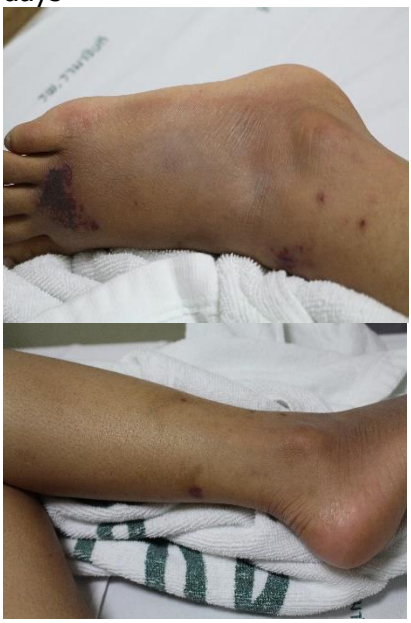
## Case 5

A 33-year-old Thai woman from Pitsanulok province
**Chief complaint**: Palpable purpura on both legs for 5 days



**Present illness**:

10 months PTA: She developed tenderness on paranasal sinus, diagnosed as sinusitis.

5 months PTA: She developed dyspnea with bronchospasm, diagnosed as acute asthmatic attack.

5 days PTA: She developed multiple palpable and non palpable purpura on dorsum of both feet and posterior aspect of right calf.

3 days PTA: She developed multiple joint swelling of both hand and ankles, diagnosed as

migratory polyarthritis.

**Past history**

She had a history of allergic rhinitis since childhood and history of chronic eczema 4 years ago.

**Physical examination**

HEENT: no malar rash or discoid rash, no oral ulcer, no alopecia

Lung: equal breath sound, no adventitious sound

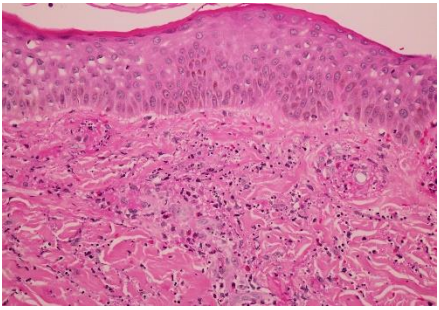
Extremities: Swelling, warm, tenderness at right 2nd-5th PIP, DIP, MCP, and right wrist, right elbow, right ankle and right foot

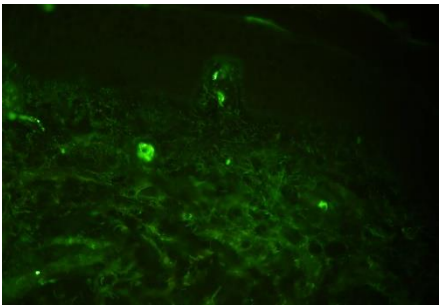
**Skin examination**

Multiple erythematous to violaceous indurated plaques and reticulate patches on dorsum of both feet and posterior aspect of right calf.

**Histopathology** (S14-030879, Rt leg)

There was dense perivascular and interstitial inflammatory cell infiltrate of mainly neutrophils, nuclear dust and extravascular erythrocytes in the superficial and deep dermis. Fibrin deposit within the wall of small blood vessel





**Direct immuofluorescence:**
- Positive IgG, IgM, C3 at superficial blood vessels
- Compatible with small vessel vasculitis

**Diagnosis:** Eosinophilic granulomatosis with polyangiitis with leukocytoclastic vasculitis.

**Investigations:**
- CBC: WBC 14,980 (N 56%, L 11%, Eo 29%, Mo 3%)
  Absolute eosinophil count 4,345 cells
  Platelet 346,000, Hb 13.1, Hct 38%
- P-ANCA: positive (1:320), C-ANCA: negative
- ANA: positive 1:80 (fine speckled), AntidsDNA: negative
- C3, C4, CH50: normal
- RF: positive(89.4), Anti CCP: negative
- Lupus anticoagulant, Anticardiolipin,
  Beta-2 Glycoprotein1: negative
- Cryoglobulin: weakly positive
- ESR: 73

- Stool exam: no parasite

**Treatment(Initial):**
- Naproxen 500 mg once a day
- Etoricoxib 90 mg once a day
- Omeprazole 20 mg once a day
- Seretide evohaler(25/125) 2 puff twice a day
- Ventolin MDI 2 puff prn for dyspnea

