Case Report

Granulomatous interstitial nephritis in granulomatosis with polyangiitis mimicking leprosy: A case report

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Abstract

Granulomatous polyangiitis (GPA) is a small vessel vasculitis commonly affecting the upper and lower respiratory tracts and kidneys. About 90% of the cases are associated with ANCA, namely, PR3-ANCA and MPO-ANCA. Herein, we describe a patient of GPA who presented with anasarca, sensory neuropathy, recurrent upper airway congestion, epistaxis, and rapidly progressive glomerulonephritis. Granulomatous interstitial nephritis and necrotizing granulomatous inflammation of the nasal septum were found on biopsy of the kidney and nasal septum, respectively both of which are rare findings. PR3-ANCA and MPO–ANCA were negative. Fulfilling the ACR criteria, this case of GPA proves that biopsy is still the gold standard of diagnosis.

Keywords: ANCA, granulomatosis with polyangiitis, interstitial lung disease, interstitial nephritis, peripheral neuropathy

Introduction

Vasculitis is an inflammation of vascular walls resulting in organ damage. As per the Chapel Hill Consensus Conference classification, it is classified into large vessel vasculitis, medium vessel vasculitis, small vessel vasculitis, variable vessel vasculitis, single organ vasculitis, vasculitis associated with systemic disease, and vasculitis with probable etiology.[1,2] The antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis includes ANCA against myeloperoxidase and proteinase-3 whereas ANCA negative vasculitis has ANCA that are undetectable by conventional methods or are of unknown specificity.[3] The four criteria laid by the American College of Rheumatology (ACR) 1990 for the diagnosis of granulomatous polyangiitis (GPA) include nasal or oral inflammation, abnormal chest radiograph, abnormal urinary sediment, and granulomatous inflammation.[3,4] The presence of two or more of these four criteria yields a sensitivity of 88% and a specificity of 92%.[4,5] Herein, we describe an unusual case of GPA presented with upper and lower respiratory tract involvement with granulomatous interstitial nephritis and peripheral neuropathy fulfilling the four criteria.[4,5]

Case Report

A 27-year-old male, a resident of northeast India, presented as an outpatient in the department of dermatology in January 2019. He was diagnosed as a case of Hansen's disease since 2013 and was on multidrug therapy (dapsone, rifampin, clofazimine) for the same. His treatment was stopped in September 2015 following which in November 2015 he developed skin lesions on the limbs with tingling and numbness. Hence, treatment was restarted and continued till January 2019 when he complained of tender erythematous skin nodules clinically diagnosed as

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erythema nodosum along with numbness of all the limbs. He also complained of nasal congestion. Slit-skin smear was negative for acid-fast bacilli (AFB). All routine investigations were normal [Table 1]. He was discharged on nortriptyline, gabapentin, and prednisolone in tapering doses.

However, after 3 months, he presented with anasarca, persisting nasal congestion, throat pain, numbness, and loss of sensation of both upper and lower limbs. He was transferred to the medicine department for further evaluation. His blood pressure on admission was 130/80 mmHg, with a heart rate of 110/min. He had a low-grade fever, pitting edema of both lower limbs, and generalized dry scaly plaques. There was no nerve thickening. On systemic examination, he had signs of peripheral neuropathy with impaired fine sensations in both lower limbs.

On detailed evaluation, he had nephritic-range proteinuria which subsequently progressed to nephrotic-range proteinuria suggesting glomerulonephritis with significant red blood cells on urine analysis [Tables 2 and 3]. He also had a clinical picture of chronic nasal septal inflammation. Thus a renal and nasal biopsy was carried out along with non-contrast imaging of the lung. The renal biopsy showed expansion of the interstitium with inflammatory infiltrates along with interstitial edema. There were a few large and small non-caseating granulomas with multinucleated giant cells in the interstitium [Figure 1a]. All the glomeruli were unremarkable. Immunofluorescence showed no immune complex deposits as IgG, IgA, IgM, C1q, and C3 were negative. Based on these findings, the renal biopsy was suggestive of granulomatosis interstitial nephritis. Nasal biopsy showed a necrotizing granulomatous lesion with evidence of leukocytoclastic [Figure 1b and 1c]. Non-contract computed tomography (CT) thorax showed ground-glass appearance in the lower zone of the lungs [Figure 2]. Thus the diagnosis of granulomatosis with polyangiitis was made with a Birmingham vasculitis activity score of 36 though his ANCA was negative.

