A RARE PRESENTATION OF ANCA ASSOCIATED VASCULITIS
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Abstract:
Churg Strauss Syndrome (CSS) is a rare antineutrophil cytoplasmic antibody (ANCA associated small vessel vasculitis with protean manifestations. A 27 years old male presented with ulcer over legs, peripheral gangrene, mononeuritis multiplex, blood eosinophilia, pANCA negativity, later developed bronchial asthma, diffuse nodular pulmonary infiltrates, pANCA positivity, granuloma and renal failure inspite of treatment. In conclusion vasculitic manifestations are protean. It may have typical and atypical presentations. Repeated clinical examination and investigations will clinch the correct diagnosis as well as its complications, relapse and treatment failure.

Keyword: Vasculitis, Churg Strauss Syndrome, Gangrene, Asthma

Introduction:
Churg- Strauss syndrome is a rare primary small vasculitis. Incidence of CSS ranges between 0.9 and 4 per million people depending upon the location considered and the classification criteria used. CSS is characterized by the presence of asthma, eosinophilia and granuloma. From 1988 to 1998, 14 cases of CSS per million inhabitants were diagnosed in the Norwich Health Authority (UK)\(^1\), where the annual incidence of Churg – Strauss syndrome, diagnosed using Lanham’s criteria, was 3.1 per million inhabitants. In 1994 Chapel Hill Consensus criteria defined the disease as an eosinophilia rich and granulomatous inflammation involving the respiratory tract and necrotizing vasculitis involving the medium sized vessels associated with asthma and eosinophilia. Very few cases are reported from India. We are reporting a case of CSS with rare presentation.

Case report:
In August 2010, a 27 year old man presented with 3 months history of ulcer over both legs, weakness of both foot and both hands of one month duration, blackish discolouration of fingers on both sides for 10 days with history of weight loss. There was no past history of URI or LRI or hemoptyisis. Examination
showed gangrene of right four fingers, tips of left thumb and little fingers. He had right wrist and both foot drop, healed ulcers and papery scars over both legs. Investigations showed ESR of 28mm/hr, eosinophilia 15%, CPR >6mg/l, RF >128IU/ml, normal renal and liver function tests. Urine examination was normal. HIV- Non Reactive, HBsAg-Neg, PR3ANCA, MPO-ANCA, ANA (Elisa) - Neg, HRCT Lung and USG abdomen- normal. Nerve Conduction Study (NCS)-showed features of mononeuritis multiplex. Sural nerve biopsy- necrotizing vasculitis with marked acute and chronic axonopathy. Initially with a diagnosis of unclassified vasculitis. patient was treated with IV methyl prednisolone pulse 1gm for 3 days followed by oral prednisolone 1mg/kg, tapered and maintained at 20mg/day. Patient also received IV Cyclophosphamide (15 mg/kg) monthly pulse for 6 months followed by IV cyclophosphamide pulse once in 3 months and was on regular follow up. In November -2011 readmitted with complaints of cough, breathlessness on exertion and blood stained sputum of 3 months duration. Examination showed acne, bilateral wheeze, right hand amputated fingers . HRCT lung showed patchy nodular infiltrates in both lung fields, suggestive of vasculitis. Renal function tests and urine examination were normal. P ANCA was 4+ positive. Patient was treated with oral prednisolone 30 mg/day, salbutamol nebulisation, antibiotics and other supportive measures. In February 2012 readmitted with complaints of burning sensation over both feet of 3 days duration. Clinical examination showed bilateral wheeze. Investigations showed blood eosinophilia 65%, Urine albumin 4+, 10-15 puscells, urine PCR -1.5, blood urea 60 mg/dl, Sr creatinine 2.2 mg/dl; Patient treated with Oral Prednisolone 1mg/kg/day and planned for IV rituximab therapy 500mg infusion once a week for 4 weeks. 

Nodules over face (Churg Strauss granuloma) Picture showing papery scars on legs. In right hand, 2nd to 5th fingers amputated.

Pictures : We have only these two pictures of the lesions which show papery scars over legs, amputated fingers of right hand and nodules over face. We have no other pictures.
RHEUMATOLOGIST OPINION:
This article is submitted from the Dept. of Rheumatology, MMC under the guidance of Professor and HOD of Rheumatology and his opinion is Churg - Strauss syndrome.

Discussion:
Churg – Strauss syndrome (CSS) is a rare small vessel vasculitis associated with anti-neutrophilic cytoplasmic antibodies (ANCA) mainly targeting myeloperoxidase (MPO)-ANCA, a disease entity that is similar to but closely distinct from polyarteritis nodosa (PAN), that involves medium sized arteries and is not usually accompanied by ANCA. Churg – Strauss syndrome (CSS) is usually diagnosed based on the following criteria. Lanham criteria\(^2\) for the classification of Churg – Strauss syndrome

All three required (Sensitivity 95%, Specificity 95%)

