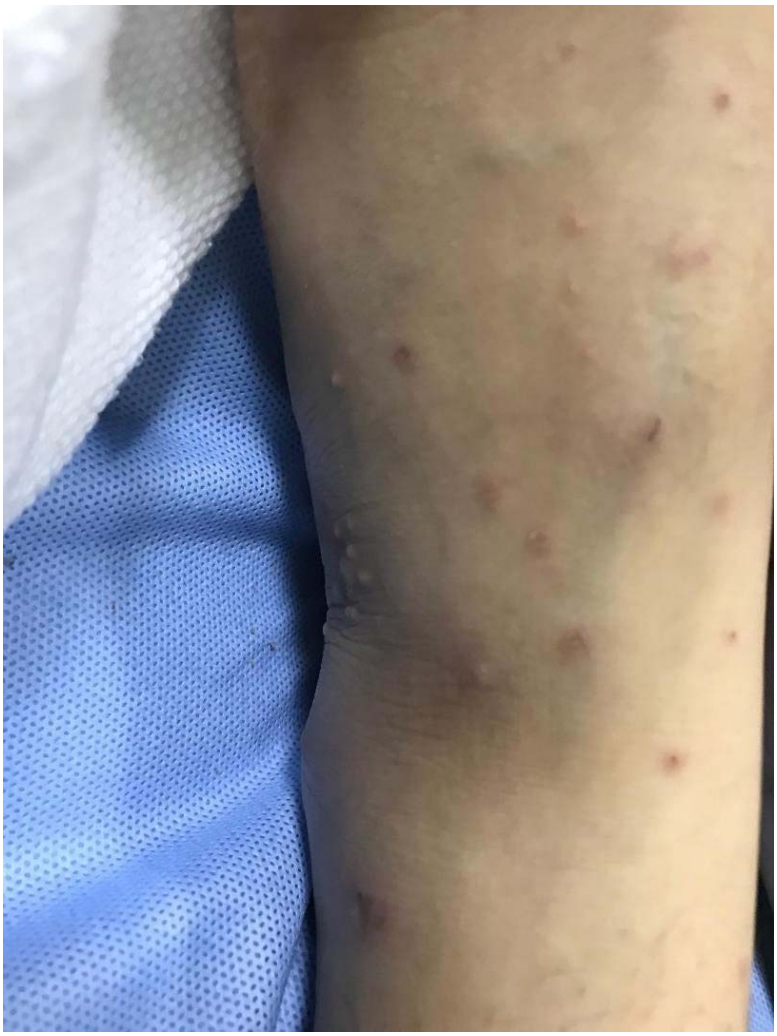

Plate 2: showed healed blisters of Stevens-Johnson syndrome with crustation.

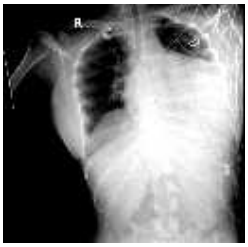

Plate 3: showed pericardial effusion with compressed of right lung.

