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LETTERS OF BIOMEDICAL AND CLINICAL RESEARCH

High prevalence of antinuclear antibodies and lupus anticoagulant in patients hospitalized for SARS-CoV2 pneumonia

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About 15–20% of patients with severe acute respiratory syndrome–coronavirus 2 (SARS-CoV2) disease experience pneumonia of variable extent and course [1]. A proportion of them have cardiovascular involvement, including myocarditis, ischemia and shock, and thrombotic disease, including venous thromboembolism, pulmonary embolism (PE), and disseminated intravascular coagulation, that can lead to death [2]. Systemic inflammation and a procoagulant state play a major pathophysiological role in these severe forms and correlate very well with disease severity and death [2]. It is unclear whether the procoagulant profile is a direct effect of infection or whether it is a consequence of inflammation [2]. Autoimmune diseases are characterized by inflammation and some of them by a procoagulant state; moreover, several viruses are involved in their development [3]. An autoimmune mechanism mediated by antiphospholipid antibodies has been suggested to explain the procoagulant state in SARS-CoV2 disease [4], but the impact of autoimmune mechanisms on SARS-CoV2 disease was never studied. The aim of our study was to evaluate markers of autoimmunity in patients hospitalized for SARS-CoV2 pneumonia.

A panel of autoimmune markers was evaluated in 45 consecutive patients admitted to our hospital for SARS-CoV2 pneumonia. Pneumonia was documented by computed tomography and infection was established by RT-PCR. Blood samples were taken on admission. Statistical analysis was performed with *t* test after log-transformation for non-normally distributed variables and with exact Fisher test for frequency comparisons.

Table 1 shows features of the patients, prevalence of autoimmune markers, and features of the patients stratified by presence/absence of ANA and lupus anticoagulant. Several autoimmune markers were present. The prevalence of antinuclear antibodies (ANA) (35.6%) and lupus anticoagulant (11.1%) was very high. Moreover, borderline values of lupus anticoagulant were present in a high percentage of subjects (35.5%). No difference was found between subjects with positive and those with borderline lupus anticoagulant, so we grouped the two together in our analysis.

The high prevalence of ANA, together with other autoimmune markers, suggests an involvement of autoimmune mechanisms in SARS2-CoV2 disease. In addition, lupus anticoagulant may be associated with the increased thrombotic risk described in a high proportion of patients and characterized by cardiac involvement, respiratory complications, and death [2]. The prevalence of lupus anticoagulant in our patients is similar to that recently reported [5]: indeed, if we group together subjects with positive and those with borderline values of lupus anticoagulant, the prevalence becomes impressively high (46.6%). On the other hand, we cannot exclude that borderline values of lupus anticoagulant early detected on admission will become positive in a subsequent short time. No significant differences in C-reactive protein, D-dimer, prothrombin time, and activated partial-thromboplastin time were observed between subjects with and without ANA or lupus anticoagulant. The lack of difference in D-dimer between patients with and without lupus anticoagulant may be surprising, but this may be due to the fact that inflammation can affect D-dimer levels and that our study population is relatively small. The significant

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Table 1 Features of patients with SARS-CoV2 pneumonia, prevalence of autoimmune markers, and features of the patients stratified by presence/absence of ANA and lupus anticoagulant

