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BMH Medical Journal 2015;2(2):47-52 **Case Report**

A Case of ANCA Negative Pauci-immune Crescentic Glomerulonephritis in Mixed Connective Tissue Disease

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Abstract:

Pauci-immune crescentic glomerulonephritis (CrGN) is one of the most common causes of rapidly progressive glomerulonephritis. The majority of patients with pauciimmune CrGN have circulating antineutrophil cytoplasmic autoantibodies (ANCA). Approximately 10% of systemic vasculitides patients test negative for ANCA. Majority of the ANCA negative pauciimmune CrGN described in the literature have not shown associations with connective tissue diseases. Only isolated case reports of associations with systemic lupus erythematosus and scleroderma have been described. We report the case of a 24 yr lady who was diagnosed to have a pauciimmune crescentic glomerulonephritis on renal biopsy, and was found to be ANCA negative. Subsequently her collagen profile revealed a mixed connective tissue disease, even though she did not have any other systemic manifestations of the disease at presentation. We presume that antiendothelial antibodies (AECA) may have a role in the pathogenesis of the disease.

Keywords: Pauci-immune crescentic glomerulonephritis, ANCA

Introduction

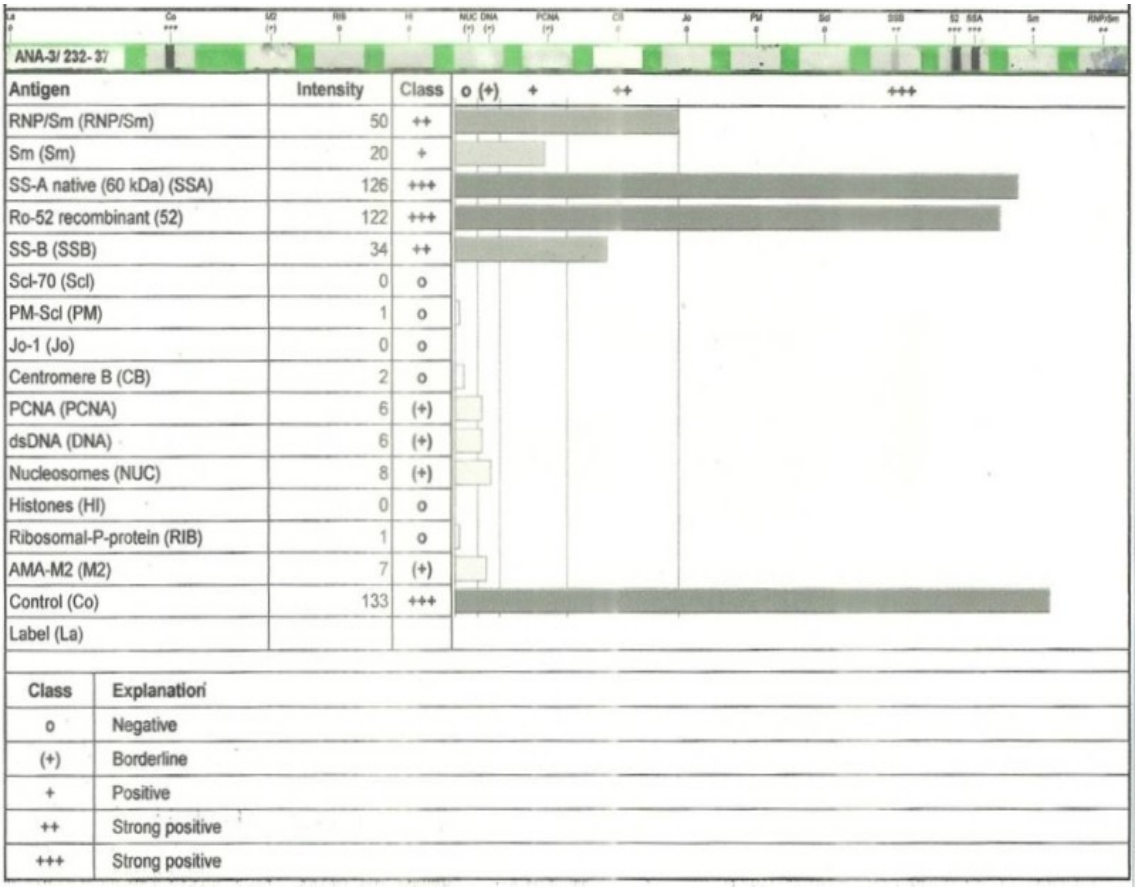
Pauci-immune crescentic glomerulonephritis (CrGN) is one of the most common causes of rapidly progressive glomerulonephritis. The majority of patients with pauciimmune CrGN have circulating antineutrophil cytoplasmic autoantibodies (ANCA). Approximately 10% of systemic vasculitides patients test negative for ANCA. Majority of the ANCA negative pauciimmune CrGN described in the literature have not shown associations with connective tissue diseases. Only isolated case reports of associations with systemic lupus erythematosus (SLE) and scleroderma have been described [1,2].