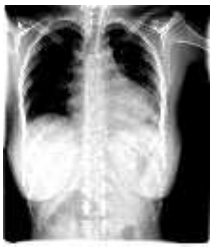

Plate 4 : showed slightly improved of pericardial effusion after treatment

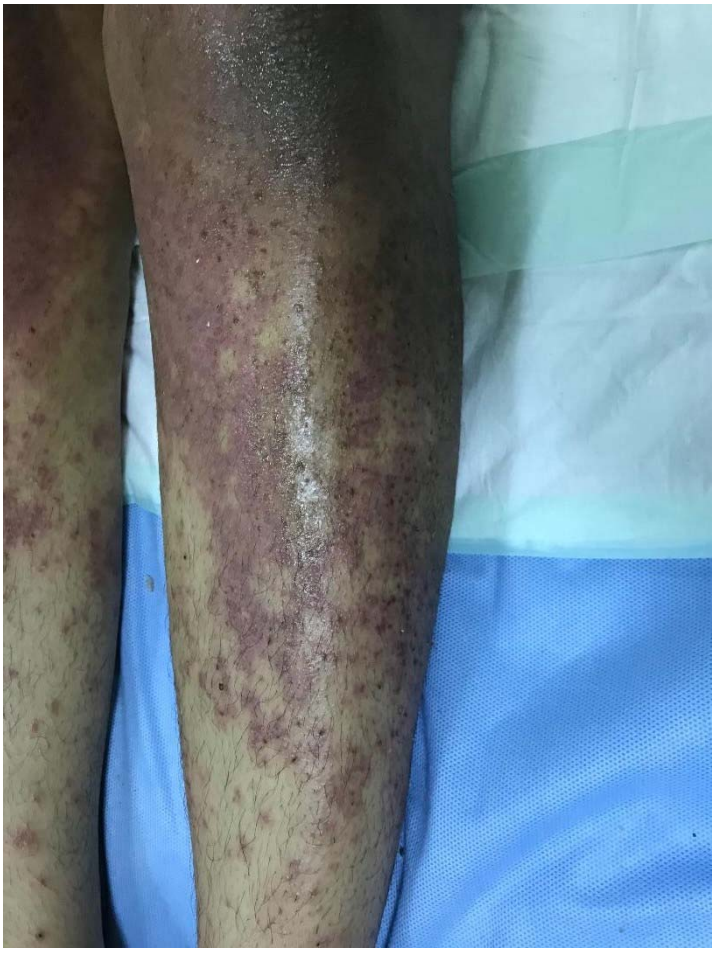

Plate 5: showed purpuric rash in both lower extremities.

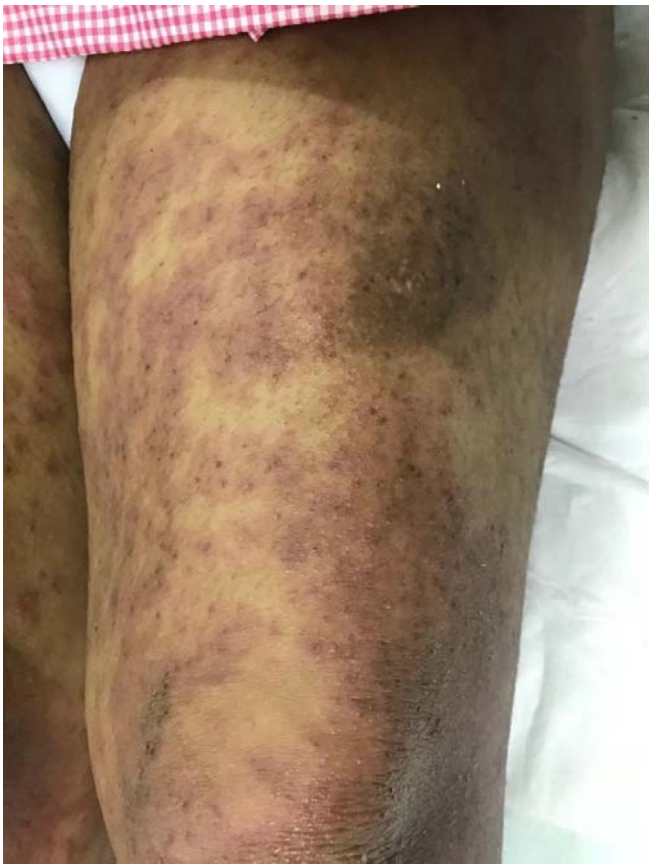

Plate 6: showed purpuric rash in both thighs.

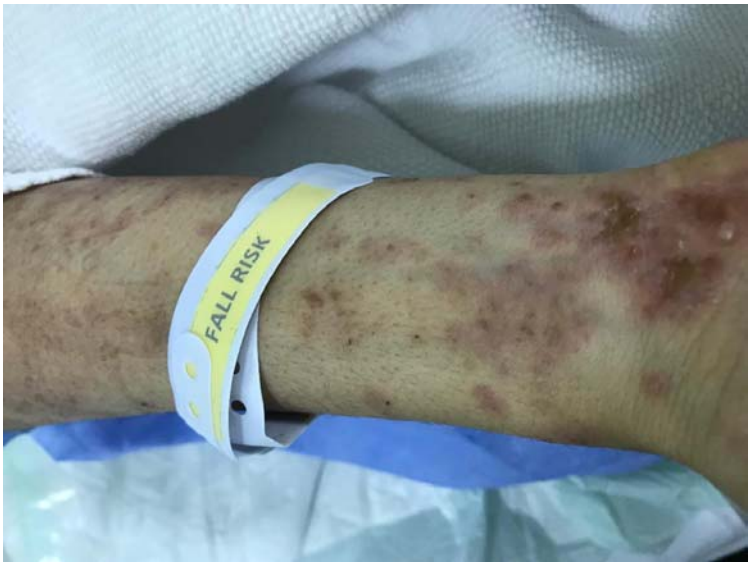

Plate 7: showed purpuric rash few healed and active blisters of Stevens-Johnson syndrome were still present as shown in wrist area of left forearm.

