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An Interesting Case of Anca Associated Vasculitis

Medical Science

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ABSTRACT

ANCA associated vasculitides are systemic autoimmune diseases that affects small to medium sized blood vessels. They often are associated with the serologic presence of antineutrophil cytoplasmic antibodies (ANCAs) against cytoplasmic proteins expressed on the surface of neutrophils.

Here we discuss a case of 50 years old female patient of ANCA associated vasculitis and digital gangrene with history of asthma but without significant eosinophilia and renal biopsy suggestive of crescentic glomerulonephritis.

The patient was treated on the lines of Cresentic glomerulonephritis, started on cyclophosphamide therapy along with steroids. There are multiple case reports of limited forms of Eosinophilic granulomatosis of polyangitis which showed the absence of eosinophilia,however the tissue biopsy showed presence of leucocytoclastic vasculitis. Thus, conclusively, there should be very high suspicion in patients with asthma who are difficult to control and associated systemic features of vasculitis. Preferably the renal biopsy to be performed in all cases who present with features of vasculitis and serological positivity to assess the extent of damage and to direct the treatment plan.

INTRODUCTION

ANCA associated vasculitides are systemic autoimmune diseases that affects small to medium sized blood vessels.[1] They show similar focal necrotizing lesions involving arterioles, venules, and capillaries.[2] They often are associated with the serologic presence of antineutrophil cytoplasmic antibodies (ANCAs) against cytoplasmic proteins (proteinase 3 [PR3] and myeloperoxidase [MPO]) expressed on the surface of neutrophils.[2]

There are three forms of ANCA associated vasculitis i.e. granulomatosis with polyangitis(GPA)(previously known as wegener's granulomatosis), eosinophilic granulomatosis with polyangitis(EGPA)(previously known as churg strauss syndrome) and microscopic polyangitis.(MPA)[3] They form part of the ANCA-associated category of vasculitides, although not all patients with GPA, MPA, or EGPA have ANCAs.[4] They often affect the kidneys and the upper and lower respiratory tract.[2]

GPA is characterized by granulomatous inflammation of the upper and lower respiratory tract[5]. Mainly associated with ANCAs against PR3[2]

MPA is characterized by small vessel vasculitis without granulomatous inflammation[5] .Mainly associated with ANCAs against MPO[2]

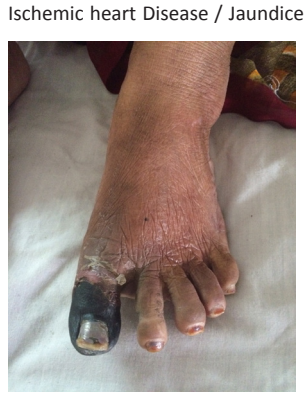
EGPA is characterized by granulomatous inflammation, asthma, and eosinophilia[5] .Mainly associated with ANCAs against MPO[5]

The significant and important potential outcome of ANCA-associated vasculitis is that it can result in damage to the vessel wall leading to vessel occlusion, tissue ischemia, and localized necrosis. These damaging effects all contribute to the clinical manifestations of GPA, MPA, and EGPA and may involve multiple organs of the body.[3,6,7]

Here we discuss an interesting rare case of ANCA associated vasculitis presented with digital gangrene.

CASE PRESENTATION

A 50 years old female, housewife, Known case Asthma since 15 years (On Tablet Deriphylline retard and Aerocort MDI) and hypertension since 3 years on regular medications was brought to DHIRAJ GENERAL HOSPITAL by relatives with complaints of Breathlessness on exertion since 3 months which was insidious in onset - Initially grade II MMRC → progressed to grade-III MMRC at present (No orthopnoea, no PND); Blackening of left great toe since 1 month which was gradually progressive involving whole of the toe upto metatarsophalangeal joint, associated with throbbing pain(on & off); Numbness & Tingling sensations over left toe since 1month ;Blackening of tip of right ring finger since 20 days which was gradually progressive, associated with throbbing pain(on & off).No history of Diabetes / Tuberculosis / Ischemic heart Disease / Jaundice / Blood transfusion.