Case Report

A 24 year old lady, presented with vomiting off and on of 2 weeks duration. She had no other illness in the past. She was a thin built lady. There was no edema or puffiness of the face. Her blood pressure was 140/90 mm Hg. Her cardiovascular, respiratory, neurological examination and abdomen were clinically normal.

Investigations revealed 2+protein and numerous RBCs in urine routine, a 24 hr urine protein of 5.2 gm, Blood urea 23mg/dl and Serum creatinine of 1.6mg/dl. CBC showed Hb 9.6gm/dl, TC 11,200/cmm, ESR 93mm/Ist hr. Lipid profile showed a Serum cholesterol Total 159mg/dl,Serum Triglycerides 129mg/dl, HDL 34mg/dl, LDL 87mg/dl and VLDL 27mg/dl. Total Proteins 7.2g/dl, Albumin 2.9g/dl,Globulin 4.3g/dl,A/G ratio 0.7. HIV, HCV, HBsAg and Mantoux test were negative.

Collagen profile showed ANA (ELISA) positive(3.80AI), antidsDNA negative(20.0IU/ml), p-ANCA(MPO)ELISA negative(4.68U/ml) and c-ANCA(PR3) ELISA negative(4.25U/ml). ANA profile showed RNP/Sm ++, Sm +, SS-A +++, Ro-52+++ and SS-B ++ (**Figure 1**). The collagen profile was consistent with Mixed Connective Tissue Disease.


ANA-3/ 232- 37

Antigen	Intensity	Class
RNP/Sm (RNP/Sm)	50	++
Sm (Sm)	20	+
SS-A native (60 kDa) (SSA)	126	+++
Ro-52 recombinant (52)	122	+++
SS-B (SSB)	34	++
Scl-70 (Scl)	0	o
PM-Scl (PM)	1	o
Jo-1 (Jo)	0	o
Centromere B (CB)	2	o
PCNA (PCNA)	6	(+)
dsDNA (DNA)	6	(+)
Nucleosomes (NUC)	8	(+)
Histones (HI)	0	o
Ribosomal-P-protein (RIB)	1	o
AMA-M2 (M2)	7	(+)
Control (Co)	133	+++
Label (La)		

Class	Explanation
o	Negative
(+)	Borderline
+	Positive
++	Strong positive
+++	Strong positive

Figure 1: ANA profile

Percutaneous renal biopsy showed a core of renal cortex without medulla. Glomeruli were upto 20 in number, 19 of them showing cellular and fibrous crescents, many of them circumferential.Some showed fibrinoid necrosis and hyaline droplets. The tufts showed normal cellularity, capillary walls and patent capillary lumina. Tubules showed focal areas of atrophy with hyaline casts, red cell casts and some showed luminal neutrophils. The interstitium showed focal dense infiltrates of lymphocytes. Blood vessels were unremarkable (**Figures 2** and **3**). Immunoflourescence showed only nonspecific trapping of IgM +. IgG, IgA,C3,C1q, Kappa and Lambda were absent (**Figure 4**).