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 was Chronic non specific inflammation and lymphocytic vasculitis as shown in Plates 8 and 9.

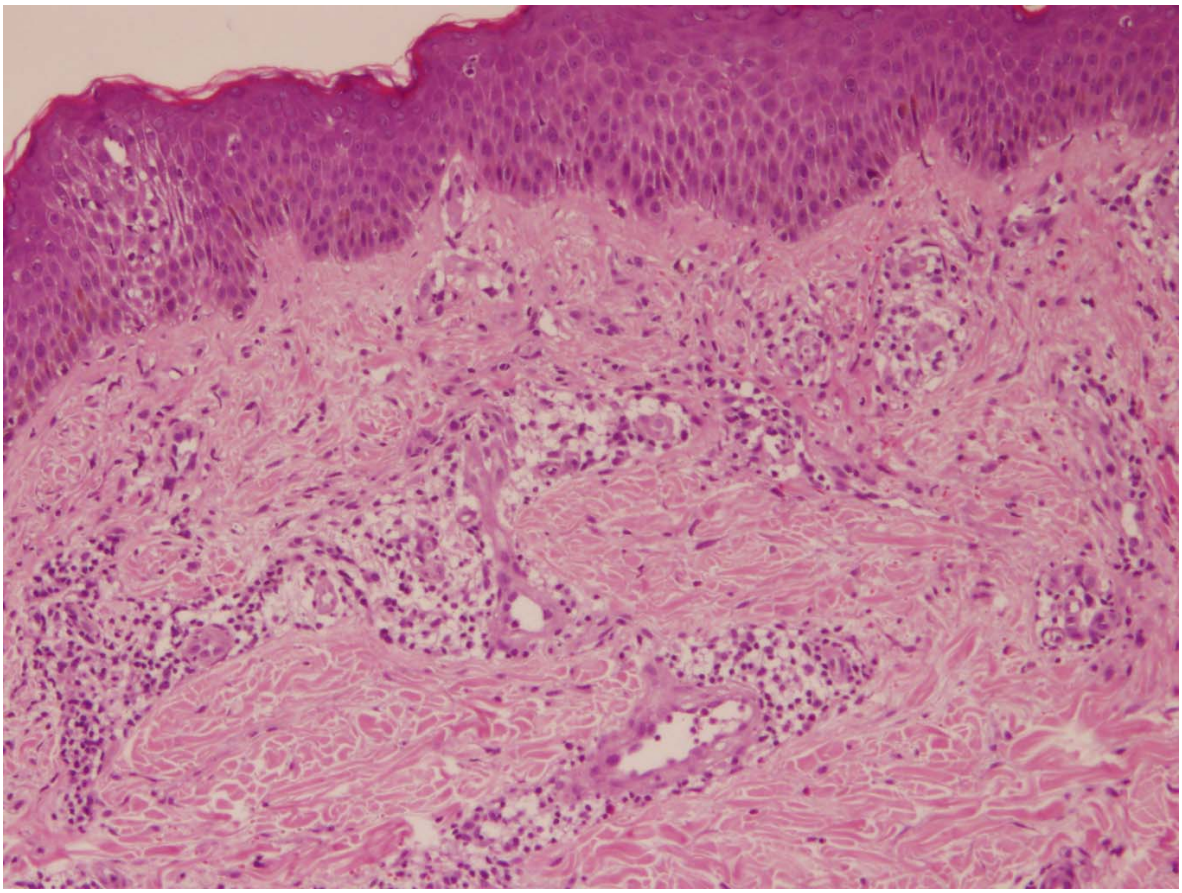

Plate 8: LPF showed minimal hyperkeratosis and parakeratosis. Papillary dermis showed perivascular edema and moderate inflammatory cellular infiltrate in the form of lymphocytes, esinophilis and histiocytes as well as extravasated red blood cells of small and medium sized vessels.

