Anti Neutrophlic Cytoplasmic Antibodies In Patients with Systemic Vasculitis

Ali Alkazzaz
Babylon University/College of Medicine

Abstract

To evaluate the prevalence of ANCA antibodies in patients with systemic vasculitis and to compare that to its prevalence in patients with different rheumatic diseases and in normal healthy control subjects.

Fifty patients with systemic vasculitis and fifty patients with different rheumatic diseases and one hundred healthy control persons, have been tested for the presence of ANCA antibodies "Anti PR3" and "Anti MPO" by ELISA technique in central public health laboratory in Baghdad-Iraq.

Seventeen patients out of fifty patients 34% with systemic vasculitis were found to be positive for ANCA antibodies ,nine patients were positive for c.ANCA " Anti - PR3 ", eight patients were positive for p.ANCA "Anti-MPO" and two patients were positive for both types with specificity of "99%" and sensitivity of 34%.

All fifty patients with different rheumatic disease were negative for ANCA antibodies , and also the healthy control persons were negative except one who was positive for c.ANCA "Anti-PR3".

ANCA antibodies should be looked for in all patients with suspected vasculitis , their absence will not rule it out ,the test through not highly sensitive 34% however it is highly specific 99% and should alert the attending physician towards further investigation including histopatho-logical tissue diagnosis.

الخـــلاصـــة

الهـــدف:

هو دراسة مدى انتشار مضادات هيولي العدل في المرضى المصابين بالتهاب الاوعيه المنتشر ومقارنتها مع المرضى الصابين بالتهاب المفاصل الرثويه المختلفة والأشخاص الأصحاء (مجموعة ضبط).

طـــرق العـــمل:

تم فحص خمسين مصابا بالتهاب الاوعيه المنتشر وخمسين مريضا بالتهاب المفاصل الرثويه المختلفة ومئة شخصا كمجموعه ضبط للكشف عن وجود مضادات هيولي العدل من النوعين مضاد بروتيناز -3 ومضاد البيروكسايداز النقوي بواسطة طريقة المقايسة المناعية للانظيمات في مختبر الصحة المركزي في بغداد

النتائـــج :

تم الكشف عن سبعة عشر مريضا من اصل خمسين مريضا (34%) كنتيجة موجبة لمضادات هيولي العدل وتسعة من هؤلاء المرضى اظهروا نتائج موجبة لمضاد بروتيناز -3 وثمانية لمضاد بيروكسايداز النقوي واثنان للمضادين في نفس الوقت وكانت نوعية الفحص(99%) وحساسية الفحص (34%).

أما بالنسبة للمرضى المصابين بالتهاب المفاصل الرثويه المختلفة فقد اظهروا نتائج سالبه وكذلك جميع أشخاص مجموعة الضبط ما عدا شخص وان اظهر نتيجة موجبة لمضاد بروتيناز -3.

الاستنتاج:

إن البحث عن مضادات هيولي العدل يجب إن يعمل في كل المرضى المشتبه بإصابتهم بالتهاب الاوعيه المنتشر وان وجود هذه المضادات سوف يثبت تشخيص المرض وان عدم وجود هذه المضادات لا يستبعد التشخيص وان نوعية هذا الفحص عالية عكس حساسية الفحص ويوجه الطبيب المعالج نحو إجراء فحوص أخرى مثل التشريح المرضي التشخيصي.

Introduction

Vasculitis mean inflammation of blood vessels,the blood vessel is primary site of inflamation,the blood vessels wall is thus infiltrated with inflammatory cells and perivascular cuffing does not equate with vasculitis , the consequence of such inflammation is destruction of the vessels wall which is seen on histology as a fibrinoid necrosis .

The vasculitis are a hetrogenous group of relatively uncommon diseases which can arise de novo e.g poly arteritis nodosa , Wegener's granulomatosis or as a secondary feature of an established clinical disease such as Rheumatoid arthritis or systemic lupus erythematosus.

