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Original Article

Association between perinuclear antineutrophil cytoplasmic antibodies and infection: a retrospective study

Shun-Ban Tai[1,2], Chen-Hung Chen[2], Chun-Chi Lu[2], Ning-Chi Wang[3], Tony Szu-Hsien Lee[4], Deh-Ming Chang[2,5]

[1]Division of Rheumatology/Immunology/Allergy, Department of Internal Medicine, Zuoying Armed Forces General Hospital, Taiwan
[2]Division of Rheumatology/Immunology/Allergy, Department of Internal Medicine, Tri-Service General Hospital, Taiwan
[3]Division of Infection, Department of Internal Medicine, Tri-Service General Hospital, Taiwan
[4]Department of Health Promotion and Education, National Taiwan Normal University, Taiwan
[5]National Defense Medical Center, Taiwan

Background & objectives: Antineutrophil cytoplasmic antibody (ANCA) is often used in laboratory tests to confirm paucicellular vasculitis. However, ANCA is also occasionally found in patients with infectious disorders independent of any vasculitic process. We retrospectively studied the association between perinuclear antineutrophil cytoplasmic antibody (p-ANCA) and clinical conditions, especially infectious diseases. **Methods:** Between 2007 and 2010, 1291 patients (118 p-ANCA-positive and 1173 p-ANCA-negative patients) were tested for ANCA. We selected the total 118 p-ANCA-positive patients, and selected 118 of the 1173 p-ANCA-negative patients randomly. They were divided into 2 equal groups according to the presence or absence of p-ANCA. Data on their medical history and hospitalization course were retrospectively analyzed using their medical records. **Results:** Overall, 44 p-ANCA-positive patients (37.3%) and 14 p-ANCA-negative patients (11.9%) had infections. From the former group, 36 patients (81.8%) had Staphylococcus aureus infection, 15 (34.1%) had multidrug resistant gram-negative bacterial infection, and 21 (47.7%) had Pseudomonas aeruginosa infection. Of the latter group, 6 patients (42.9%) had Staphylococcus aureus infection, 4 (28.6%) had multidrug resistant gram-negative bacterial infection, and 5 (35.7%) had Pseudomonas aeruginosa infection. Further, 21 p-ANCA-positive patients (17.8%) and 7 p-ANCA-negative patients (5.9%) were diagnosed with vasculitis. Lastly, 37 p-ANCA-positive patients (31.4%) and 16 p-ANCA-negative patients (13.8%) required intensive care unit admission. **Conclusions:** p-ANCA is significantly associated with some infections. Patients with severe infections may produce p-ANCA, especially those requiring ICU admission. Those who test positive for p-ANCA should be thoroughly investigated not only for vasculitis but also for infectious conditions.

Key words: Antineutrophil cytoplasmic antibody, infection

Corresponding author: Deh-Ming Chang, M.D., Ph.D.
Division of Rheumatology/Immunology/Allergy, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center. No. 325, Cheng-Kung Rd., Sec. 2, Neihu 114, Taipei, Taiwan.
Tel: +886-2-87927135; Fax: +886-2-87927136
E-mail: pang1175@yahoo.com.tw
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Introduction

Over the past few decades, several studies have been conducted on the role of antineutrophil cytoplasmic antibody (ANCA) in the pathogenesis of vasculitis.

These antibodies are directed against enzymes present in the granules of polymorphonuclear leukocytes [1]. Indirect immunofluorescence (IIF) analysis to detect

ANCA indicates 3 subtypes of ANCA according to the staining patterns: cytoplasmic ANCA (c-ANCA), an antibody that is most specific to proteinase-3 (PR3), which is a serine protease present in the azurophilic granules of neutrophils; perinuclear ANCA (p-ANCA), an antibody against the myeloperoxidase (MPO) antigen, which is an enzyme present in the azurophilic granules of neutrophils; and atypical ANCA [2]. Further, enzyme-linked immunosorbent assay (ELISA) has shown that ANCA may also react with elastase, cathepsin G, azurocidin, lactoferrin, lysozyme, and bactericidal permeability-increasing protein (BPIP) [3].