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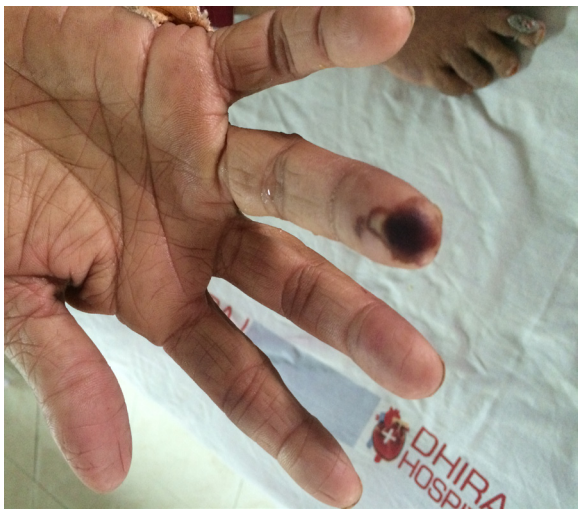


Patient was averagely built ,afebrile ,conscious and oriented. Pulse showing sinus tachycardia, Blood pressure was 106/76 mm of Hg, blood pressure show no significant difference in all four limbs. Respiratory Rate was 22/min, thoraco-abdominal,SPO2 97 % at room air. Pallor present; No Oedema/ Lymphadenopathy/ Icterus/ Cyanosis/ Clubbing.

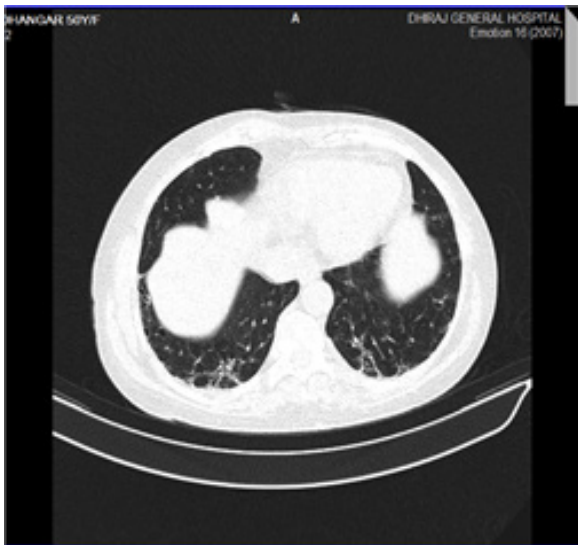
On respiratory system examination bilateral minimal Rhonchi present in mid and lower zones. Cardiovascular System S1S2 +, no murmur ; Central nervous system examination showing numbness and tingling sensations over left toe till metatarsophalangeal joint, ankle reflex bilateral diminished, all these findings suggestive of bilateral symmetrical motor sensory(mixed) peripheral neuropathy. Rest neurological examination was normal. Abdominal system soft, no organomegaly.

On blood investigations in complete blood count **Hb** was **8.6 gm%**, **total count** was **11600 cell/cumm**(N-69, L-22, E-4, M-5), Platelets 4.18 lacs/cumm; **ESR** was raised **50 mm/hr**; Peripheral blood smear was normocytic normochromic picture; Absolute eosinophil count was in normal range 374 per cumm; Random blood sugar 133 mg/dl; **Urine routine microscopy** suggestive of **proteinuria +++, RBCs:10-12/hpf ,Pus cells:5-6/ hpf, RBC casts and granular casts are present**; In renal function tests, **Urea 75 mg%** and **Serum creatinine** was raised **2.8 mg%**; Liver function tests and Serum electrolytes were within normal limits; S.Calcium 8.5mg/dl, S.phosphorus 4.2mg/dl, S.Uric acid 6.6 mg/dl; PT INR was 1.014; HIV/ HbsAg/ HCV results negative; Thyroid stimulating hormone 2.516 u/ml; Serum ferritin and Serum Vitamin B_{12} level were within normal limits; **RA factor** was borderline **19.663 IU/ml**; CRP level 7.2 mg/L.

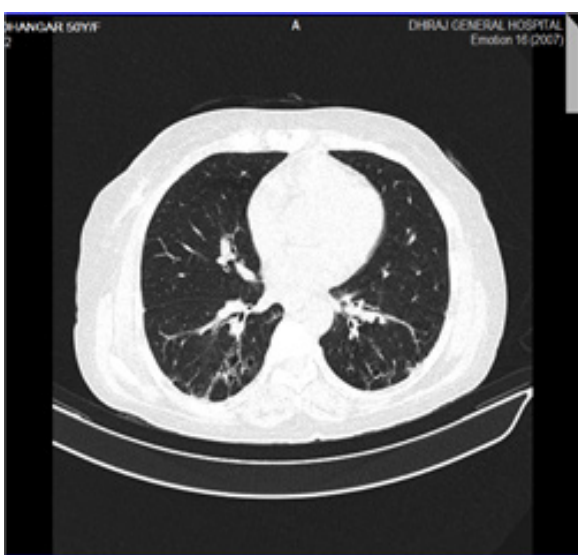
ECG showing **Sinus Tachycardia**; Chest Xray PA view and USG Abdomen pelvis Normal,