The consequence of such vascular inflammation depend upon size ,site ,and the number of blood vessels involved , vasculitis can occasionally localized and clinically insignificant but commonly is generalized and potentially life threating , especially when small muscular arteries are involved .

The classification of vasculitis is confusing because of the considerable overlap between the different vasculitis syndromes and because the cause of the vasculitis is usually unknown .

In 1993 an Chpel Hill consensus conference [CHCC] which deve-loped definition for the nomenclature of systemic vasculitis based on clinical and laboratory features and classification scheme based on vessel size:-

-Large vessel vasculitis :-

-Medium-sized vessel vasculitis

-Small vessel vasculitis:-

(1)

because of the developments of ANCA antibodies assay some physic-ians feel that the [CHCC] system was inadequate and they developed modification which reflects not only dominant vessel size but also ANCA antibodies , this had split Wegner's granulomatosis , Churg – Strauss syndrome and microscopicpolyang from rest because:-

1- They often involve small arteries.
2- They often associated with ANCA.
3- They associated with high risk of glomeralnephritis.
4- They are diseases which respond best to immunosuppresion with cyclophosphamide.

The ANCA antibodies constitute a family of antibodies directed against various components of neutrophil cytoplasm (2).

The over all incidence of systemic vasculitis is greater than was previously thought and it is estimated to be around " 10 per million per year" , this may represent a real increased incidence with time or increased physician awareness especially with the availability of the ANCA tests(3)(4).

Davies and associates in 1982 were first to report that certain IgG antibodies were directed against intracyptoplasmic antigens of the neutrophil cells in patients with glomeralonephritis and systemic vasculitis.

Vander wode and associates in 1985 termed these as "Antineutrophil Anti - cytoplasmic antibodies and have recognized their connection with Wegener's granulomatosis as well as their apparent specificity for the disease , they also suggested that their titer correlated with the disease activity(5)(6).

The classical methods for the determination of ANCA are immuno-fluorescent methods,with these indirect immunofluorescence echniques two main patterns are recognized , [c.ANCA] , [p.ANCA] and other pattern which non specific stain[a.ANCA].

I- c.ANCA:-Anti-PR3

Show a diffuse granular staining cytoplasm, with some accentuation near center of cells , and the main target antigen is proteinase - 3 (PR3), and this pattern is chiefly found in Wegener's granulomatosis and related disorders.

II- p.ANCA :- Anti-MPO

Show perinuclear to nuclear staining pattern , the main target antigens are : myeloperoxidase (MPO) , granulocyte-

specific elastase ,lactoferrin , lysozyme, cathepsin G , B-glucnronidase and defensin the Anti – MPO is found in microscopic polyangitis and other related disorders.

III- a.ANCA:-

Show non - specific staining (7) (8).

Unlike c.ANCA the p.ANCA is not specific for a single disease , antibodies of p.ANCA positive sera are mainly directed to (MPO) , antibodies to other antigens often result in a similar p.ANCA pattern , they seen in wide spectrum of diseases including most of systemic vasculitis and other diseases like inflammatory bowel disease and IDDM . This makes a clear interpretation and classification of IIF patterns diffcult , threfore every positive IF-ANCA finding specially p.ANCA should be differentiated by ELISA techniques using purified antigens(9).

Immune pathogenesis of ANCA:-

All ANCA associated vasculitis have uncommon , contrary to immune complex vasculitis ,that they occur without complement consumption(10).

1-Neutrophil granuloprotiens (PR3 , MPO) will be released into circulation and may bind indothelium through charges interactions, leading to further proteolytic damage.

2-In the case of PR3 the enzyme may also be carried as immuno-complex with c.ANCA .(11)

The other apparent co-factor in ANCA associated vasculitis is infec-tion leading to activation of neutrophils , therefore it appears that c.ANCA in association with infections is sufficient to induce vasculitic lesions(4)(11).Figure (2)

Diagnosis of systemic vasculitis including Wegener's granulomatosis and necrotizing vasculitis should not be based on the detection of specific ANCA antibodies alone but should be considered in the correct clinical background , tissue biopsy is still needed sometimes to confirm the diagnosis (1)(3).

