Life-threatening onset of systemic vasculitis requiring intensive care unit admission: a case series

S. Monti[1], C. Montecucco[1], S. Pieropan[2], F. Mojoli[3], A. Braschi[3], R. Caporali[1]

[1]*Division of Rheumatolgy, University of Pavia, IRCCS Policlinico San Matteo Foundation, Pavia, Italy;*
[2]*Division of Rheumatology, Azienda Ospedaliera Universitaria Integrata, Verona, Italy;*
[3]*Department of Clinical, Surgical, Diagnostic and Paediatric Sciences, Section of Surgery and Anesthesiology, Unit of Anesthesia, Intensive Care and Pain Therapy, University of Pavia, Italy and Anaesthesia and Intensive Care Division I, Emergency Department - IRCCS Policlinico San Matteo Foundation, Pavia, Italy.*

Sara Monti, MD
Carlomaurizio Montecucco, MD
Sara Pieropan, MD
Francesco Mojoli, MD
Antonio Braschi, MD
Roberto Caporali, MD

Please address correspondence to:
Dr Sara Monti,
Pz.le Golgi 2,
27100 Pavia, Italy.
E-mail: sara.saramonti@gmail.com

Received on March 31, 2015; accepted in revised form on April 21, 2015.

Clin Exp Rheumatol 2015; 33 (Suppl. 89): S126-S131.

Key words: systemic vasculitis, anti-neutrophil cytoplasmic antibody-associated vasculitis, intensive-care units.

Competing interests: none declared.

ABSTRACT

Objective. *Onset of ANCA-associated vasculitis (AAV) can be abrupt with life-threatening manifestations requiring Intensive Care Unit (ICU) admission. A high level of suspicion leading to prompt diagnosis is essential. Our objective was to investigate the epidemiologic characteristics and the type of life-threatening manifestations.*

Methods. *Medical records of AAV patients were analysed, selecting those with an ICU onset to identify predictive signs or symptoms and past medical history warnings useful for diagnosis.*

Results. *Out of 90 patients with AAV, 10 (11.1%) showed an ICU onset. The most frequent AAV diagnosed in the ICU was eosinophilic granulomatosis with polyangiitis (EGPA) (60%), followed by granulomatosis with polyangiitis (GPA) (20%) and microscopic polyangiitis (MPA) (20%). Cardio-pulmonary involvement was the main cause for ICU admission (70%) and significantly distinguished the ICU onset group from other AAV. The most frequent anamnestic warnings were history of asthma (50%), nasal polyps (30%), eosinophilia (30%). Symptoms shortly preceding ICU admission were arthralgia, fever (30%) and purpuric lesions (20%). ANCA were positive in 60% of patients. Mean Birmingham Vasculitis Activity Score (BVAS) at diagnosis was 16±8.43 and 0.88±1.45 at the end of follow up. All patients survived with a 10% rate of chronic kidney disease and a mean Vasculitis Damage Index (VDI) of 2±1.15.*

Conclusions. *Keeping a high level of suspicion for AAV is mandatory, particularly when treating life-threatening onset manifestations in the ICU. A history of asthma, nasal polyps, eosinophilia and arthralgia should always be investigated. ANCA are negative in about half of cases, therefore clinical expertise and strict collaboration with the rheumatologist are still pivotal.*

Introduction

Systemic vasculitides are a diverse set of diseases characterised by the presence of blood-vessel inflammation which can present with a multitude of organ manifestations and different levels of severity, morbidity and outcomes. Systemic vasculitides are often associated with life-threatening complications, sometimes representing the first sign of disease onset (1, 2).

The nomenclature of vasculitides has been recently updated with the second Chapel Hill Consensus Conference (CHCC2012) with the acknowledgement of additional diseases (secondary vasculitides) and the replacement of eponyms (3). CHCC2012 offers a standardised nosologic definition but is not intended for classification or diagnostic purposes. The categorisation of vasculitides according to the predominant size of the blood vessels involved (small, medium or large) was maintained and can provide a framework to predict the predominant organ manifestations to be expected in clinical care. Nevertheless, it is important to remember that, despite classification, vasculitides can potentially affect vessels of any size (3).