**Presenter:** Noppanun Chalermroj, MD

**Consultant:** Kumutnart Chanprapaph, MD

**Discussion:**

Our patient presented with multiple palpable purpura on lower legs. Skin biopsy and direct immunofluorescence was done to confirm the diagnosis of small vessel vasculitis. Leukocytoclastic vasculitis (LCV) is a small-vessel vasculitis where the skin is the most commonly involved organ. The most frequent skin manifestation of LCV is palpable purpura. [1,2] Other skin manifestations include maculopapular rash, bullaes, papules, plaques, nodules, ulcers, and livedo reticularis. The differential diagnosis for LCV can divided in primary and secondary vasculitis. Multiple etiologies including drugs, infections, autoimmune diseases, collagen vascular diseases, and malignancies have been associated with LCV. Laboratory tests including complete blood count, erythrocyte sedimentation rate, biochemistry profile with liver and renal function and urinalysis are useful in excluding other vasculitides, determining the presence of systemic disease, and identifying an associated disorder, which can provide

prognostic information. In this case, the patient present with LCV and had history of allergic rhinitis, asthma and paranasal abnormalities. Her lab investigation reveals eosinophilia and P-ANCA positive. Therefore, EGPA was suspected and our patient satisfied four out of six criteria for the diagnostic criteria of Churg-Strauss syndrome proposed by the American college of rheumatology as shown in table 1.[3]

Eosinophilic granulomatosis with polyangiitis (EGPA)[4], formerly named Churge Strauss syndrome. EGPA was first described in 1951 by Jacob Churg and Lotte Strauss. EGPA is a rare ANCA-associated vasculitis characterized by eosinophil rich and granulomatous necrotizing vasculitis of the small- to medium-sized arteries. Affected patients usually have a prolonged history of allergic syndromes, including rhinosinusitis, nasal polyposis, and persistent, difficult-to-control asthma.

EGPA usually presents in 3 phases: The prodromal phase characterized by asthma with or without allergic rhinitis, the eosinophilic phase characterized by eosinophilia in the blood and tissue, and the vasculitic phase. The vasculitic phase may occur in multiple organs, including the nerves, lungs, heart, gastrointestinal tract, kidneys, and skin. Cutaneous lesion has been observed in approximately two-third EGPA patients. Palpable purpura was the most common type. There were a variety of other cutaneous lesions such as erythematous vesicles or bullae, nodular erythema, subcutaneous nodules, hemorrhagic bullae, livedo reticularis and erythema multiforme-like eruption. All patients had skin eruptions on the lower extremities.[5]

Although the syndrome can occur at any age, the prevalence is highest at a mean age of 48 (range 14-74 year), with an equal gender distribution.[6] The annual incidence is low in the general population, ranges from 10.7[7]to 13[8]cases/million inhabitants, with an annual incidence of 0.5 to 6.8 new cases/million inhabitants. [9-11]

The pathophysiology of EGPA is not well understood, but its association with ANCA, rheumatoid factor, hypergamma- globulinemia, and elevated IgE levels suggests autoimmunity.

ANCAs are present in about 40% of patients with EGPA,
with a perinuclear ANCA pattern (antimyeloperoxidase) found in most patients. ANCA-positive findings has been shown in many studies to be associated with more glomerulonephritis, alveolar capillaritis, and neuropathy. Patients with ANCA-negative findings have been shown to have more cardiac involvement.[12-14]

There are three primary histopathologic findings: (1) vasculitis (which may be an eosinophil-rich small vessel leukocytoclastic vasculitis involving venules and arterioles or cutaneous polyarteritis nodosa-like vasculitis of medium sized vessels), (2) dermal eosinophilia and (3) extravascular granulomas, which can often manifest as a palisading neutrophilic and granulomatous dermatitits, with or without eosinophils.[15] In fact, extravascular necrotizing granulomas are reported by some to be pathognomonic, however, many believe that it could be observed in a number of other autoimmune disorders.[3,16]

Diagnosis of EPGA by presence of any four or more of the six classification criteria developed by the

American College of Rheumatology [Table 1] yielded a sensitivity of 85% and a specificity of 99.7%.[3]

**Table 1**

| **Churg Strauss syndrome : American College of Rheumatology classification criteria** |
|---|
| Asthma<br>Eosinophilia<br>History of allergy<br>Pulmonary infiltrates, non fixed<br>Paranasal sinus abnormalities<br>Extravascular eosinophilias |
| 4 out of 6 criteria should be present |

Management of EGPA depends on the major organ affected. If patient manifest with life and/or organ threatening disease (i.e., heart, GI, central nervous system, severe peripheral neuropathy, severe ocular disease, alveolar hemorrhage and glomerulonephritis) then aggressive remission-induction regimen comprising of glucocorticoids and another immunosuppressant (e.g.cyclophosphamide, azathioprine, methotrexate, mycophenolate mofetil and IVIG).[17]Biologic agents such as the anti-interleukin-5 (mepolizumab), rituximab and anti TNF alpha blocking agents are promising treatment options.[18,19]The overall prognosis of EGPA is generally good and largely depends on initial degree of disease extension and organ involvement.

Our patient presented with EGPA in the vasculitic phase of the disease. She had history of allergic rhinitis, recurrent sinusitis, well controlled asthma. During follow up, she developed mononeuritis multiplex, cerebral vasculitis. She has been treated with pulse

methyprednisolone combined with pulse cyclophosphamide and then switched to oral prednisolone and azathioprine.

Skin manifestations can be the presenting feature of EPGA. Therefore, early recognition is essential for appropriate treatment and prevention of irreversible organ damage.

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