AIM OF STUDY

The aim of this study was to find out the prevalence of ANCA antibodies in patients with systemic vasculitis in order to help in the evaluation of such patients and in their management and also to find the prevalence of these antibodies in different rheumatic diseases and in healthy normal subjects.

PATIENTS AND METHODS

One hundred patients have been included in this study, they were divided into two groups:-

Group I: -

This included fifty patients with a primary or secondary systemic vasculitis , twenty seven female (54%) their ages ranged between 15-65 years with a mean age of 38 years , and twenty three males (46%) ,their ages ranged between 18-70 years ,with a mean age of 40 years , most of the patients were from three major hospitals in Baghdad (Baghdad teaching hospital alnhrian teaching hospital and AL- Yarmok hospital) , the rest were referred to the central public health laboratory from other hospitals or clinics table (2).

Group II :

This included fifty patients with different rheumatic diseases with out vascular involvement , all of them were from Baghdad teaching hospital , twenty five females(50%) with ages ranged between 14-70 years and a mean age of 40 years, twenty five males (50%) , their ages ranged between 12-63 years with a mean age of 42.5 years table(3).

Group III:control group

This included one hundred healthy persons , their ages ranged between 15-70 years with a mean age of 42.5years.

All the three group subjects were evaluated for the presence of ANCA antibodies and for the presence of ANA table(4)..

The diagnosis was made by the attending physicians using the stan-dard criteria [ACR criteria] before the results of the ANCA test bec-ame available.

All patients in group I had a clinical diagnosis of active systemic vasculitis with laboratory markers of active disease

or a clinical sus-picion of vasculitis was there in some patients.
Patients of group II were also diagnosed according to the ACR criteria and all the patients had clinically active disease.
Twenty patients of group I were already on some sort of immuno suppressive therapy either steroid or with a cytotoxic therapy but none of them were in a clinical remission state.
A tissue diagnosis for vasculitis was only done for one patient who was diagnosed as having Wegener's granulomatosis, the histological result supported the diagnosis.

The detection of ANCA antibodies:-

The identification of auto antibodies against neutrophils ANCA is primarily based on indirect immuno fluorescence (IIF) and followed up by monospecific enzyme linked immunosorbent assay (ELISA) and immunoblots.
In this study ELISA method have used for the detection of both types of ANCA "Anti-PR3 and Anti-MPO"and also for ANA.

The ELISA values:-
For c.ANCA "Anti-PR3":
Positive :- value above 5 U/ML
[Mean +2SD of normal control]
Negative :- value below 5U/ML

For p.ANCA "anti-MPO":-
Positive: value above 8 U/ML
[Mean+2SD of normal control]
negative:- value below 8U/ML
The type of immunoglobin which been tested by ELISA is IgG3 (12)

RESULTS

Patients groupI:-
This group included fifty patients with a different types of systemic vasculitis with a different systemic involvement out of them seven-teen patients were positive for either c or p ANCA antibodies (34%)table(7).

Positive c.ANCA "Anti-PR3"patients:-
Nine patients (18%) out of the total patients with systemic vasculitis were positive for c.ANCA.
The patients were distributed equally between age groups of 20 -39 years, 40-59 years and above 60 years table(6).
Three of them were positive for ANA (33%) table (7), the respiratory system was mostly involved (66.6%) followed by the locomotor system (55.5%) and renal involvement was found in (33.3%) table(8).