The ANCA test is mainly indicated to diagnose ANCA-associated systemic vasculitis (AASV), which includes conditions like Wegener's granulomatosis (WG), microscopic polyangiitis (MPA), Churg-Strauss syndrome (CSS), and pauci-immune crescentic glomerulonephritis. The clinical manifestations for which the ANCA test is warranted include glomerulonephritis, especially rapidly progressive glomerulonephritis; pulmonary hemorrhage, especially pulmonary renal syndrome; cutaneous vasculitis, especially with systemic features; multiple lung nodules; chronic destructive disease of the upper airways; long-standing sinusitis or otitis; subglottic tracheal stenosis; mononeuritis multiplex or peripheral neuropathy; and a retro-orbital mass [4].

Previous studies have suggested that ANCA is detected in patients with infections such as Staphylococcus aureus bacteremia [5,6], bacterial endocarditis [7], leprosy [8], tuberculosis [9], viral infections [10,11], and invasive amebiasis [12]. Studies have also indicated that peptides released by S. aureus trigger the production of antibodies to both PR3 and its mimic, complementary PR3, and that these autoimmune antibodies are involved in the pathogenesis of WG [13]. One study suggested that unmethylated CpG oligodeoxynucleotide, found in bacterial and viral DNA, may mediate the stimulation of ANCA production in patients with vasculitis [14]. Further, studies have proposed theories on the possible roles played by microbial superantigens and CpG oligodeoxynucleotide in infections accompanied by ANCA production. Although the critical factors that trigger the interaction between neutrophils and ANCA in vasculitis have been identified [15-17], those involved in triggering ANCA production in other infections have not yet been recognized.

The c-ANCA staining pattern is strongly associated with and is specific for WG, a rare vasculitis affecting small arteries and veins. In contrast, p-ANCA is far less specific than c-ANCA and is found in patients with a range of inflammatory conditions, including glomerulonephritis and other vasculitic syndromes as well as inflammatory bowel disease. It is even found in patients with non-vasculitic disorders, e.g., infections, and in normal subjects [18]. The association between p-ANCA and infectious disease has been strongly suggested in several studies. We retrospectively analyzed the medical records of an equal number of patients with and without p-ANCA and sought to assess the correlation between the presence of p-ANCA and the associated clinical conditions.

Materials and methods

Patient population

Between 2007 and 2010 at our institution, 1291 patients (118 p-ANCA-positive and 1173 p-ANCA-negative patients; the rate of p-ANCA positivity was 9.14%) underwent laboratory tests for the presence of ANCA. We selected the total 118 p-ANCA-positive patients, and selected 118 of the 1173 p-ANCA-negative patients randomly. We divided the 236 patients into 2 equal groups (n = 118, each).

Most of the patients had secondary or tertiary referrals for the ANCA test from specialists, i.e., nephrologists, pulmonologists, rheumatologists, gastroenterologists, and gynecologists, and general physicians. All consecutive ANCA test requisition forms received from in- and outpatient units were examined and reviewed for clinical data and ANCA results. Data collected were used to determine whether the patients fulfilled the 1999-guideline criteria [18]. If a patient had one of the recommended clinical indications for ANCA testing at the time the ANCA test was ordered, the patient was considered to have fulfilled the criteria for ANCA testing. Data on the patients' medical history and hospitalization course were retrospectively obtained from the medical charts. They were then analyzed to evaluate the relationship between p-ANCA production and infections. Nephropathy was divided into glomerulonephritis, diabetic nephropathy, shock nephropathy, uremia, lupus nephritis, and others (e.g. hypertensive nephropathy and analgesic nephropathy), according to the pathophysiological information obtained from renal biopsy. This study protocol was approved by the Ethics Committee of the Tri-Service General Hospital.

Laboratory tests for p-ANCA detection

An IIF antibody kit was purchased from IMMCO Diagnostics, Inc. (Buffalo, NY). All tests were performed by the same technician. Serum samples obtained from patients were incubated with optimized preparations of human polymorphonuclear leukocytes (PMNs) to allow binding of the antibodies to the substrate. Unbound antibodies were removed by phosphate buffered saline (PBS). The bound IgG antibodies were then detected by incubating the substrate with fluorescein-labeled anti-human IgG conjugate. The resultant reactions were observed under a fluorescence microscope. The PMNs were then treated with ethanol for antigen fixation. Subsequently, ANCA was detected and classified into c-ANCA and p-ANCA on the basis of the staining pattern.