Table 1: Baseline investigations

Investigations	Results
Hb 14 g %	Total protein 6.4
Plt 180000	Albumin 3.7
TC 6100	SGOT/SGPT 29/38
Creatinine 0.9 mg/dL	Bilirubin 0.6
Slit-skin smear	Negative for AFB

During his hospital stay, he developed a catheter-related bloodstream infection resulting in worsening of renal function for which he received broad-spectrum antibiotics and responded. The glomerulonephritis picture persisted even on recovery from bacteremia along with constitutional symptoms. Hence, after the 7th day of antibiotic with low procalcitonin level, the patient was initiated on methylprednisolone pulse therapy and injection cyclophosphamide (cyclophosphamide-based regime 0.5 g/m^2 fortnightly for 3 to 6 months).[6] His renal function test subsequently improved with proteinuria of 724 mg/24 h. He was continued on oral steroids and injection cyclophosphamide every fortnight for 6 months with BVAS of 13 from 25 on discharge. He received pneumococcal and influenza vaccinations and oral prophylaxis of trimethoprim-sulfamethoxazole. On follow-up, he was responding well to pulse therapy of injection cyclophosphamide with normal

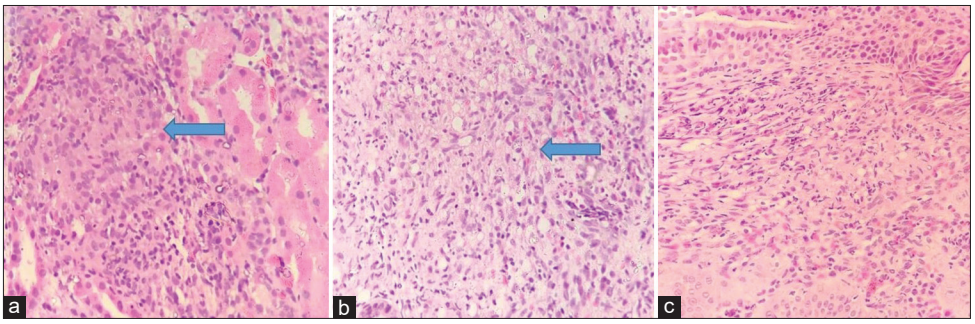

Figure 1: (a) Renal biopsy showing interstitial non-caseating granuloma marked by the arrow (H and E, 400×); (b) Nasal biopsy showing granuloma marked by the arrow (H and E, 400×); (c) Nasal biopsy showing leucocytoclasia (H and E, 400×)

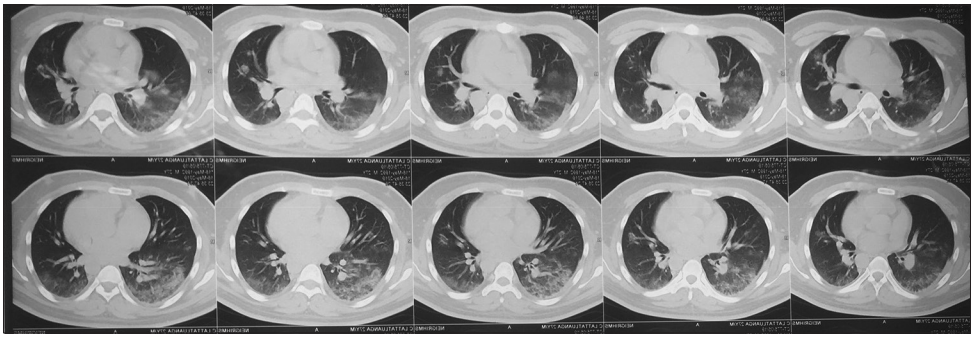

Figure 2: NCCT thorax showing ground-glass appearance in the lower zone of the lungs