Positive p.ANCA "Anti-MPO"patients:-
Eight patients (16%) out of the total patients with systemic vasculitis were positive for p.ANCA , four of them were between age of 20-39 years , (50%) table(6).
Three patients were positive for ANA (37.5%) in the p.ANCA group table(7).
Six patients(75%) had renal involvement either as primary or secondary vasculitis table (8).
From the total number of patients of group I , eighteen patients had renal involvement ,six of them were positive for p.ANCA (33.3%) .
Two patients were positive for both types (c+p) , the first patients was 35 years old male with idiopathic acute renal failure and arthritis of knee joint ,the second patient was a 65 years old female with a clinic-al diagnosis of temporal arteritis and visual impairment but a normal brain scan ,both patients were negative for ANA.
As whole seventeen patients were positive for ANCA antibodies, seven patients between age of 20-39 years ,six patients between age 40-59 years and rest above 60 years table(6).
Renal system and locomotor system have been involved equally followed by respiratory system table(8).
Six patients were positive for ANA (35.2%) table(7).

Patients group II:-
Fifty patients with different rheumatic diseases from different age groups table (3,4) have been tested for both types of ANCA antibodies " Anti-PR3 , Anti-

MPO" and for ANA , none of them was positive for ANCA antibodies,twenty three of them were positive for ANA (46%) .

Control group III:-

One hundered healthy persons from different age groups , all were tested for both types of ANCA antibodies "Anti-PR3 ,Anti-MPO"and also for ANA, all were found to be negative for ANCA except one person who had diabetes on oral hypoglycemic agent , his age was 65 years old was positive for c.ANCA antibody.

ANAwas positive (2.66%) .

The specificity of ANCA antibodies test for detection of systemic vasculitis was 99% but the sensitivity of test was (34%).

The positive predictive value of test was (75%) and the negative predictive value is (94%).

DISCUSSION

In some patients , especially those with limited form of the disease , the diagnosis can difficult to substantiate , with ANCA assay may help in early diagnosis of those patients,given the high specificity of ANCA for Wegener's granulomatosis it may help in making earlier diagnosis , before full range of symptoms , or it may be the decisive diagnositic factor in cases that appear clinically typical but in which a histopath-ological diagnosis cannot be made.

Parlevliet and associates described eleven patients with symptoms that strongly suggested Wegener's granulomatosis , in only two patients a firm histologic diagnosis was made , ten patients had a positive ANCA test which were considered diagnostic and influenced the treatment decisions(13).

A negative ANCA tests will not rule out a diagnosis of vasculitis, however none of untreated patients with active generalized disease remain negative , in most of them , ANCA test were detected a few weeks after the onset of full range of symptoms consequently if vascu-litis is suspected several serial tests determination are recommended.

There was reports about detection of ANCA in other disease e.g type I diabetes mellitus , anti - MPO antibody was detected in the serum patients with type I diabetes mellitus , state of chronic neutrophil activ-ation has been described in diabetes(14).

In this study one healthy subject with type II diabetes mellitus on oral hypoglycimic agent developed weak positive result for Anti-PR3.

In this study the titers of ANCA antibodies were not correlated with disease activity i.e only a positive or a negative value is measured and further studies are needed to correlate the titer with disease activity ,this will help to follow the activity of the disease and will help to distin-guish relapses from other intercurrent illness mainly infections which remain always a threat to patients on immunosuppressive therapy(12).

To compare this study with similsr study by Crista etal , in which one hundered ten patients of presumptive diagnosis of systemic vasculitis and idiopathic crescentric glomeralonephritis with vascular manif-estation , they found twenty-five patients (22.7%) were positive to either c or p ANCA ,however , no histological diagnosis was available (15) table(9).

In another study by Bartunkova-J etal (1010) sera samples from a diff-erent diseases including (systemic vasculitis , autoimmune diseases, isolated glomeralonephritis,inflammatory intestinal diseases ,opthalmic inflammatory diseases and other diseases)have been screened for both anti PR3 and anti MPO " antibodies , they found one hundred and fifteen patients positive for either : twenty-six cases of systemic vascu-litis ,twelve cases of other auto-immune diseases , nine cases of isola-ted glomeralonephritis, seven cases of inflammatory intestinal diseases, six cases of opthalmic inflammatory diseases , and six cases of other diseases(16).