Statistical analysis

For statistical analysis, SPSS Version 15.0 for Windows (SPSS Inc., Chicago, USA) was used. The correlation between different events was calculated using crosstabs (chi-square and Pearson tests). The means of parametric data were determined by analysis of variance (ANOVA), and the ranks of nonparametric data were determined by the Mann-Whitney, Wilcoxon, and Kruskal-Wallis tests. A p value of ≤ 0.05 was considered significant.

Results

Although this study showed several interesting findings, its focus was findings pertinent to the association between p-ANCA production and the following infections: (a) S. aureus infection, including methicillin-resistant S. aureus (MRSA) and methicillin-sensitive S. aureus (MSSA); (b) infection with multidrug-resistant gram-negative bacilli (MDR GNB), including extended spectrum beta-lactamase GNB (ESBL GNB); and (c) Pseudomonas aeruginosa infection. The clinical characteristics of the patients are summarized in Table 1. Among 44 p-ANCA-positive patients with infections, 36 (81.8%) had S. aureus infection, 15 (34.1%) had MDR GNB infection, and 21 (47.7%) had Pseudomonas aeruginosa infection. Of the 14 p-ANCA-negative patients with infections, 6 (42.9%) had S. aureus infection, 4 (28.6%) had MDR GNB infection, and 5 (35.7%) had Pseudomonas aeruginosa infection.

To evaluate the usefulness of p-ANCA testing in clinical practice, we focused on analyzing the association between vasculitis and p-ANCA. Vasculitis was diagnosed in 21 p-ANCA-positive patients (17.8%) and 7 p-ANCA-negative patients (5.9%) (p=0.005). Vasculitis due to MPA was detected in 10 patients from the former group and 1 patient from the latter group (8.5% vs. 0.8%; p=0.005). Further, vasculitis associated with CSS was detected in 1 patient each in both groups. Two patients from the positive group had vasculitis due to WG, while none from the negative group had this condition.

Since AAV may also occur in some autoimmune diseases, we analyzed the relationship between autoimmune diseases and p-ANCA. Thirty-two (27.1%) of p-ANCA-positive patients and twenty-two (18.6%) of the p-ANCA-negative patients had autoimmune diseases. To analyze the association between p-ANCA and infections across different organ systems, we evaluated p-ANCA positivity according to the involved organ systems, including the skin and nervous system and the opthalmic, gastroenteric, and hematologic systems.

Table 2 shows the clinical characteristics of p-ANCA-positive and p-ANCA-negative patients with MRSA infection. Among the 33 patients with MRSA infection, 29 tested p-ANCA positive and 4 tested negative. In the p-ANCA-positive group, 3 patients (10.3%) had vasculitis, 5 (17.2%) had autoimmune diseases, 13 (44.8%) had nephropathy, and 19 (65.5%) required ICU admission. In contrast, only 2 p-ANCA-negative patients had nephropathy and 2 required ICU admission. Tables 3 and 4 summarize the data on the incidence of p-ANCA-positive and p-ANCA-negative patients with MDR GNB infection and ESBL GNB infection, respectively.

Discussion

Recent studies have shown that both PR3-ANCA and MPO-ANCA are produced in some infections [15-17]. This finding prompted us to determine the types of infections associated with ANCA production. A previous study showed that microorganisms, including S. aureus, express sequences complementary to those of PR3-encoding genes, implying that these microorganisms produce complementary PR3, which triggers the production of anti-idiotypic antibodies cross-reactive with PR3 [13]. Another study showed that the high relapse rate of WG among S. aureus nasal carriers can be attributed to bacterial superantigens, which serve as trigger factors [19].