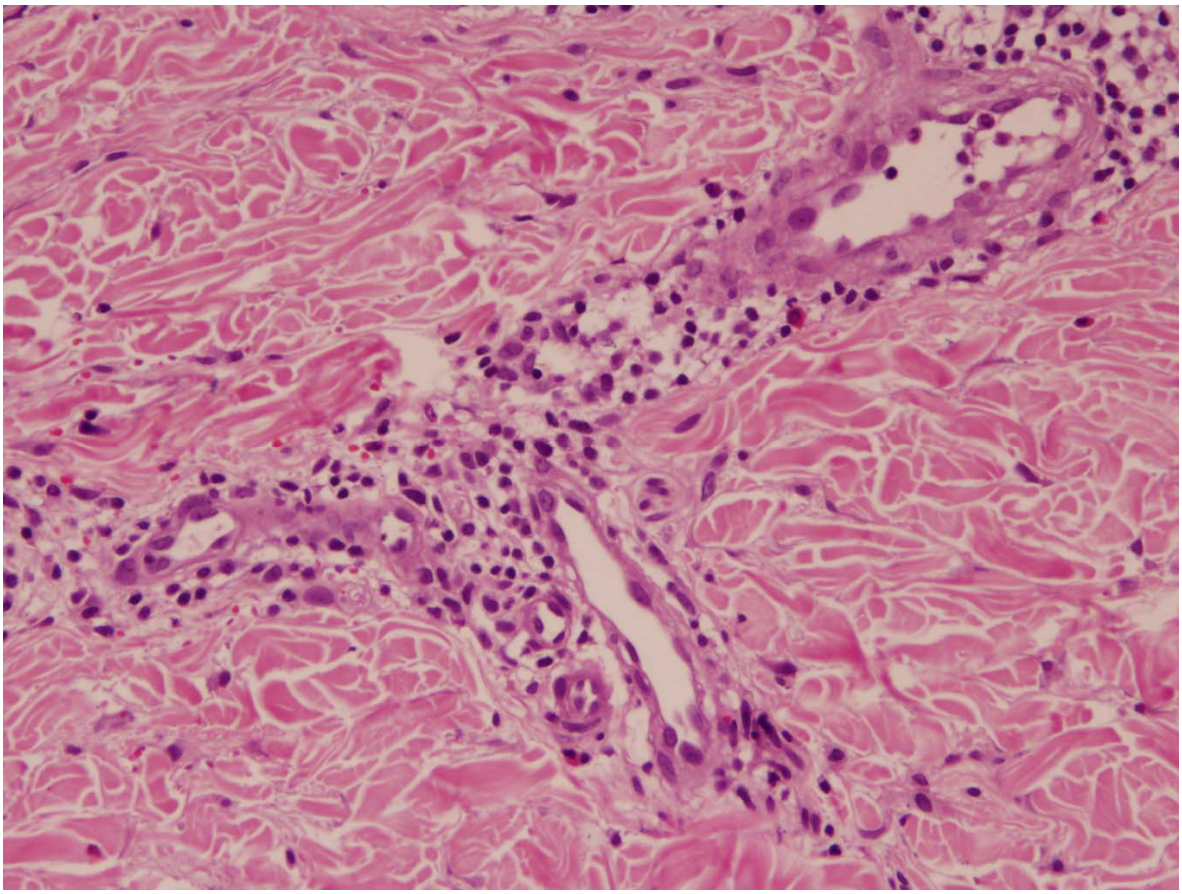

Plate 9 HPF showed: endothelial cell swelling and fibrinoid necrosis of blood vessels. There was also extravasated red blood cells.

Discussion

Diagnosis of Churg-Strauss syndrome (allergic granulomatosis and angiitis) was suspected firstly due to high eosinophilia (10.70%), purpuric rash, protinuria and pericardial effusion, and the histopathological findings was not go with allergic granulomatosis and angiitis diagnosis. 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] Asthma, neuropathy, pulmonary infiltrates, Sinus problems, extravascular eosinophils in histological findings were not be present.

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

In spite of lympocytic vasculitis was developed, few healed and active blisters of Stevens-Johnson syndrome were still present as shown in wrist area of left forearm in plate 7.