In the Bernhard etal study the overall sensitivity of ANCA was 60%and specificity was :-
-proven biopsy patients:- 160/222 (72%)
-clinical diagnosis patients:- 35/55 (63%)
-control subjects :- 0/119 (0%) (5).
In study by Ronald J etal , described that the perinuclear pattern predominated in patients with renal limited disease ,and all patients with documented necrotizing inflammation in the lung had auto anti-bodies that produced the cytoplasmic pattern , however the perinuclear and the cytoplasmic pattern were found with equal frequency in those patients with glomeralonephritis and pulmonary disease when the pulmonary disease was defined clinically by the prescence of hemo-ptysis or radiographic evidence of nodules , cavites or infiltrates (17).
In this study the cytoplasmic patteren predominated in patients with pulmonary involvement six patients (66.6%) and the perinuclear patt-ern predominated in patients with renal involvement six patients tab-le(8) (75%) .
Regarding c.ANCA antibody to compare with another study by Cohen Tervant etal which detected a specificity of (97%) for Wegener's gran-ulomatosis and a sensitivity of (93%) (18).
Gross etal study detected a specificity (97%) and sensitivity (81%) for proven biopsy disease(8).
In this study four patients with clinical diagnosis of Wegener's granu-lomatosis , three of them were positive for c.ANCA antibodies (75%).
Regarding the p.ANCA it was found to be less specific and sensitive than c.ANCA and it is usually positive in patients with microscopic polyargitis and cresecentric glomeralonephritis , a study by Flak etal, which found that (27/35) (77%) of patients with idiopathic glomera-lonephritis " Microscopic polyangiyis " were positive for p.ANCA,
(5/11) (45%) of lupus nephritis were positive and none in control group(7).
The sensitivity in patients with diffuse systemic vasculitis with renal involvement was (50%)and for Microscopic polyangitis was (80%)(1).
In this study six patients (33.3%) with idiopathic glomeralonephritis or patients with renal impairment associating systemic vasculitis were positive for p.ANCA "Anti-MPO".
Regarding ANA association with ANCA,a study by Saviage etal found that patients who were positive for c.ANCA were (19%) positive for ANA and patients with p.ANCA were (47%)positive for ANA(19).

In this study three patients (33.3%) who were positive for c.ANCA were positive for ANA and three patients (37.5%) who were positive for p.ANCA were positive for ANA i.e six patients of total patients with positive ANCA (35.2%)were positive for ANA.

We conclude that ANCA antibodies detection should be looked for in all patients with suspected vasculitis , their pres-ence will confirm a suspected clinical diagnosis , their abse-nce will not rule it out , the test though not highly sensitive 34% however it is highly specific 99% and should alert the atten-ding physician towards further investigation including histopa-thological tissue diagnosis.

REFERENCES

1-David I,Scottand A. Primary vasculitis,classification of vasculitis , Disease association of ANCA .Oxford text book of Rheumatology 2nd.ed.New York.Oxford University Press,Inc.1998;1319-29
2-Lesavre P. The diagnostic and prognostic significance of ANCA .Renal Failure. 1996.Sep;18(5):803-12.
3-Savage COS,Jones S ,etal : Prospective study of Radioimmuno-assay for antibodies against neutrophil cytoplasm in diagnosis of vasculitis.Lancet.1987;1:1389-93.
4-Cona L.Vasculitis,epidemiology ,pathology and pathogensis.Primer on

Rheumatic Disease 11th ed.Atlanta,Georgin .Arthritis foundation.1997;291-97

5-Noll B. Anticytoplasmic auto antibodies , their immuno diagnostic value in Wegener's granulomatosis .Annals of Internal Medicin. 1989;111:28-40.

6- Andreini B. ANCA in dialysis patients :role for biocmpatibility?.Int-J-Artif – Organs-2000;Feb ;23(2):67-103.