Table 1. Comparison of the clinical profiles and infections between p-ANCA (−) and p-ANCA (+) patients

	p-ANCA (−)	p-ANCA (+)	p value
Age	51.86 ± 21.13	60.86 ± 22.46	0.317
Sex			
Female	61 (51.7%)	53 (44.9%)	
Male	57 (48.3%)	65 (55.1%)	0.297
Infection	14 (11.9%)	44 (37.3%)	0.001
SA	6 (5.1%)	39 (33.1%)	0.001
MSSA	2 (1.7%)	10 (8.5%)	0.018
MRSA	4 (3.4%)	29 (24.6%)	0.001
Blood	0 (0%)	5 (4.2%)	0.060
Wound	1 (0.8%)	4 (3.3%)	0.036
Sputum	2 (1.7%)	9 (7.6%)	0.001
Empyema	0 (0%)	4 (3.4%)	0.122
CVP catheter	1 (0.8%)	7 (5.9%)	0.066
MDR GNB	4 (3.4%)	15 (12.7%)	0.008
MDR PA	0 (0%)	3 (2.5%)	0.247
Urine	0 (0%)	1 (0.8%)	1.000
Sputum	0 (0%)	3 (2.5%)	0.247
MDR AB	2 (1.7%)	7 (5.9%)	0.171
Urine	2 (1.7%)	3 (2.5%)	1.000
Sputum	1 (0.8%)	6 (5.1%)	0.119
ESBL GNB	2 (1.7%)	9 (7.6%)	0.031
ESBL KP	1 (0.8%)	6 (5.1%)	0.119
Blood	0 (0%)	1 (0.8%)	1.000
Urine	0 (0%)	2 (1.7%)	0.498
Wound	0 (0%)	1 (0.8)	1.000
Sputum	1 (0.8%)	4 (3.4%)	0.375
ESBL E. coli	1 (0.8%)	4 (3.4%)	0.370
Urine	1 (0.8%)	2 (1.7%)	0.623
Wound	0 (0%)	3 (2.5%)	0.247
PA	5 (4.2%)	21 (17.8%)	0.001
Urine	0 (0%)	7 (5.9%)	0.014
Sputum	4 (3.4%)	14 (11.9%)	0.014
Other sites	2 (1.7%)	8 (6.8%)	0.051
Nephropathy	30 (25.4%)	48 (40.7%)	0.013
Glomerulonephritis	10 (8.5%)	11 (9.3%)	0.819
DM nephropathy	3 (2.5%)	7 (5.9%)	0.196
Shock nephropathy	12 (10.2)	17 (14.4%)	0.321
Uremia	1 (0.8%)	1 (0.8%)	1.000
Lupus nephritis	1 (0.8%)	9 (7.6%)	0.010
Other nephropathy	3 (2.5%)	3 (2.5%)	1.000
Vasculitis	7 (5.9%)	21 (17.8%)	0.005
WG	0 (0%)	2 (1.7%)	0.498
MPA	1 (0.8%)	10 (8.5%)	0.005
CSS	1 (0.8%)	1 (0.8%)	1.000
Non-AAV	5 (4.2%)	8 (6.8%)	0.392
Autoimmune disease	22 (18.6%)	32 (27.1%)	0.121
SLE	4 (3.4%)	14 (11.9%)	0.014
Others	18 (15.3%)	18 (15.3%)	1.000
Malignancy	7 (5.9%)	6 (5.1%)	1.000
Drug-induced	2 (1.7%)	6 (5.1%)	0.332
Other organ/tissue manifestation			
Skin eruption	27 (22.9%)	21 (17.8%)	0.123
Neuropathy	8 (6.8%)	3 (2.5%)	1.000
Hematologic disease	2 (1.7%)	2 (1.7%)	0.354
Gastroenterologic disease	4 (3.4%)	7 (5.9%)	1.000
Ophthalomologic disease	1 (0.8%)	1 (0.8%)	0.281
Patient origin			
General ward	98 (83.0%)	80 (67.8%)	
ICU	16 (13.6%)	37 (31.4%)	0.010
OPD	4 (3.4%)	1 (0.8%)	0.370

Abbreviations: SA = Staphylococcus aureus; MSSA = Methicillin-sensitive Staphylococcus aureus; MRSA = Methicillin-resistant Staphylococcus aureus; CVP = Central venous puncture; MDR GNB = Multidrug-resistant gram-negative bacilli; PA = Pseudomonas aeruginosa; AB = Acinetobacter baumannii; ESBL = Extended-spectrum beta-lactamase gram-negative bacilli; KP = Klebsiella pneumoniae; DM = Diabetes mellitus; WG = Wegener's granulomatosis; MPA = Microscopic polyangiitis; CSS = Churg-Strauss syndrome; AAV = ANCA-associated vasculitis; ICU = Intensive care unit; OPD = Out-patient department