Small-vessel vasculitis, and particularly anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), have been described as the most frequent rheumatologic diseases leading to intensive care unit (ICU) admission (4). Up to 20% of cases can be diagnosed in the critical care setting due to life-threatening manifestations at disease onset (4). A high level of suspicion leading to prompt diagnosis and treatment is essential to improve organ survival and reduce mortality (5).

We conducted a retrospective observational cohort study of patients diagnosed with AAV in the ICU, investigating the epidemiologic characteristics and the type of life-threatening manifestations. Secondarily, we attempted to

Table I. Type and frequency of AAV manifestations requiring ICU admission.

Disease onset manifestation	n. (%)	Pathologic finding	Type of AAV
Respiratory failure	3 (30%)	DAH (Pulmonary-renal ssyndrome in 2 cases)	2 MPA 1 GPA
Dyspnoea, signs of congestive heart failure	4 (40%)	Cardiomyopathy with severely reduced ejection fraction	4 EGPA
Acute abdomen	2 (20%)	Intestinal ischemia leading to surgical resection	2 EGPA
Dyspnoea and stridor	1 (10%)	Subglottic stenosis	1 GPA

DAH: diffuse alveolar haemorrhage; AAV: ANCA-associated vasculitis; MPA: microscopic polyangiitis; GPA: granulomatosis with polyangiitis; EGPA: eosinophilic granulomatosis with polyangiitis.

identify predictive signs or symptoms and past medical history warnings that can be useful to suggest a diagnosis of AAV in patients admitted to the ICU.

Materials and methods

Medical records of all patients followed at our Department up to February 2015 with a diagnosis of AAV were analyzed, selecting those with an ICU onset of disease. Patients or their relatives provided informed consent according to local guidelines.

All patients fulfilled the American College of Rheumatology and Chapel Hill nomenclature criteria. Full anamnestic, clinical, organ-involvement, laboratory, histologic, induction and maintenance treatment data were available for all patients. Detailed history of the causes leading to ICU admission, the presence of prodromic signs or symptoms or the presence of relevant past medical warnings was investigated. ANCA positivity by immunofluorescence was always confirmed with ELISA for proteinase-3 (PR3) or myeloperoxidase (MPO). Clinimetric evaluation was retrospectively performed with *Birmingham Vasculitis Activity Score* (BVAS) version 3 (6), *Vasculitis Damage Index* (VDI) (7) and *Five Factor Score* (FSS) (8). A comparison of the baseline characteristic of AAV with ICU onset and the remaining 80 AAV patients followed at our Department was also performed. Descriptive statistical data were presented as means ± standard deviation (SD) and percentages. Parametric statistic tests were performed when appropriate.

Results

A total of 90 patients with AVV were followed at our Rheumatology Department. The most frequently represented AAV in our cohort was eosinophilic granulomatosis with polyangiitis (EGPA) (n=51 patients; 56.6%), followed by granulomatosis with polyangiitis (GPA) (n=35 patients; 38.9%), and microscopic polyangiitis (MPA) (n=4 patients; 4.4%).

Within this group, we selected 10 (11.1%) patients whose disease onset was characterised by life-threatening manifestations leading to ICU admission.

Mean age of patients diagnosed in the intensive care setting: 46±15.2, male/female: 4/6. The type and frequency of different disease manifestations requiring intensive care management are reported in Table I.

The most frequent AAV diagnosed in the ICU in our case series was (EGPA) (60%), followed by (GPA) (20%) and (MPA) (20%).

Cardio-pulmonary acute involvement was the main cause for ICU admission, accounting for 70% of cases. Diffuse alveolar haemorrhage (DAH) represented the leading cause of respiratory failure in our population; concomitant infections were excluded with extensive microbial investigations also on bronchoalveolar lavage. Patients complained of dyspnea and cough, associated with acute hypoxemic respiratory failure and rapid anaemisation requiring multiple red blood cells (RBC) transfusions. Haemoptysis was present in 2 cases.

Out of 3 patients presenting with DAH, 2 (20% of the study population) had a pulmonary-renal syndrome with acute kidney injury (AKI), nephrotic-range proteinuria and microhaematuria. Renal histology disclosed pauci-immune necrotising and crescentic glomerulonephritis. Both patients were diagnosed with MPA.

Table II presents a comprehensive overview of the demographic and clinical characteristics of the study population. ANCA were positive in 60% of our cases: 30% c-ANCA (PR3), 30% p-ANCA (MPO). Prodromic signs or symptoms and anamnestic warnings preceding the diagnosis are also listed.