ANA profile was sent which is Negative, **ANCA was sent which reveals positive(P-ANCA: Strongly positive-by IF assay; by ELISA-Anti MPO positive; C-ANCA: Negative; Initial dilution-1:20, End point titre-1:640)**

Pulmonary function test was Normal, **CT Thorax(plain) suggestive of thin fibrous strands in bilateral lower zones, few small air filled cysts in both lungs predominately in subpleural region.**



(fibrotic bands seen)



(few small air filled cyst)

2D Echo was normal, LVEF 60%

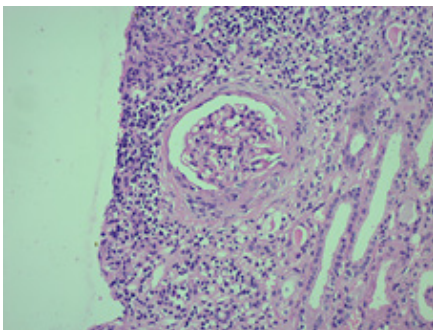
NCV shows median sensory-motor neuropathy & right peroneal and right tibial neuropathy

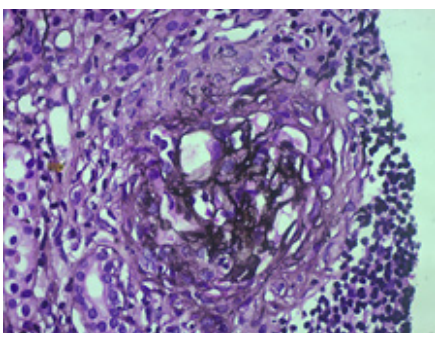
Arterial doppler of left lower limb and right upper limb showed atherosclerotic changes,

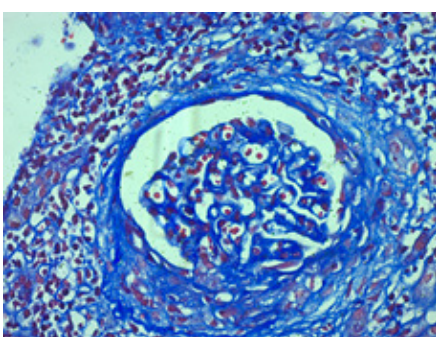
Renal biopsy was done which shows,

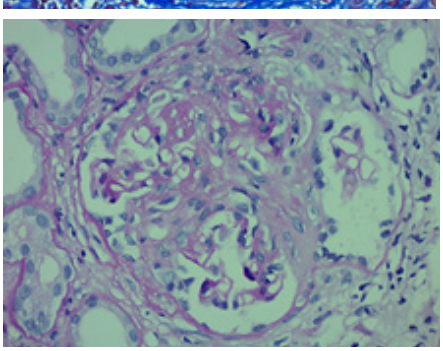
- 9 glomeruli--- in which 5 showing crescent.
- 4/5 showing fibrous/fibrocellular crescents.
- Remaining 4 glomeruli are normal with no necrotizing lesions.
- Mild focal interstitial fibrosis seen.
- IF study- Negative.
- The immunofluorescence findings are consistent with **pauci-immune crescentic glomerulonephritis**. This appears

to be a burnt out lesion with only occasional cellular crescents seen.









DISCUSSION

This patient presented with features suggestive of systemic vasculitis syndrome which on serological evaluation directed the differentials towards either Churg strauss syndrome or Microscopic polyangitis.

She underwent renal biopsy in view of ANCA positivity associated with renal dysfunction and active urinary sediments.

The renal biopsy suggested presence of cresentic glomerulonephritis, however, no evidence of necrotizing vascuitis could be identified. Scattered neutrophils, some eosinophils and periglomerular fibrosis was seen. The possibility of GPA was ruled out clinically as well as absence of granulomatous lesions in the renal biopsy.

The difficulty of differentiating between EGPA and MPA on the basis of biopsy is great considering the similar features, however clinically presence of asthma points towards EGPA.