7-Falk l, Jennette C.Antineutrophil cytoplasmic auto antibodies with specificity for myloperoxidase in patients with systemic vasculitis and idiopathic necrotising and cresceutric glomeralonephritis .New England Journal of Medicine.1988;318:1651-7.

8-Gross Wl: Antineutrophil cytoplasmic auto antibodies,auto antigens,and systemic vasculitis.APIMS .1995 Feb;103(2):81-97.

9-Bueno C,Bonfa D .Comparism between Immuno fluorescence techniques and ELISA using whole neutrophil extract and primgranules for detection of antineutrophil cytoplasmic antibodies . Revision of hospital-clinics.1995 March;50(2):101-9.

10-Gross Wl , Reinlold E .ANCA associated vasculitis (Wegener's granulomatosis , Churg – Strauss syndrome , microscopic polyangitis : systemic aspects , pathogensis and clinical aspects Z-Rheumatology – 1995;279-90

11- Peakman M .Necrotizing vasculitis .Basic and clinical Immunology. 1997;224-28.

12- Boomsma M. Predication of relapses in Wegener's granulomatosis by measurment of antineutrophil cytoplasmic antibody levels.Arthritis and Rheumatism. 2000:43(9):2025-33.

13-Parlevliet J. Antibodies to components of neutrophil cytoplasm: a new diagnostic tool in patients with Wegener's granulomatosis and systemic vasculitis .Q J Med.1988:66;55-63.

14- Accardo A . Detection of antimyloperoxidase antibodies in serum of patients with type I diabetes mellitus .Acta Diabetology .1996 Jul:33(2);103-7.

15- Crista A.Clinical evaluation of antineutrophil cytoplasmic auto antibodies in ANCA associated disease .Journales of clinical labe and Immunology .1995:46(2);85-94.

16- Bartunkora J . The spectrum of diseases associated with antineutrophil cytoplasmic antibodies .Cas-Les –Cesk .1995:4;134(1);18-21.

17- Ronald J. Clinical course of antineutrophil cytoplasmic auto-antibody-associated glomeralonephritis and systemic vasculitis.Annals of Internal Medicine .1990;113:656-67.

18- Cohen W . Association between active Wegener's granulomatosis and cytoplasmic antibodies . Arch of Internal Medicine .1989:149;2461-85.

19- Saviage A . Auto antibodies and target antigen in ANCA associated vasculitis. Rheumatology International.1996:16(3);109-14.

Table (1): Documented clinical indication for ANCA antibodies

Systemic vasculitis syndromes	IF "Immuno Flurescence"	Target antigen
Wegener's granulomatosis	c.ANCA,rare p.ANCA	PR3,rare MPO
Microscopic polyangitis	c.ANCA,p.ANCA	PR3,MPO
Churg-strauss-syndrome	p.ANCA	MPO
Unclassified vasculitis	Rare ANCA	Rare PR3,MPO
Polyarteritis nodosa	Rare ANCA	Rare PR3,MPO
Collagen disease and other Rheumatic disorder		
Rheumatoid arthritis	Gs-ANA, p.ANCA, a typical ANCA	Unknown,ANA,rare MPO, loctoferrin
SLE	p.ANCA	MPO,Lactoferrin
Other diseases		
Ulcerative colitis	p.ANCA	Cathepesin-G,Lacto ferrin
Morbus chron	p.ANCA	Cathepesin- G, Lactoferrin

Table(2): Clinical diagnosis of group (I)

	Clinical diagnosis	No.of patients
1	Idiopathic G.N or acute renal impairment with possibility of vasculitis	8
2	SLE vasculitis	7
3	Idiopathic unclassified vasculitis	7
4	Rheumatic arthritis vasculitis	6
5	Wegener's granulomatosis	4
6	Hypersenstivity vasculitis	4
7	Polymylgia rheumatica	3
8	Sjogren syndrome vasculitis	2
9	Henoch-sholine purpura	2
10	Good pasture syndrome	1
11	Temporal arteritis	1
12	Still disease vasculitis	1
13	Dermatomyositis with vasculitis	1
14	Gastrointestinal vasculitis	1
15	C.N.S vasculitis	1
16	Bacterial endocorditis vasculitis	1

Total=50 patients

Table 3: Subsets of group (II) patients of different rheumatic diseases.