Table 2. Clinical profiles of p-ANCA (−) and p-ANCA (+) patients with MRSA infection

MRSA Infection	p-ANCA (−)	p-ANCA (+)	p value
Age	64.75 ± 20.39	72.28 ± 17.67	0.786
Sex			
Female	1 (25.0%)	13 (44.8%)	
Male	3 (75.0%)	16 (55.2%)	0.620
Vasculitis			
No	4 (100.0%)	26 (89.7%)	
Yes	0 (0%)	3 (10.3%)	1.000
Autoimmune Disease			
No	4 (100.0%)	24 (82.8%)	
Yes	0 (0%)	5 (17.2%)	1.000
Nephropathy			
No	2 (50.0%)	16 (55.2%)	
Yes	2 (50.0%)	13 (44.8%)	1.000
Others			
No	2 (50.0%)	21 (72.4%)	
Yes	2 (50.0%)	8 (27.6%)	0.567
ICU admission			
No	2 (50.0%)	10 (34.5%)	
Yes	2 (50.0%)	19 (65.5%)	0.610

Abbreviations: MRSA = Methicillin-resistant Staphylococcus aureus; ICU = Intensive care unit

Previous studies showed that 36 of the 57 p-ANCA-positive patients with infections (63%) had S. aureus [20], compared with our study, among 44 p-ANCA-positive patients with infections, 36 (81.8%) had S. aureus infection. S. aureus infection was found to play a significant role in p-ANCA production; both MRSA and MSSA infections were significantly associated with p-ANCA. A statistically significant association was noted between S. aureus infection, with both MSSA (p=0.018) and MRSA (p<0.001), and p-ANCA production (p<0.001). On the basis of these findings, a theory on the enhancement of neutrophil extracellular traps (NETs) by S. aureus infection was proposed [21]. Under normal conditions, neutrophils release NETs, which can capture bacteria. In AAV, however, the NETs express ANCA autoantigens, accumulate in the kidneys, and promote an autoimmune response against neutrophils [21]. This finding appears to support our results suggesting a relationship between S. aureus infection and p-ANCA production.

Similarly, a significant association was noted between ESBL GNB infection and p-ANCA production (p=0.031). However, neither ESBL K. pneumoniae nor ESBL E. coli infection was found to be independently associated with p-ANCA. A previous study showed that infection with fimbriated bacteria, such as E. coli and K. pneumoniae, may trigger a cross-reactive autoimmune response to the ANCA antigen lysosomal membrane protein-2 (LAMP-2), which is located on the membranes of the intracellular vesicles that contain MPO and PR3 and is abundant on the surface of endothelial cells. LAMP-2 is involved in antigen presentation and in the adhesion of peripheral blood mononuclear cells to the vascular endothelium [22,23].

Interestingly, we also found that P. aeruginosa infection was strongly associated with p-ANCA production (p<0.001). P. aeruginosa was cultured from the urine (5.9%) in cases of urinary tract infection (UTI) and sputum (11.9%) in cases of infectious lung disease. A previous study demonstrated that P. aeruginosa colonization was associated with ANCA against BPIP

Table 3. Clinical profiles of p-ANCA (−) and p-ANCA (+) patients with MDR GNB infection

	MDR AB			MDR PA			MDR GNB		
	p-ANCA (−)	p-ANCA (+)	p	p-ANCA (−)	p-ANCA (+)	p	p-ANCA (−)	p-ANCA (+)	p
Sex									
Female	1 (50.0%)	2 (28.6%)		0	3 (100%)		2 (50.0%)	5 (33.3%)	
Male	1 (50.0%)	5 (71.4%)	1.000	0	0 (0%)	N	2 (50.0%)	10 (66.7%)	0.603
Vasculitis									
No	2 (100%)	5 (71.4%)		0	1 (33.3%)		4 (100%)	11 (63.6%)	
Yes	0 (0%)	2 (28.6%)	1.000	0	2 (66.7%)	N	0 (0%)	4 (36.4%)	0.530
Autoimmune Diseases									
No	2 (100%)	7 (100%)		0	2 (66.7%)		4 (100%)	13 (84.6%)	
Yes	0 (0%)	0 (0%)	N	0	1 (33.3%)	N	0 (0%)	2 (15.4%)	1.000
Nephropathy									
No	1 (50.0%)	5 (71.4%)		0	1 (33.3%)		2 (50.0%)	10 (66.7%)	
Yes	1 (50.0%)	2 (28.6%)	1.000	0	2 (66.7%)	N	2 (50.0%)	5 (33.3%)	0.603