The patient was treated on the lines of Cresenteric glomerulonephritis, started on cyclophosphamide therapy along with steroids.

The ACR criteria proposed the following six criteria for diagnosis of Churg-strauss syndrome. The presence of four or more criteria yields a sensitivity of 85% and a specificity of 99.7%.[8] which is-

- Asthma(wheezing, expiratory rhonchi)
- Eosinophilia >10% in peripheral blood
- Paranasal sinusitis
- Pulmonary infiltrates(may be transient)
- Histological proof of vasculitis with extravascular eosinophils
- Mononeuritis multiplex or polyneuropathy

It defines the disease (EGPA) as presence of 4/6 features which has very specificity ,which is not fully fulfilled in the present patient but considering the fact that disease has evolving characteristic and renal biopsy suggestive of burnt out lesions, the absence of eosinophils may be indicative of postvasculitic phase.[9,10,11]

Even though defining the disease does play a role in understanding the epidemiology of the disease, the treatment is mainly directed depending on the severity of the organ damage.

There are multiple case reports of limited forms of EGPA which showed the absence of eosinophilia, however the tissue biopsy showed presence of leucocytoclastic vasculitis, thereby fulfilling the criteria.[12]

Considering the rarity of the occurrence of the EGPA, diagnosing the disease helps in understanding the disease characteristics greatly.

The presence of gangrene in this case might be related to the history of hypertension and also atherosclerotic changes noted in arterial doppler.

Thus, conclusively, there should be very high suspicion in patients with asthma who are difficult to control and associated systemic features of vasculitis. Preferably the renal biopsy to be performed in all cases who present with features of vasculitis and serological positivity to assess the extent of damage and to direct the treatment plan.

REFERENCES

1. Jennette JC, Falk RJ, Andrassy K, et al. Nomenclature of systemic vasculitides. Proposal of an international consensus conference. Arthritis Rheum. 1994;37(2):187-192.
2. Pallan L, Savage CO, Harper L. ANCA-associated vasculitis: from bench research to novel treatments.Nat Rev Nephrol. 2009;5(5):278-286.
3. Bosch X, Guilabert A, Espinosa G, Mirapeix E. Treatment of antineutrophil cytoplasmic antibody associated vasculitis: a systematic review. JAMA. 2007;298(6):655-669.
4. Falk RJ, Jennette JC. ANCA disease: where is this field heading? J Am Soc Nephrol. 2010;21(5):745-752.
5. Langford CA. Vasculitis. J Allergy Clin Immunol. 2010;125(2 Suppl 2):S216-225.
6. Gota CE, Vasculitis: Introduction. The Merck Manual for Healthcare Professionals http://www.merckmanuals.com/professional/musculoskeletal_and_connective_tissue_disorders/vasculitis/overview_of_vasculitis.html?qt=red%20blood%20cell%20casts&sc=&alt=sh. 2008.Masi AT, Hunder GG, Lie JT, et al. The American College of Rheumatology 1990 criteria for the classification of Churg-strauss syndrome (allergic granulomatosis and angitis). Arthritis Rheum. 1990 Aug. 33(8):1094-100.

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7. Gómez-Puerta JA, Bosch X. Anti-neutrophil cytoplasmic antibody pathogenesis in small-vessel vasculitis: an update. Am J Pathol. 2009;175(5):1790-1798.
8. Masi AT, Hunder GG, Lie JT, et al. The American College of Rheumatology 1990 criteria for the classification of Churg-strauss syndrome (allergic granulomatosis and angitis). Arthritis Rheum. 1990 Aug. 33(8):1094-100.
9. Churg J. Churg-Strauss syndrome.In: Thurlbeck WM, Churg A, editors.*Pathology of the lung*. 2nd ed. New York: Thieme Medical Publishers; 1995.p. 425–435
10. Lanham JG, Churg J. Churg-Strauss syndrome.In: Churg A, Churg J, editors.*Systemic vasculitides*. New York: Igaku-Shoin; 1991.pp. 101–120.
11. Lanham JG, Elkon KB, Pusey CD, Hughes GRV. Systemic vasculitis with asthma and eosinophilia: A clinical approach to the Churg-Strauss syndrome.*Medicine (Baltimore*) 1984; 63: 65–81.
12. Lie JT. Limited forms of Churg-Strauss syndrome.*Pathol Annu* 1993; 28: 199-220.