Variable			
Age (years)		66.1 ± 12.5	
Men (%)		80	
C-reactive protein (mg/L)		174.2 ± 95.7	
D-dimer (ng/ml)		2854 ± 7495.2	
Ultra-sensitivity cardiac troponin (pg/ml)		48.6 ± 86.6	
Prothrombin time (sec)		12.1 ± 1.6	
Activated partial-thromboplastin time (sec)		30.3 ± 4.1	
Oxygen saturation (%)		88.1 ± 6.7	
Complement C3 (mg/dl)		148.4 ± 41.5	
Complement C4 (mg/dl)		30.5 ± 15.0	
ANA (%)		35.6	
ENA (anti RNP; anti Scl70, anti Sm, anti SS-A/Ro52; anti SS-A/Ro60; anti SS-B/La) (%)		4.4 (anti SS-A/Ro52)	
p-ANCA c-ANCA (%)		6.6	
Anti MPO (%)		2.2	
Anti PR3 (%)		0	
Anticardiolipin IgM (%)		2.2	
Anticardiolipin IGG (%)		2.2	
Anti-beta2-glycoprotein IgM (%)		2.2 4.4 (borderline)	
Anti beta2-glycoprotein IgG (%)		4.4 (borderline)	
Lupus anticoagulant (%)		11.1 35.5 (borderline)	
Variable	Patients with positive ANA ($n = 16$)	Patients with negative ANA ($n = 29$)	p value
Age (years)	68.5 ± 13.4	64.7 ± 12.0	0.3372
Men (%)	75	82.8	0.6998
C-reactive protein (mg/L)	184.9 ± 108.2	168.3±	0.7593
D-dimer (ng/ml)	1821.2 ± 1742.3	3424.1 ± 9257.8	0.6815
Ultra-sensitivity cardiac troponin (pg/ml)	48.5 ± 100.1	48.6 ± 80.2	0.1522
Prothrombin time (sec)	12.3 ± 1.6	11.9 ± 1.6	0.3823
Activated partial-thromboplastin time (sec)	30.2 ± 4.7	30.3 ± 3.7	0.9021
Oxygen saturation (%)	88.1 ± 5.5	88.1 ± 7.4	0.9329
Lupus anticoagulant (%)	50	44.8	0.7648
Variable	Patients with positive or borderline lupus anticoagulant ($n = 21$)	Patients with negative lupus anticoagulant ($n = 24$)	p value
Age (years)	69.2 ± 12.9	63.3 ± 11.7	0.1118
Men (%)	85.7	75	0.4689
C-reactive protein (mg/L)	200.3 ± 99.2	151.3 ± 88.3	0.0868
D-dimer (ng/ml)	2006.9 ± 2665.6	3595.6 ± 10,003.1	0.6172
Ultra-sensitivity cardiac troponin (pg/ml)	82.9 ± 115.8	18.5 ± 25.6	0.0025
Prothrombin time (sec)	12.0 ± 1.3	12.1 ± 1.8	0.7883
Activated partial-thromboplastin time (sec)	31.1 ± 4.5	29.6 ± 3.5	0.2139
Oxygen saturation (%)	85.8 ± 7.6	90.1 ± 5.6	0.0336
ANA (%)	38.1	33.3	0.7648

SARS-CoV2, severe acute respiratory syndrome–coronavirus 2; *ANA*, antinuclear antibodies; *ENA*, extractable nuclear antigen; *anti RNP*: anti-ribonucleoprotein; *anti Sm*, anti Smith; *anti Scl70*, anti-scleroderma; *anti SS-A*, anti Sjögren's syndrome A; *anti SS-B*, anti-Sjögren's syndrome B; *p-ANCA*, perinuclear antineutrophil cytoplasmic antibodies; *c-ANCA*, cytoplasmatic antineutrophil cytoplasmic antibodies; *anti MPO*, anti-myeloperoxidase; *anti PR3*, anti proteinase 3

association of both cardiac troponin and oxygen saturation with lupus anticoagulant may be of clinical interest, as it may predict a worse course of pneumonia, characterized by thrombotic complications and death. However, specific studies have to confirm this hypothesis. In conclusion, our data suggest a possible role of autoimmune mechanisms in SARS-CoV2 pneumonia requiring hospitalization and this may imply specific treatments. Other studies should clarify whether lupus anticoagulant can be used to stratify patients at high risk for cardiovascular involvement and thrombosis and whether it can predict poorer outcomes of viral pneumonia, including death.

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Compliance with ethical standards

Disclosures None.

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