Abbreviations: MDR = Multidrug-resistant gram-negative bacilli; AB = Acinetobacter baumannii, PA = Pseudomonas aeruginosa; GNB = gram-negative bacilli

Table 4. Clinical profiles of p-ANCA(-) and p-ANCA(+) patients with ESBL GNB infection

	ESBL KP			ESBL E. coli			ESBL GNB		
	p-ANCA (−)	p-ANCA (+)	p	p-ANCA (−)	p-ANCA (+)	p	p-ANCA (−)	p-ANCA (+)	p
Sex									
Female	0 (0%)	1 (16.7%)		1 (100%)	3 (75.0%)		1 (50.0%)	4 (44.4%)	
Male	1 (100%)	5 (83.3%)	1.000	0 (0%)	1 (25.0%)	1.000	1 (50.0%)	5 (55.6%)	1.000
Vasculitis									
No	1 (100%)	5 (83.3%)		1 (100%)	3 (75.0%)		2 (100%)	7 (77.8%)	
Yes	0 (0%)	1 (16.7%)	1.000	0 (0%)	1 (25.0%)	1.000	0 (0%)	2 (22.2%)	1.000
Autoimmune disease									
No	1 (100%)	6 (100%)		1 (100%)	3 (75.0%)		2 (100%)	8 (88.9%)	
Yes	0 (0%)	0 (0%)	N	0 (0%)	1 (25.0%)	1.000	0 (0%)	1 (11.1%)	1.000
Nephropathy									
No	1 (100%)	3 (50%)		0 (0%)	2 (50.0%)		1 (50.0%)	5 (55.6%)	
Yes	0 (0%)	3 (50%)	1.000	1 (100%)	2 (50.0%)	1.000	1 (50.0%)	4 (44.4%)	1.000

Abbreviations: ESBL GNB = Extended-spectrum beta-lactamase gram-negative bacilli; KP = Klebsiella pneumoniae; E. coli = Escherichia coli

in cystic fibrosis (CF) [24]. BPIP is also a target antigen of ANCA and can be detected by IIF as perinuclear/cytoplasmic staining in patients with WG or MPA [25]. However, BPIP-ANCA is also frequently expressed in chronic inflammatory bowel disease [26] and primary sclerosing cholangitis [27], besides CF and chronic airway infection [24, 28]. Another study reported the concomitant expression of MPO-ANCA and BPIP-ANCA in patients with MPA and chronic bronchiectasis [29]. Further, BPIP-ANCA may play a critical role in the autoimmune response in gram-negative bacterial infections. The BPIP sequence exhibits 44% homology with the amino acid sequence of lipopolysaccharide (LPS) protein, and the production of BPIP-ANCA may reflect the influence of long-term chronic airway infection. Elevated serum BPIP-ANCA levels inhibit the bactericidal activity of neutrophils, which results in prolonged bacterial colonization, and render chronic airway infections intractable [30]. Although clinical and experimental animal data support a link between gram-negative bacterial infections and the generation of BPIP-ANCA [31], it is unclear whether the antibody is involved in the pathogenesis of AAV, which may be triggered by gram-negative bacterial infections in the case of chronic lung disease. Using the data from the present study, we can further analyze p-ANCA-positive patients by using ELISA to identify the specific ANCA target antigen in patients with P. aeruginosa infection.