She was started on Inj. Methyl prednisolone 1g daily for 3 days followed by oral prednisolone 40 mg and 100mg Azathioprine daily.

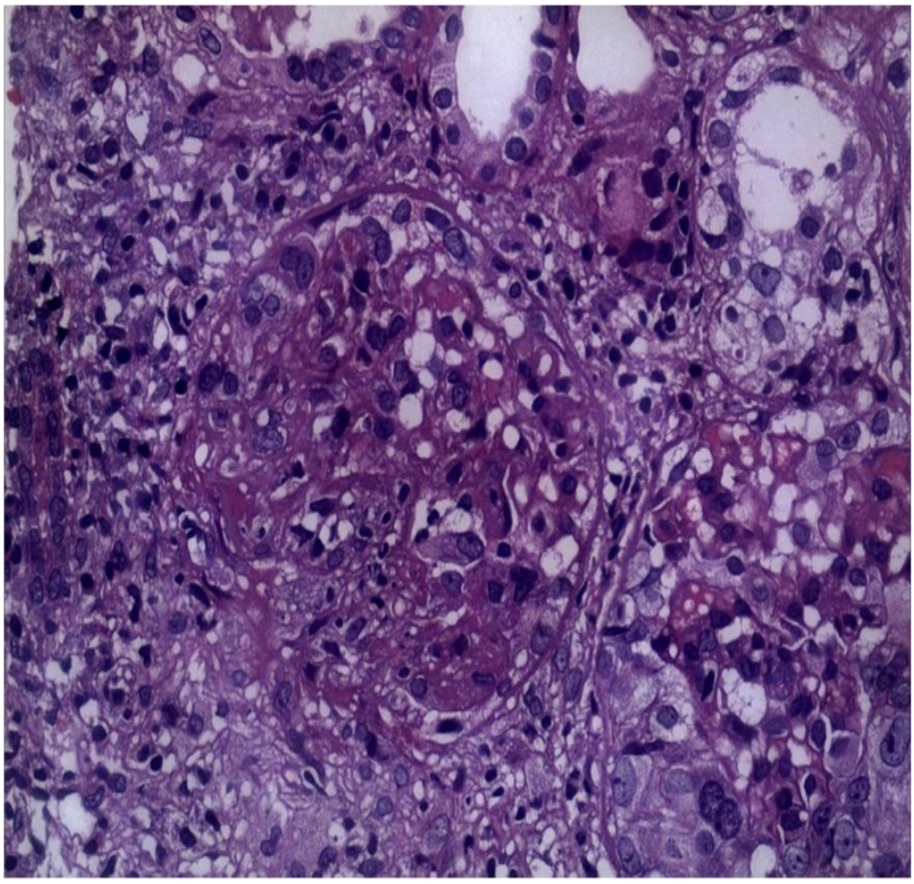


Figure 2: Glomerulus with crescent

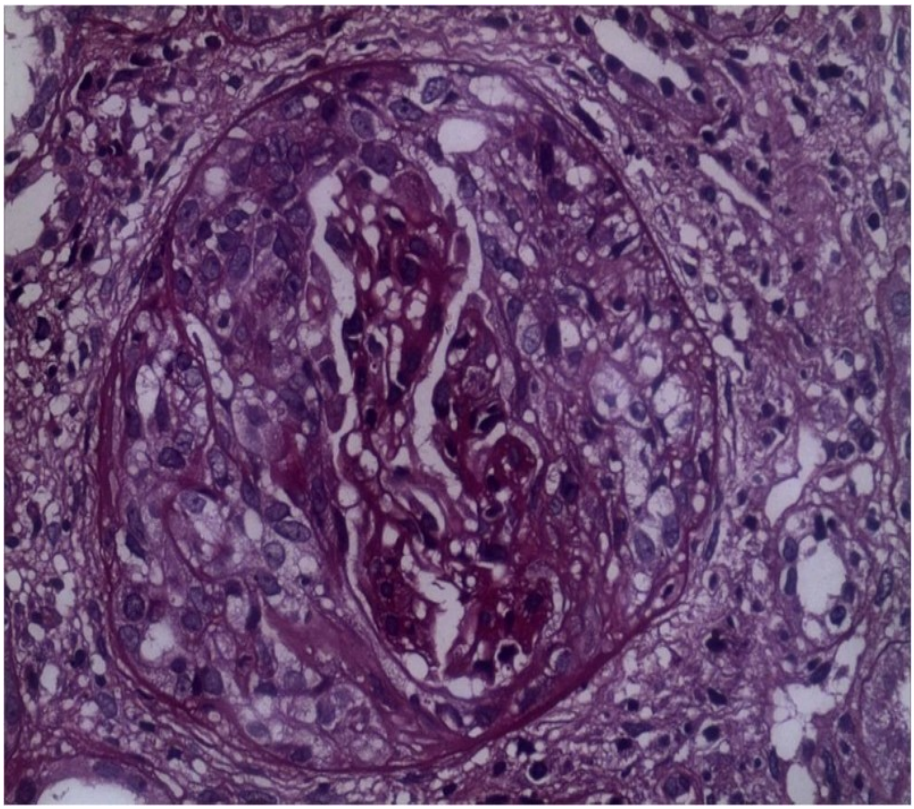


Figure 3: Glomerulus with circumferential crescent

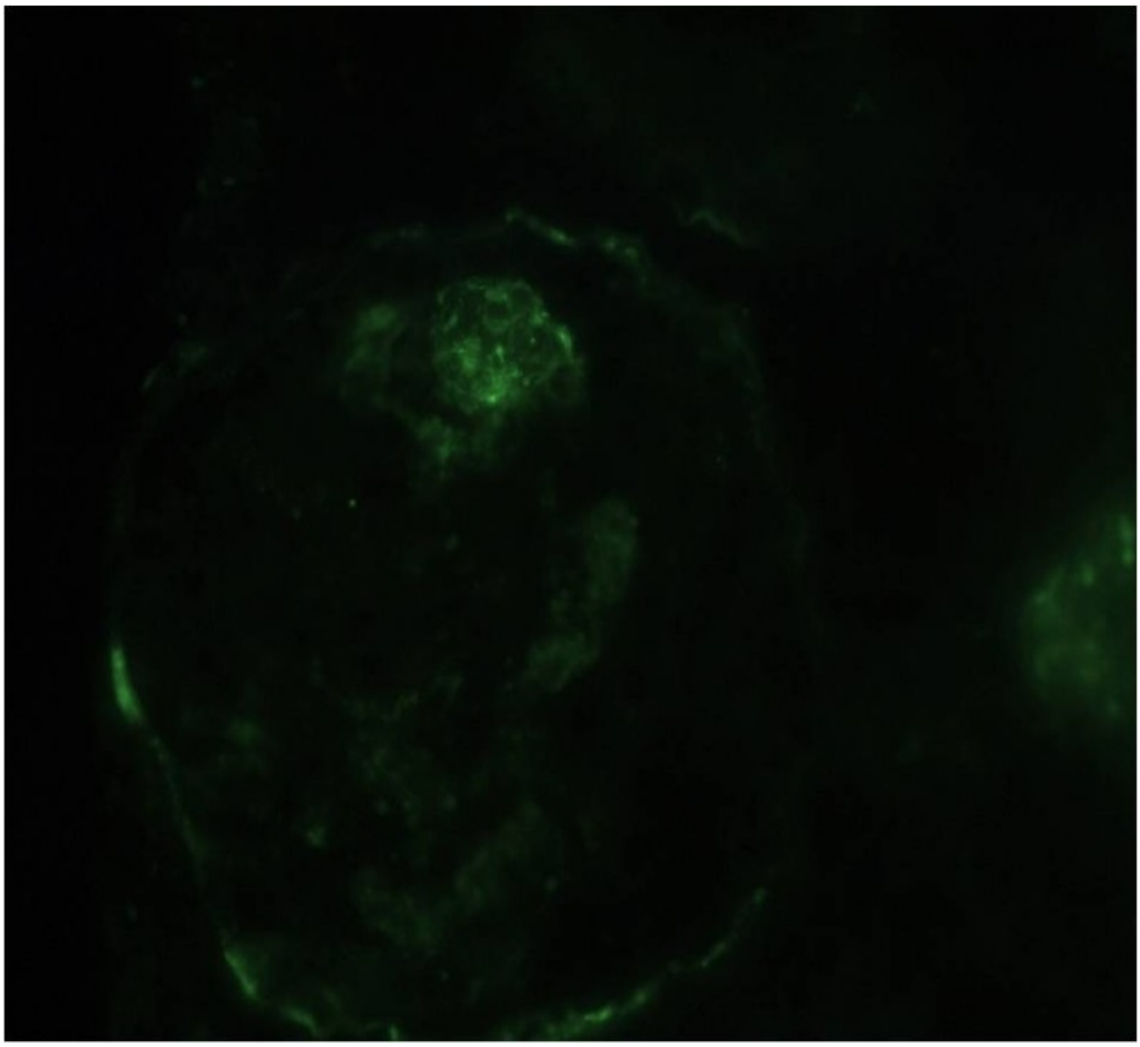


Figure 4: Immunoflourescence showing only nonspecific trapping of IgM

Discussion

There is a wealth of literature on ANCA positive systemic vasculitides with regards to clinical presentation, pathogenesis, pathology and treatment. But, approximately 10% of systemic vasculitides test negative for ANCA and there is only limited literature on the associations of ANCA negative renal limited pauciimmune crescentic glomerulonephritis. Hedger et al investigated 35 patients with ANCA negative rapidly progressive glomerulonephritis and found that they had fewer airway symptoms than the ANCA positive cases [3]. Min Chen et al compared the clinical and histologic variables in 57 ANCA positive patients and 28 ANCA negative cases and found that the ANCA negative patients were much younger and the levels of urinary protein and the prevalence of nephrotic syndrome were