The most frequent anamnestic warning was history of asthma, presented by 50% of patients and lasting up to 30 years before the acute exacerbation leading to the ICU diagnosis occurred. 30% of patients reported recurrent nasal polyps, often treated with frequent surgical procedures without a conclusive diagnosis. Mild eosinophilia, characteristically and significantly increasing at the time of disease flare and ICU admission, was detectable in 30% of cases, often being recognisable several years before the diagnosis. The most frequent symptoms shortly preceding ICU admission were arthralgia and fever (30% of cases). Purpuric lesions were observed in 20% of patients.

Treatment

The majority of our patients required mechanical ventilation and/or extracorporeal life support when admitted to ICU (Table III). Antibiotic therapy was empirically prescribed to all patients. Once the diagnosis of AAV was established, patients were promptly initiated on a remission induction therapeutic strategy. High dose glucocorticoids (at least 1 mg/kg or, more frequently, high dose pulse therapy of methylprednisolone 1 g/day for 3 days) were the mainstay of treatment, usually in association with plasma exchange and/or *i.v.* cyclophosphamide cycles at the dosage of 15 mg/kg every two weeks for 3 to 6 infusions, eventually adjusted according to

Table II. Demographic and clinical characteristics of the study population. Analysis of the prodromic signs and symptoms and anamnestic warning preceding the event leading to the diagnosis in ICU.

Patient	Sex	Age at diagnosis	Type of AAV	ANCA positivity	Manifestation leading to ICU admission	Other associated signs/symptoms at ICU admission	Prodromic signs/symptoms and anamnestic warnings	Duration of prodromic and anamnestic warning before diagnosis	Outcome	Duration of follow-up (mts)
Case 1	F	46	MPA	p-ANCA (MPO)	DAH	Haemoptysis, Anaemia, arthritis, haematuria	Fever, arthralgia	2 weeks	Moderate restrictive pattern at RFTs	84
Case 2	F	46	EGPA	-	Cardiomyopathy	CNS vasculitis, significantly increasing eosinophilia, ENT	Asthma, nasal polyps, eosinophilia	29 years	Cardiac function fully recovered. chronic asthma	14
Case 3	M	71	EGPA	-	Cardiomyopathy	PN, significantly increasing eosinophilia, pericarditis, ENT	Asthma, nasal polyps, previous eosinophilic pneumonia	30 years	EF 40%. chronic asthma	60
Case 4	M	43	EGPA	p-ANCA (MPO)	Intestinal ischemia	Increasing eosinophilia, ENT	Asthma, nasal polyps	12 months	Recovered after bowel resection	120
Case 5	M	56	EGPA	-	Cardiomyopathy	Increasing eosinophilia, pericarditis	Asthma, eosinophilia	12 months	EF 45%. chronic asthma	96
Case 6	F	16	GPA	c-ANCA (PR3)	DAH	AKI, proteinuria, haematuria haemoptysis, anemia	Fever, arthralgia	2 days	Mild restrictive pattern at RFTs. Normal renal function	9
Case 7	F	29	GPA	c-ANCA (PR3)	Subglottic stenosis	Pulmonary cavitary lesions, ENT	Chronic ENT involvement	7 years	Permanent tracheostomy. Proptosis	120
Case 8	F	53	MPA	c-ANCA (PR3)	DAH	AKI, proteinuria, haematuria, haemoptysis, anaemia, arthritis	Fever, arthralgia	7 days	Moderate restrictive pattern at RFTs. End stage CKD	36
Case 9	M	56	EGPA	-	Intestinal ischemia	AKI, proteinuria, haematuria, cutaneous leukocytoclastic vasculitis	Purpuric lesions, arthralgia	2 months	Recovered after bowel resection. Normal renal function	24
Case 10	F	49	EGPA	p-ANCA (MPO)	Cardiomyopathy	ILD, cutaneous leukocytoclastic vasculitis	Asthma, purpuric lesions, arthritis	4 years	Cardiac function fully recovered. Chronic Asthma	18

DAH: diffuse alveolar hemorrhage; AAV: ANCA-associated vasculitis; MPA: microscopic polyangiitis; GPA: granulomatosis with polyangiitis; EGPA: eosinophilic granulomatosis with polyangiitis; ENT: ear, nose, throat involvement; CNS: central nervous system; PN: peripheral neuropathy; AKI: acute kidney injury; MTS: months; RFTs: respiratory function tests; EF: cardiac ejection fraction; CKD: chronic kidney disease.

renal function. One patient with pulmonary-renal syndrome was successfully treated with Rituximab (375 mg/m^2 every week for 4 administrations). Specific immunosuppressive treatment was promptly introduced within 4 days from ICU admission in the majority of cases. Maintenance treatment mainly consisted in low dose glucocorticoids and weekly methotrexate, usually preferred to azathioprine in our cohort.