Some of the examined patients had mild nephropathy with signs such as hematuria and reduced creatine clearance. Bacterial infection with severe sepsis or multiorgan failure can also manifest concomitant renal failure. However, infection combined with a vasculitis-like syndrome may present as renal failure with or without the deterioration of pulmonary lesions. Under such clinical conditions, it is necessary to determine whether the patients test positive for p-ANCA expression. Patients with p-ANCA positivity who show symptoms suggestive of underlying insidious vasculitis should be promptly evaluated to determine the cause of the vasculitis. Analysis of tissue biopsy samples obtained from the lung, kidney, or skin and confirmation of the presence of ANCA-specific antigens by ELISA will facilitate the selection of an appropriate management strategy. Patients with MRSA infection (including ventilator-associated pneumonia, central line catheter infection, and soft tissue infections) and MDR GNB infections (including ventilator-associated pneumonia, UTI, and intra-abdominal infection) can develop severe sepsis or septic shock with multiorgan failure syndrome, manifesting as acute renal failure, acute respiratory failure, or cutaneous eruptions.

The International Consensus Statement on Testing and Reporting ANCA advocates that all laboratories screen for ANCA by using the IIF method; it also recommends that any serum sample with cytoplasmic, perinuclear, or nuclear fluorescence that might mask an ANCA should be tested for both the major ANCA types, i.e. PR3-ANCA and MPO-ANCA, by ELISA. This should be done even though the IIF test is more sensitive than ELISA for ANCA detection [32]. Recent studies have shown that well-designed tests adhering to these recommendations, and the use of both IIF tests and solid-phase ELISA tests directed against PR3 and

MPO can minimize false-positive results [33]. For these reasons, we used a modified method for ANCA detection, screened patients thoroughly in consultation with experts, and carefully examined the clinical manifestations to confirm the diagnosis.

We found that p-ANCA may be expressed in several kinds of infections, of which S. aureus, MDR GNB, and P. aeruginosa infections were significantly associated with the autoantibody. ANCA-associated vasculitis may mimic nephropathy, pulmonary infiltration, and skin eruption in patients with severe infections who present with multiorgan failure syndrome, especially those requiring ICU admission. If p-ANCA is detected in patients with infections, these patients should be evaluated by histological examination, ANCA-specific IIF, and confirmatory ELISA tests to help prevent misdiagnosis. Although the current study showed that p-ANCA is associated with some kinds of infections, further research is essential for investigating the clinical significance of p-ANCA in severe infections.

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核周型抗嗜中性球細胞質抗體與感染之關聯性

戴舜邦[1,2] 陳政宏[2] 盧俊吉[2] 王甯棋[3] 李思賢[4] 張德明[2,5]

[1]國軍左營總醫院 風濕免疫過敏科
[2]三軍總醫院 風濕免疫過敏科
[3]三軍總醫院 感染科
[4]國立師範大學 衛生教育學系
[5]國防醫學院

目的：核周型抗嗜中性球細胞質抗體（perinuclear antineutrophil cytoplasmic antibody, p-ANCA）常作為診斷血管炎的依據。核周型抗嗜中性球細胞質抗體有時也會出現在受感染病人的血液中。經由回朔分析，探討核周型抗嗜中性球細胞質抗體及感染的關係。**方法：**選擇2006年至2010年之間，p-ANCA陽性的病人118位，及隨機選擇1173位p-ANCA陰性病人中的118位，將p-ANCA的陽性與否分為兩組，經由病例記錄及住院病程做回朔性分析。**結果：**44位（37.3%）p-ANCA陽性及14位（11.9%）p-ANCA陰性的病人有感染情形。在44位p-ANCA陽性合併感染的病人中,分別有36位（81.8%）受到Staphylococcus aureus的感染，15位（34.1%）受到multidrug resistant gram-negative bacterial感染，及21位（47.7%）受到Pseudomonas aeruginosa感染。在14位p-ANCA陰性合併感染的病人中，分別有6位（42.9%）受到Staphylococcus aureus感染，4位（28.6%）受到multidrug resistant gram-negative bacterial感染，及5位（35.7%）受到Pseudomonas aeruginosa感染。21位（17.8%）p-ANCA陽性病人及7位（5.9%）p-ANCA陰性病人被診斷為血管炎。37位（31.4%）p-ANCA陽性病人及16位（13.8%）p-ANCA陰性病人住進加護病房。**結論：**p-ANCA與感染之間有顯著的關聯性，且嚴重的感染可能引起p-ANCA的產生，特別是在加護病房的病人。對於p-ANCA陽性的病人，除了血管炎之外，還應該徹底的探查其潛藏著感染的可能性。

關鍵詞：核周型抗嗜中性球細胞質抗體、感染