significantly higher in the ANCA negative group [4]. Our patient also presented with nephrotic range proteinuria. However, the prevalence of extrarenal involvement was significantly lower in ANCA negative patients. The renal pathology was more severe in the ANCA negative group and the renal survival was poorer [4]. Our case did not have extrarenal manifestations at presentation.

Sampathkumar et al have described 4 cases of ANCA negative pauciimmune crescentic glomerulonephritis with systemic involvement, arthralgias, fever, neurological manifestations, accelerated hypertension and pulmonary renal syndrome [10].

Regarding the associations of ANCA negative pauciimmune crescentic glomerulonephritis, there are isolated case reports in SLE [1], and in a patient with endometrial small cell carcinoma [5], but we could not find published literature of an association with MCTD, even though antiendothelial

antibodies have been described in MCTD [8].

Antiendothelial cell antibodies(AECA) have been implicated to have a causal role in ANCA negative vasculitis. AECA were first reported in the early 1970s during an immunohistochemical study of kidney biopsy specimens. The examined sera were from patients with various rheumatic diseases, including SLE and Scleroderma [6,7]. They have been described in various autoimmune diseases like Granulomatous Polyangitis, Churg-Strauss disease,Takayasu arteritis, Rheumatoid arthritis, Systemic Sclerosis, MCTD, Polymyositis and in other diseases like Inflammatory Bowel Disease and Diabetes mellitus [8]. Antiendothelial antibodies have also been classified into those against either microvascular or macrovascular endothelium [8].

In a study involving sera from 19 patients with ANCA negative glomerulonephritis, 10 were serum IgG-AECA positive and seven bands reactive with endothelial antigens could be blotted. In the sera of 26 ANCA positive cases, 23 were AECA positive and 11 bands could be recognized [9].

Whether there are some other mechanisms, such as lymphocytes or unidentified autoantibodies involved in the pathogenesis of ANCA negative pauciimmune CrGN needs further investigation.

Conclusions

Among patients with pauciimmune CrGN, ANCA negative cases are not rare, but their associations in the literature are limited. Our case exemplifies the rarity of the association with Mixed Connective Tissue Disease.

References

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