Prognosis

The survival rate in our cohort of patients was 100% up to 10 years since ICU admission. Mean *Birmingham Vasculitis Activity Score*, version 3 (BVAS) at diagnosis was 16±8.43 and dropped to 0.88±1.45 at latest follow up visit. We recorded a 10% rate of end-stage chronic kidney disease (CKD) requiring haemodialytic treatment. Cardiac function significantly improved in all patients with cardiomyopathy due to EGPA, with a residual slightly reduced ejection fraction (40–45%) in two patient. DAH always resulted in

Table III. Treatment strategies in AAV diagnosed in ICU.

Acute treatment	n (%)
Mechanical ventilation	5 (50%)
Tracheostomy	1 (10%)
CRRT	2 (20%)
ECMO	1 (10%)
Remission induction treatment	n (%)
High dose corticosteroids	10 (100%)
Plasma exchange	3 (30%)
Cyclophosphamide	5 (50%)
Rituximab	1 (10%)
Maintenance treatment	n (%)
Low dose corticosteroids	10 (100%)
Methotrexate	7 (70%)
Azathioprine	1 (10%)

CRRT: continuous renal replacement therapy; ECMO: extracorporeal membrane oxygenation; AAV: ANCA-associated vasculitis; MPA: microscopic polyangiitis; GPA: granulomatosis with polyangiitis.

Table IV. Comparison of baseline characteristics of ICU-onset AAV patients and the AAV control group not diagnosed in the ICU.

Variable	ICU-onset AAV	AAV control group	*p*-value
n	10	80	
Sex (M/F)	4/6	33/47	
Age (mean ± SD)	46 ± 15.2	55 ± 16.6	NS
Type of AAV n (%):			
EGPA	6 (60%)	45 (56%)	NS
GPA	2 (20%)	33 (41%)	NS
MPA	2 (20%)	2 (2%)	**0.05**
p-ANCA (MPO)	3 (30%)	33 (41%)	NS
c-ANCA (PR3)	3 (30%)	16 (20%)	NS
Type of organ involvement at onset n (%):			
Lung	10 (100%)	45 (56%)	**0.01**
Kidney	3 (30%)	17 (21%)	NS
Heart	4 (40%)	13 (16%)	NS
ENT	4 (40%)	43 (54%)	NS
Gastrointestinal	2 (20%)	4 (5%)	NS
PN	1 (10%)	28 (35%)	NS
CNS	2 (20%)	4 (5%)	NS
Cutaneous	2 (20%)	22 (28%)	NS
Arthritis/arthralgia	5 (50%)	24 (30%)	NS
Systemic symptoms	3 (30%)	17 (21%)	NS
FFS positivity n (%)*	7 (70%)	13 (16%)	**0.0005**
BVAS at onset	16 ± 8.4	15 ± 7.1**	NS
BVAS at end of follow-up	0.88 ± 1.4	1.4 ± 2.1	NS
VDI at end of follow-up	2.2 ± 1.1	1.4 ± 0.8	**0.007**

*FFS: five factor score was calculated only for EGPA and MPA; **Data available for 63 pts at baseline. AAV: ANCA-associated vasculitis; MPA: microscopic polyangiitis; GPA: granulomatosis with polyangiitis; EGPA: eosinophilic granulomatosis with polyangiitis; ENT: ear, nose, throat involvement; CNS: central nervous system; PN: peripheral neuropathy; FFS: five factors score.

some degree of asymptomatic mild to moderate restrictive pattern at pulmonary function tests. The life-threatening symptom leading to ICU admission did not relapse in any of our patients during maintenance treatment. Mean *Vasculitis Damage Index* (VDI) was 2±1.15 at the end of follow-up.