Table 2: Investigations

INVESTIGATIONS	On admission	After 10 days of admission	After 1 week of methyprednisolone and cyclophosphamide	After 2 weeks of methyprednisolone and injection cyclophosphamide
URINE ANALYSIS				
	2+	3+	1 +	
	5.5	5.5	5.0	
	1/hpf	9-19/hpf	5.0-9.9/hpf	
Cast cells	1.45	1-3/lpf	1.45-2.90/hpf	
Hy cast	1.45	1.45/lpf	5.0-9.9/hpf	
Path cast	1.45	1.45/lpf	-	
Bact	0-342	0-342/hpf	-	
24 h urine protein	1585 mg	4161 mg	724 mg	
ELECTROLYTES				
POTASSIUM	3.77	4.83	3.64	3.77
SODIUM	142	141	143.7	140.5
CL	109	116	112.3	115.4
iCa	1.31	1.05	1.26	1.02
TCa	2.56	2.05	2.46	1.99
KIDNEY FUNCTION TEST				
Creatinine	0.8	7.5	3.6	0.5
Urea	28	239	132	28
LIVER FUNCTION TESTS				
Total bilirubin	1.2	0.6	0.8	0.9
SGOT	49	72	41	67
SGPT	53	25	26	89
AlkPhos	324	303	223	193
Protein	5.6	4.3	5.2	6.0
Albumin	2.9	2.2	3.1	3.7
TG	186			
CHOL	116			
HDL	23			
HEMATOLOGICAL INVESTIGATIONS				
Hb	12	6.8	7.7	10.3
TC	6300	6100	6300	10000
DC	N75/L19/M05/E01	N75/L16/M08/E01	N78/L20/M02/E00	N92/L05/M03/E00
PLT	180000	200000	100000	300000
MCV	84	85	87	80
ESR	11	15	24	21
PS	Mild anisopoikilocytosis with normoblastic normochromic RBC, admixed with microcytic hypochromic RBCs, teardrops, polychromatophils.			
Procalcitonin		>2	<0.5	<0.5
CULTURES				
Blood culture		Streptococcus		Sterile
Central line tip		Streptococcus with *Candida albicans*		
Imaging and Biopsy report				
Ultrasound of abdomen and pelvis	Enlarged liver with raised echogenicity. Normal kidney size with corticomedullary differentiation			
Echocardiography	Normal LV function.No features of IE			
NCCT thorax	Diffuse areas of ground-glass opacities in both lung fields			
Renal biopsy	Granulomatous interstitial nephritis showing the expansion of the interstitium with inflammatory infiltrates (composing of lymphocytes, plasma cells, and eosinophil cells) and edema with focal areas of large and small noncaseating granulomas with multinucleated giant cells. Immunoflorescence shows IgG 1+, IgA trace, IgM negative, C3 trace, and kappa and lambda 2+			
Biopsy nasal mucosa	A necrotizing granulomatous lesion with leucocytoclasia.			

Table 3: Serological investigations

Investigations	Results
PR3-ANCA and MPO- ANCA	Negative
ASO	Negative
Widal	Negative
Cortisol (01/05/2019)	15.58
TSH	1.63
FT3	2.85
FT4	0.99
H/H/H	Negative
Uric acid	5.7
Phosphorus	4.9
CRP	26 (high)
s. ACE	9 U/L

hematological, renal, liver function tests (Hb 12 g %, creatinine 0.8 mg/dL, AST 28, ALT 41, protein 5.7 gm/dL, albumin 3.7 gm/dL, 24 h urine protein <150 mg).

Discussion

Our patient presented with ANCA negative GPA having upper, lower airway involvement, sensory neuropathy with rapidly progressive glomerulonephritis with nasal biopsy suggestive of the necrotizing granulomatous lesion with leukocytoclastic and renal biopsy suggestive of granulomatous interstitial nephritis. Though the diagnosis of small vessel vasculitis includes ANCA positivity either to PR3 or myeloperoxidase, this is one rare case where ANCA was negative with three organ involvement, which was upper airway, lungs, and kidneys.[6-8] GPA is a disease with diverse manifestations involving the respiratory tract and kidneys with positive biopsy findings and ANCA being positive.[9] The presence of granulomatous interstitial nephritis in GPA is rare. In a case report of 32 patients with granulomatous interstitial nephritis by Mignon *et al.*, 28% were due to drugs, 16% were due to GPA, and 9% were attributed to sarcoidosis and tuberculosis.[10] This paper is important to primary healthcare physicians because patients presenting with clinical manifestations suggesting more than one organ involvement mandates a thorough workup to rule out inflammatory disorders like vasculitis, connective tissue diseases, and immunological disorders.

Conclusion

This case shows the rare presentations of GPA; firstly, the granulomatous interstitial nephritis on renal biopsy; secondly, nasal biopsy showed necrotizing granulomatous lesions; and thirdly, ANCA negativity despite the severity of the disease. Hence, the ACR criteria with a biopsy-proven granulomatous involvement are still the gold standard method of diagnosing the disease.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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