1. Asthma
2. Eosinophilia >10% (1500/mm\(^3\))
3. Systemic vasculitis involving two or more extrapulmonary organs.

1990 ACR classification criteria\(^3\) for Churg – Strauss syndrome

<table>
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<tr>
<th>Criteria</th>
<th>Definition</th>
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<tr>
<td>Asthma</td>
<td>History of wheezing or diffuse high pitched rhales on expiration</td>
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<tr>
<td>Eosinophilia</td>
<td>Eosinophilia &gt;10% of white blood cell differential count</td>
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<tr>
<td>Mononeuropathy/polyneuropathy</td>
<td>Development of mononeuropathy, multiple mononeuropathies or polyneuropathy (glove, stocking distribution) attributable to vasculitis</td>
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<tr>
<td>Pulmonary infiltrates non-fixed</td>
<td>Migratory or transitory pulmonary infiltrates on radiographs (not including fixed infiltrates) attributable to systemic vasculitis</td>
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<tr>
<td>Paranasal sinus abnormality</td>
<td>History of acute or chronic paranasal sinus pain or tenderness or radiographic opacification of the paranasal sinuses</td>
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<tr>
<td>Extravascular eosinophils</td>
<td>Biopsy including artery or venule showing accumulations of eosinophils in extravascular areas</td>
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For classification purposes, a patient with vasculitis shall be said to have CSS if at least four of these six criteria are present. The presence of any four or more criteria yields a sensitivity of 85% and a specificity of 99.7% Adapted from Masi et al\(^3\).Pathogenesis is complex and unclear. It involves ANCA directed against MPO, endothelial damage,tissue infiltration of eosinophils. Th2 lymphocytes, cytokines like TNF\(\alpha\), IL1\(\beta\), IL-4, IL-5 and IL-13.Churg – Strauss syndrome has three phases\(^5\). The first prodromal period may last for years and consists of asthma and other allergic manifestations like allergic rhinitis and or nasal polyposis. The second phase is characterized by the onset of peripheral blood and tissue eosinophilia. The third phase is systemic vasculitis usually associated with remission of eosinophilic infiltrating disease. These three phases do not necessarily follow one another in this order.

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Clinical features of CSS are protean with mean age at the time of diagnosis is 48.2 ± 14.8 years with sex ratio of around 1. CSS patient may have fever or weight loss. Asthma is the central feature of CSS and precedes the systemic manifestations nearly all cases.

**Clinical manifestations**

- **General Symptoms:** Fever, Weight Loss
- **Pulmonary Manifestations**
  - Asthma (Late Onset, Precedes atleast 10 years before vasculitis)
  - Pulmonary infiltrates
- **Pleural effusion**
- **Ear, Nose and throat**
  - Sinusitis (70%)
  - Allergic rhinitis
  - Nasal Polyps.
- **Neurological Manifestations**
  - Peripheral neuropathy (50-78%)
  - Mononeuritis multiplex (60-71%)
  - Asymmetrical Polyneuropathy (5-29%)
  - Symmetrical Polyneuropathy (0-35%)
  - CNS involvement rare
- **Cutaneous lesions (40-70%)**
  - Purpura, papules, vesicles, bullae, skin necrosis, Raynaud’s phenomenon,
  - Subcutaneous nodules
  - Toe or finger ischemia
- **Renal involvement (16-49%)**
  - Focal segmental glomerulonephritis
  - Usually mild and carries poor prognosis.
- **Cardiac Involvement (60%)**
  - Cardiomyopathy
  - Myocarditis
  - Pericardial effusion
  - Mitral regurgitation
  - Myocardial fibrosis
  - Arrhythmias
  - Gastrointestinal involvement (37 – 62%)
  - Abdominal pain
  - Diarrhea
  - Bleeding
  - Perforation
  - Other Manifestations
    - **Arthralgias, Arthritis**
    - uveitis, episcleritis, nodules, retinal vasculitis,
    - Lymph adenopathy, hepatosplenomegaly

Main histology of CSS are angitis and extravascular necrotizing granuloma usually accompanied with eosinophilic infiltrates.
Churg – Strauss Syndrome is a rare ANCA associated small vessel vasculitis usually presenting with asthma, hypereosinophilia, extravascular granuloma and systemic small vessel vasculitis and occurs in individuals with asthma and allergic rhinitis. But our case presented with initial features of vasculitis (Wt. loss, gangrene, Leg ulcers, mononeuritis multiplex) eosinophilia and MPO ANCA-negativity. 1) During followup, after 16 months from the initial presentation of vasculitis, our patient developed asthma, diffuse nodular infiltration of lung and pANCA (MPO) Positivity. Usually asthma precedes atleast 10 years to vasculitic manifestation. Lung infiltrates are usually patchy and transient in CSS. 2) Granuloma is non specific. Our patient developed cutaneous extravascular granulomotous lesion over face and forearms during follow up.3) Our patient developed eosinophilia along with new onset of renal failure which is suggestive of renal vasculitis and failure of I.V.Cyclophosphamide, a time tested drug for the management of ANCA- associated vasculitis.

**CONCLUSION:**

v Vasculitis will have protean manifestations. v Churg-Strauss Syndrome (CSS) may have atypical presentation like in our case, early age of onset (27 years), absence of allergic rhinitis and sinusitis, initially with digital gangrene, later development of asthma, nodular pulmonary infiltrates, cutaneous Churg-Strauss granuloma and pANCA postivity later. v Regular follow up and repeated investigations are must to arrive a correct diagnosis, to look for the development of new organ involvement, relapse and treatment failure. v This case was reported for its rarity and atypical presentation and evolving nature of vasculitis during its course.

**Reference:**


3. Masi AT et al. The American College of Rheumatology 1990 criteria for the classification of