Comparison with the AAV control group

Data on demographic, type of clinical presentation, disease activity and outcome of the study group of patients with AAV onset leading to ICU admission were compared with the remaining 80 AAV patients followed at our Department (Table IV).

Although not reaching statistical significance, patients with ICU-onset were about 10 years younger at diagnosis compared to the control AAV group (mean age at diagnosis 46±15.2 *vs*. 55±16.6; p=0.09). MPA significantly led to ICU admission at disease onset due to pulmonary-renal syndrome more frequently compared to the control group (p=0.05). ANCA status did not significantly differ among the two groups. Considering the type of organ involvement at disease onset, the pulmonary system was significantly more affected in patients with life-threatening manifestations leading to ICU admission (p=0.01). Cardiac and central nervous system (CNS) involvement were also more frequently represented in the ICU-onset group.

While mean BVAS disease activity scores did not significantly differ at disease onset nor at the end of follow up, a positive *Five Factor Score* (FFS) in patients with EGPA and MPA was recorded far more frequently in patients admitted to the ICU compared to patients managed in the rheumatologic ward or outpatient clinic (p=0.0005). 16% of patients in the control group presented with a FFS ≥1, mainly due to AKI requiring haemodialitic support and highly intensive treatments but did not require ICU admission. Reflecting the prognostic role of the FFS, patients with ICU-onset, despite good prognosis and 100% survival in our cohort, presented a significantly higher VDI at the end of follow up (p=0.007).

Discussion

This study investigated the frequency, epidemiologic characteristics and outcome of patients diagnosed with AAV in the ICU. While the majority of published data concentrates on the causes leading to ICU admission in patients already diagnosed with rheumatologic diseases, this is, to our knowledge, the first study investigating the prodromic signs, symptoms and anamnestic warnings that can be useful to elicit the suspect of AAV and guide a prompt diagnosis.

Rheumatologic diseases can be diagnosed for the first time in the ICU in up to 20% of cases. More than one third of these patients are represented by systemic vasculitides (4). Vasculitides, together with rheumatoid arthritis and systemic lupus erythematosus represent the rheumatologic diseases most frequently admitted to the ICU, mainly for infectious complications or disease flares (9-12). Cruz *et al*. (13) reviewed medical records of 210 patients with systemic necrotising vasculitis, selecting 26 patients admitted to the ICU, reporting a 5% rate of ICU diagnosis (42% of patients admitted to ICU due to vasculitis). In our cohort we found that 11.1% of AAV were diagnosed for

the first time in ICU. EGPA was the AAV most frequently leading to ICU admission at disease onset. Supportive data from the literature are scarce in differentiating between different types of AAV in the ICU setting, usually considering systemic vasculitides as a whole group, but GPA was reported as the prevalent diagnosis (14). This finding is not solely explained by the epidemiologic distribution of AAV that would report EGPA as the least frequent diagnosis both in terms of incidence and prevalence compared to GPA and MPA (12). The possibility of an increasing diagnostic confidence supported by specific objective findings should also be excluded since 60% of EGPA patients were ANCA negative. Moreover, EGPA is probably not the AAV with the most hyper-acute disease onset, since it shows the highest frequency of disregarded anamnestic warnings such as asthma and nasal polyps, often lasting several years before ICU admission and diagnosis, further underlying the importance of searching for this information. The higher frequency of EGPA in our cohort is probably the result of several months of unrecognised disease finally leading to a life-threatening exacerbation requiring ICU admission.

Cardio-pulmonary acute involvement was the main cause for ICU admission, accounting for 70% of cases, with DAH representing the leading cause of respiratory failure. This is in line with previous evidence (10, 15, 16). Lung involvement was the only type of organ involvement at disease onset significantly distinguishing patients with an ICU-onset from the AAV control group. Pulmonary involvement manifested as alveolar capillaritis-induced DAH is reported in 25–55% of patients with MPA (15,17) and is being increasingly recognised as a prominent manifestation of GPA, also at disease onset (18, 19). DAH has been demonstrated as the main cause for hospitalisation and ICU admission in AAV in other case series (5, 14). Also in our cohort, MPA was the most common cause of pulmonary-renal syndrome and was significantly more represented in the ICU-onset group compared to AAV not diagnosed in the intensive care setting (1). Endomyocardic involvement led to ICU admission in 66% of patients diagnosed with EGPA in our cohort and was associated with significantly increase of peripheral eosinophilia, known to reflect tissue infiltration (20). Also in our case series, myocardial involvement was more common in EGPA patients without ANCA positivity (21).