Differential diagnosis

As regarded these vasculitic lesions with high eosinophilia (10.70%), protinuria and pericardial effusion, we suspected these differential diagnosis:

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

Lymphocytic Vasculitis

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

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

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

Eosinophilic granulomatosis with polyangiitis (EGPA)

Eosinophilic granulomatosis with polyangiitis (EGPA) (alternatively termed Churg-Strauss syndrome or allergic granulomatosis and angiitis) is a rare disorder characterized by a small- and medium-sized vessel vasculitis with severe asthma and tissue eosinophilia. [7] The combination of allergic granulomatosis and angiitis associated with asthma, typically of adult onset, 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]

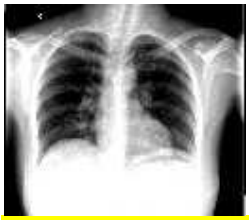

Plate 10 showed improvement of pericardial effusion with treatment.

Final diagnosis

Lymhocytic vasculitis on top of Stevens-Johnson syndrome.

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.

Conclusion

Although lymhocytic vasculitis is a rare and controversial disease , it could be presented on top of Stevens-johnson syndrome.

Competing interest:

No competing interest exists

Ethical consideration

Ethical approval was obtained from ethical committee of College of Applied Medical Science Taif University ,written consent was taken from the patient.

References

1. Steph C.F, Andrew A D, Rola B.A, Erik L., Steven J. P., Stevens-Johnson Syndrome. Medscape. Updated: Dec. 29,2017. https://emedicine.medscape.com/article/1197450-overview.

2. Masi A.T., Hunder G.G., Lie J.T., Michel B.A., Bloch D.A., Arend W.P., Calabrese L.H., Edworthy S.M., Fauci A.S., Leavitt R.Y., The American College of Rheumatology 1990 criteria for the classification of Churg-Strauss syndrome (allergic granulomatosis and angiitis). *Arthritis Rheum.* 1990 Aug. 33(8):1094-100.

3. Cutaneous Vasculitis. *DermNet NZ*. September 2014; http://dermnetnz.org/vascular/vasculitis.html. Accessed 11/13/2014.
4. Carlson JA, Ng BT, Chen KR. Cutaneous vasculitis update: diagnostic criteria, classification, epidemiology, etiology, pathogenesis, evaluation and prognosis. *The American Journal of Dermatopathology*. 2005; 27(6):504-528. http://www.ncbi.nlm.nih.gov/pubmed/16314707. Accessed 11/13/2014.

5. Carlson JA, Chen KR. Cutaneous vasculitissupdate: neutrophilic muscular vessel and eosinophilic, granulomatous, and lymphocytic vasculitis syndromes. *Am. J. Dermatopathol.* 2007,29(1): 32–43.
6. Kossard S. Defining lymphocytic vasculitis. *Australas. J. Dermatol.* 2000, 41, 149–155 .
7. Mouthon L, Dunogue B, Guillevin L. Diagnosis and classification of eosinophilic granulomatosis with polyangiitis (formerly named Churg-Strauss syndrome). *J Autoimmun.* 2014 48,49:99-103.
8. Chen KR, Carlson JA. Clinical approach to cutaneous vasculitis. *Am J Clin Dermatol*. 2008. 9 (2):71-92.
9. Churg J, Strauss L. Allergic granulomatosis, alletic angiitis, and periarteritis nodosa. *Am J Pathol*. 1951. 27:277.
10. Ramentol-Sintas M, Martinez-Valle F, Solans-Laque R. Churg-Strauss Syndrome: An Evolving Paradigm. *Autoimmunity Reviews*. 2012. 12:235-240.
11. Fujikawa K1, Kawakami A, Hayashi T, Iwamoto N, Kawashiri SY, Aramaki T, Ichinose K, Tamai M, Arima K, Kamachi M, Yamasaki S, Nakamura H, Ida H, Origuchi T, Eguchi K. Cutaneous vasculitis induced

by TNF inhibitors: a report of three cases. *Mod Rheumatol*. 2010 , 20(1):86-9.

12. Lowry MD, Hudson CF, Callen JP. Leukocytoclastic vasculitis caused by drug additives. *J Am Acad Dermatol*. 1994 , 30(5):854-855.
13. Pendergraft WF 3rd, Niles JL. Trojan horses: drug culprits associated with antineutrophil cytoplasmic autoantibody (ANCA) vasculitis. *Curr Opin Rheumatol*. 2014 , 26(1):42-49.
14. Loricera J, Calvo-Rio V, Ortiz-Sanjuan F, Gonzalez-Lamuno D, Martínez-Taboada VM, González-Gay MA, et al. The spectrum of paraneoplastic cutaneous vasculitis in a: defined population. *Medicine (Baltimore)*. 2013. 92:331.