	Clinical diagnosis	No. of patients
1	Rheumatoid arthritis	10
2	SLE	10
3	Systemic sclerosis	5
4	JRA	5
5	Seronegative arthritis	5
6	Inflammatory myositis	5
7	Sjogren syndrome	5
8	Overlap syndrome	5

Total=50 patients
ANA positive in(46%)

Table (4):-Sex and age distrubution for different groups

group	No. of patients	sex	No.	%	Mean age(years)
(GI)patients with vasculitis	50	female	27	54%	38
		male	23	46%	40
(GII)patients with different rheumatic disease	50	female	25	50%	40
		male	25	50%	42.5
(GIII)control healthy persons	100	female	50	50%	42.5
		male	50	50%	

Table (5): Patients and control age groups

	Age groups	Group I patients	%	Group II patients	%	Group III control	%
1	0-19 years	6	12	4	8	8	8
2	20-39 years	18	36	19	38	38	38
3	40-59 years	16	32	17	34	34	34
4	Above 60 years	10	20	10	20	20	20

Table (6): age groups for ANCA positive patients

		c.ANCA		p.ANCA	
	Age groups(years)	patients	%	patients	%
1	0-19 years	----	----	---	---
2	20-39 years	3	33.3	4	50
3	40-59 years	3	33.3	3	37.5
4	>60 years	3	33.3	1	12.5
	total	9	52.9	8	47

Table (7): Clinical diagnosisof ANCA positive patients and relation to ANA

ANCA	No.	Sex		Clinical diagnosis	ANA		
		female	male		No	Sex	%
c.ANCA	9	3		Wegener's granulomatosis	1	Male	
			3	Unclassified vasculitis	1	female	
		1		Acute renal failure	1	male	
			1	Temporal arteritis			
			1	C.N.S vasculitis			
		4 44.4%	5 55%		3		33
p.ANCA	8		2	Idiopathic vasculitis	1	Female	
		1	2	Idiopathic G.N,acute renal failure	1	Male	
			1	Temporal arteritis			
		1	1	SLE vasculitis	1	female	
		2 25%	6 75%		3		37.5
c+p ANCA	17	6 35.2%	11 64.7 %				
					6		35.2

Table(8): Systemic involvement in ANCA positive patients

		c.ANCA	
	system	No = 9	%
1	Respiratory	6	66.6
2	Locomotor	5	55.5
3	Skin	4	44.4
4	Renal	3	33.3
5	C.N.S	3	33.3
6	C.V.S	1	11.1
7	C.I.T	-	-
		p.ANCA	
	System	No = 8	%
1	Renal	6	75
2	Locomotor	4	50
3	Skin	3	37.5
4	C.N.S	2	25
5	Respiratory	2	25
6	C.V.S	-	-
7	C.I.T	-	-
		C+p ANCA	
	SYSTEM	NO. = 17	%
1	LOCOMOTOR	9	52.9
2	RENAL	9	52.9
3	RESPIRATORY	8	47
4	C.N.S	5	29.4
5	Skin	6	35.2
6	C.V.S	-	5.8
7	C.I.T	-	-

Table (9): Sensitivity and specificity of ANCA in different studies

	Present study	Bernhard1990	Gross 1993	Crista 1995
Specificity	99% clinical diagnosis	98% clinical diagnosis	97% clinical+patho+logical diagnosis	96% clinical diagnosis
Sensitivity	34% clinical diagnosis	60% clinical + clinical and pathological diagnosis	81% clinical and pathological diagnosis	22.7% clinical diagnosis