We demonstrated a lower mortality rate compared to other traditional series reporting percentages as high as 29-54% (10, 13, 22). Improved prognosis has also been reported by other authors for systemic rheumatologic diseases admitted to ICU, reporting mortality rates of 16.7% and excluding correlation with pulmonary-renal syndrome secondary to vasculitides among the leading causes of death (23). The mortality rate of patients with small-vessel vasculitis admitted to the ICU has been demonstrated to be lower than predicted despite DAH being the most common reason for admission (14). Bouachour *et al*. (4) compared the prognosis of rheumatologic patients (including systemic vasculitides) diagnosed in the ICU with the outcomes of patients admitted to ICU with a previously known rheumatologic condition. Survival was better for patients diagnosed in the ICU; iatrogenic complications and particularly infections were the main factors associated with increased mortality.

Age >60, previous chronic disease, use of corticosteroids, underlying lung disease, need for mechanical ventilation, comorbidities and particularly infectious diseases are recognised as independent factors associated with grim prognosis in the ICU, despite the severity of the rheumatologic condition itself (10, 13, 22, 24, 25, 26). Our cohort of patients was younger and treatment was promptly initiated within few days from ICU admission, probably halting the course of disease, leading to 100% survival rate. It is also possible that the mortality rate in the ICU is underestimated due to missed diagnosis and premature deaths never classified as AAV. Despite the excellent survival rate, the comparison with the AAV control group demonstrated that ICU-onset significantly leads to worse VDI scores that can be efficiently be predicted by dedicated prognostic factors such as the FFS (8).

We demonstrated that some specific prodromic signs/symptoms and anamnestic warnings are consistently detectable in patients diagnosed with AAV in the ICU and should always be investigated to avoid missed or delayed diagnosis. A history of adult-onset asthma was presented by 50% of patients, often lasting several years before the acute exacerbation leading to the ICU diagnosis occured. Nasal polyps, often treated with frequent surgical procedures without a conclusive diagnosis and eosinophilia, characteristically and significantly increasing at the time of disease flare and ICU admission, were detectable in 30% of cases. Diagnostic difficulties in recognising EGPA probably arise from the close relationship with other eosinophilic disorders (27) and the frequency of asthma in the general population leading often to misclassification of EGPA into an idiopathic or allergic disorder (28). Vasculitis typically develops in a previously asthmatic and eosinophilic middle-aged patient; asthma is severe, associated with eosinophilia, nasal polyps and sinusitis and possibly other extrapulmonary symptoms (29). Other important signs and symptoms, although aspecific, to be searched for are arthralgias, fever and purpuric lesions, often shortly preceding ICU admission.

The advances in treatment strategies for AAV have certainly and dramatically improved outcomes. Our patients were treated with intensive remission induction regimens as soon as the diagnosis was confirmed. Plasma-exchange was associated for the most severe cases of DAH (30% of our cohort). The use of plasma-exchange together with corticosteroid and cyclophosphamide has dramatically changed the prognosis of AAV and has been associated with increased renal recovery and reduction of end-stage renal disease (30, 31, 32, 33). Rituximab was highly efficacious in inducing remission also in our experience (34, 35). Despite comprehensible concerns, introduction of immunosuppressive therapy did not appear to be a risk factor for mortality in this and other cohorts (25).

Our study has some limitations: the retrospective design exposes conclusions to several biases; nevertheless, a prospective study would require very large cohorts to address rare events (diagnosis in the ICU setting) in rare diseases (AAV). The single-centre experience may have been influenced by local attention to rheumatologic conditions and routine combined management of intensivists and rheumatologists in the diagnostic and therapeutic approach to suspected cases of vasculitides. Specific baseline ICU prognostic scores such as the APACHE-II (acute physiology and chronic health evaluation), the SAPS-II (simplified acute physiology score) or the SOFA (sequential organ failure assessment) were not available for our cohort of patients, and we acknowledge that this should be regarded as a limitation of our study. As a matter of fact, available data from the literature suggest that the value of such traditional prognostic scores applied to rheumatologic diseases is controversial and has often proved not to be reliable (8, 9, 23). Nevertheless vasculitis-specific prognostic factors were available and demonstrated to be effective in predicting long-term outcomes also in our cohort (8).

Conclusions

Keeping a high level of suspicion for AAV is mandatory, particularly when treating life-threatening onset manifestations of disease in the ICU. A history of asthma, nasal polyps, eosinophilia and arthralgia should always be investigated. ANCA are negative in about half of cases, therefore clinical expertise and strict collaboration with the rheumatologist are still pivotal.

References

1. WILFONG EM, SEO P: Vasculitis in the intensive care unit. *Best Pract Res Clin Rheumatol* 2013; 27: 95-106.
2. CAPORALI R, MONTI S, MAGRASSI L, MONTECUCCO C: Pneumocephalus due to granulomatosis with polyangiitis. *Rheumatology* (Oxford) 2014; 53: 2269.
3. JENNETTE JC, FALK RJ, BACON PA *et al*.: 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum* 2013; 65:1-11.
4. BOUACHOUR G, ROY PM, TIROT P, GUERIN O, GOUELLO JP, ALQUIER P: [Prognosis of systemic diseases diagnosed in intensive care units]. *Presse Med* 1996; 25: 837-41.
5. HOLGUIN F, RAMADAN B, GAL AA, ROMAN J: Prognostic factors for hospital mortality and ICU admission in patients with ANCA-related pulmonary vasculitis. *Am J Med Sci* 2008; 336: 321-6.
6. MUKHTYAR C, LEE R, BROWN D *et al*.: Modification and validation of the Birmingham Vasculitis Activity Score (version 3). *Ann Rheum Dis* 2009; 68: 1827-32.
7. EXLEY AR, BACON PA, LUQMANI RA *et al*.: Development and initial validation of the Vasculitis Damage Index for the standardized clinical assessment of damage in the systemic vasculitides. *Arthritis Rheum* 1997; 40: 371-80.
8. GUILLEVIN L, PAGNOUX C, SEROR R *et al*.: The Five-Factor Score revisited: assessment of prognoses of systemic necrotizing vasculitides based on the French Vasculitis Study Group (FVSG) cohort. *Medicine* (Baltimore) 2011; 90: 19-27.
9. MOREELS M, MÉLOT C, LEEMAN M: Prognosis of patients with systemic rheumatic diseases admitted to the intensive care unit. *Intensive Care Med* 2005; 31: 591-3.
10. JANSSEN NM, KARNAD DR, GUNTUPALLI KK: Rheumatologic diseases in the intensive care unit: epidemiology, clinical approach, management, and outcome. *Crit Care Clin* 2002; 18: 729-48.
11. POURRAT O, BUREAU JM, HIRA M, MARTIN-BARBAZ F, DESCAMPS JM, ROBERT R: [Outcome of patients with systemic rheumatic diseases admitted to intensive care units: a retrospective study of 39 cases]. *Rev Med Interne* 2000; 21: 147-51.
12. GODEAU B, MORTIER E, ROY PM *et al*.: Short and longterm outcomes for patients with systemic rheumatic diseases admitted to intensive care units: a prognostic study of 181 patients. *J Rheumatol* 1997; 24: 1317-23.
13. CRUZ BA, RAMANOELINA J, MAHR A *et al*.: Prognosis and outcome of 26 patients with systemic necrotizing vasculitis admitted to the intensive care unit. *Rheumatology* (Oxford) 2003; 42: 1183-8.
14. KHAN SA, SUBLA MR, BEHL D, SPECKS U, AFESSA B: Outcome of patients with small-vessel vasculitis admitted to a medical ICU. *Chest* 2007; 131: 972-6.
15. WILKE L, PRINCE-FIOCCO M, FIOCCO GP: Microscopic polyangiitis: a large single-center series. *J Clin Rheumatol Pract Rep Rheum Musculoskelet Dis* 2014; 20: 179-82.
16. QUINTERO OL, ROJAS-VILLARRAGA A, MANTILLA RD, ANAYA J-M: Autoimmune diseases in the intensive care unit. An update. *Autoimmun Rev* 2013; 12: 380-95.
17. GÓMEZ-PUERTA JA, HERNÁNDEZ-RODRÍGUEZ J, LÓPEZ-SOTO A, BOSCH X: ANti-neutrophil cytoplasmic antibody-associated vasculitides and respiratory disease. *Chest* 2009; 136: 1101-11.
18. BOSCH X, GUILABERT A, FONT J: Antineutrophil cytoplasmic antibodies. *The Lancet* 2006; 368: 404-18.
19. ARORA R: Massive alveolar haemorrhage: a rare life threatening complication of Wegener's granulomatosis-report of a rare case. *Quant Imaging Med Surg* 2014; 4: 509-11.
20. GUILLEVIN L, COHEN P, GAYRAUD M, LHOTE F, JARROUSSE B, CASASSUS P: Churg-Strauss syndrome. Clinical study and long-term follow-up of 96 patients. *Medicine* (Baltimore) 1999; 78: 26-37.
21. SABLÉ-FOURTASSOU R, COHEN P, MAHR A *et al*.: Antineutrophil cytoplasmic antibodies and the Churg-Strauss syndrome. *Ann Intern Med* 2005; 143: 632-8.
22. ANTÓN JM, CASTRO P, ESPINOSA G *et al*.: Mortality and long term survival prognostic factors of patients with systemic autoimmune diseases admitted to an intensive care unit: a retrospective study. *Clin Exp Rheumatol* 2012; 30: 338-44.
23. CAMARGO JF, TOBÓN GJ, FONSECA N *et al*.: Autoimmune rheumatic diseases in the intensive care unit: experience from a tertiary referral hospital and review of the literature. *Lupus* 2005; 14: 315-20.
24. RANZANI OT, BATTAINI LC, MORAES CE *et al*.: Outcomes and organ dysfunctions of critically ill patients with systemic lupus erythematosus and other systemic rheumatic diseases. *Braz J Med Biol Res* 2011; 44: 1184-93.
25. FAGUER S, CIROLDI M, MARIOTTE E *et al*.: Prognostic contributions of the underlying inflammatory disease and acute organ dysfunction in critically ill patients with systemic rheumatic diseases. *Eur J Intern Med* 2013 24: e40-4.
26. LUQMANI RA, FLOSSMANN O: Outcome in small-vessel systemic vasculitis. *J Rheumatol* 2006 Jul; 33: 1224-7.
27. LANHAM JG, ELKON KB, PUSEY CD, HUGHES GR: Systemic vasculitis with asthma and eosinophilia: a clinical approach to the Churg-Strauss syndrome. *Medicine* (Baltimore) 1984; 63: 65-81.
28. AGUILAR PR, WALGAMA ES, RYAN MW: Other Asthma Considerations. *Otolaryngol Clin North Am* 2014; 47: 147-60.
29. MOUTHON L, DUNOGUE B, GUILLEVIN L: Diagnosis and classification of eosinophilic granulomatosis with polyangiitis (formerly named Churg-Strauss syndrome). *J Autoimmun* 2014; 48-49: 99-103.
30. JAYNE DRW, GASKIN G, RASMUSSEN N *et al*.: Randomized trial of plasma exchange or high-dosage methylprednisolone as adjunctive therapy for severe renal vasculitis. *J Am Soc Nephrol* 2007; 18: 2180-8.
31. WALSH M, CATAPANO F, SZPIRT W *et al*.: Plasma exchange for renal vasculitis and idiopathic rapidly progressive glomerulonephritis: a meta-analysis. *Am J Kidney Dis* 2011; 57: 566-74.
32. JAYNE D, RASMUSSEN N, ANDRASSY K *et al*.: A randomized trial of maintenance therapy for vasculitis associated with antineutrophil cytoplasmic autoantibodies. *N Engl J Med* 2003; 349: 36-44.
33. DELLA ROSSA A, CIOFFI E, ELEFANTE E *et al*.: Systemic vasculitis: an annual critical digest of the most recent literature: *Clin Exp Rheumatol* 2014; 32: S98-105.
34. JONES RB, FURUTA S, COHEN TERVAERT JW *et al*.: Rituximab versus cyclophosphamide in ANCA-associated renal vasculitis: 2-year results of a randomised trial. *Ann Rheum Dis* 2015 Mar 4;
35. GUILLEVIN L: Rituximab for ANCA-associated vasculitides: *Clin Exp Rheumatol* 2014; 32 (Suppl. 82): S118-21.