Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

International Journal of Infectious Diseases 98 (2020) 225–226

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Letter to the Editor

Occurrence of Acute Pulmonary Embolism in COVID-19—A case series

To the Editor,

Since the outbreak of the COVID-19 pandemic, growing attention has been paid to the emerging association between severe forms of novel coronavirus pneumonia and abnormalities in coagulation parameters, in particular elevated D-dimer and fibrin degradation product (FDP) levels, that seem to relate to a poor prognosis and are seen as potential predictors of acute thrombotic complications including Acute Pulmonary Embolism (APE) (Tang et al., 2020).

Although isolated reports exist about this issue (Danzi et al., 2020; Casey et al., 2020), its real incidence still remains unknown, possibly due to the preferential use of High-Resolution Computed Tomography (HR-CT) rather than Computed Tomography Pulmonary Angiography (CTPA) to demonstrate inflammatory parenchymal changes.

Herein, we present a series of eight confirmed cases of peripheral multifocal APE in a cohort of 20 hospitalized patients, who consecutively underwent CTPA between March 25 and April 21, 2020, because of abnormal D-dimer levels (>1000 μg/L) and at least one among the following inclusion criteria: risk factors for APE, clinical signs of APE, severe pneumonia (requiring minimum oxygen support of 10 L/min and/or need for Non-Invasive Ventilatory Support, NIV).

The YEARS algorithm, Well's score, and revised Geneva score were applied, although CTPA was performed regardless of their results.

Characteristics of the study population (40% males, median age 58 years) are reported in Table 1.

Notably, the predictors of APE were higher D-Dimer levels ($p = .030$), and higher Revised Geneva Score ($p = .025$). Age, major comorbidities, high oxygen flux requirement or need for invasive mechanical ventilation, Well's Score, and the YEARS algorithm were not associated with APE. In fact, among the eight patients presenting APE, one was a 32-year-old female with no comorbidities who did not require oxygen supplementation.

Remarkably, all patients except one developed EPA despite prophylactic treatment with enoxaparin.

To conclude, the occurrence of APE in our case series was higher than expected. Of note, APE was detected even in young patients with mild symptoms; conversely, critically ill patients did not necessarily show signs of embolism, suggesting other pathogenetic mechanisms apart from blood clotting.

Table 1
Characteristics of 20 Patients with Covid-19 who performed a CTPA for suspected pulmonary embolism.

Characteristics	Total (N = 20)	Absence of Pulmonary Embolism (N = 12)	Pulmonary Embolism (N = 8)	p value
Median Age (IQR) - yr	62 (56–80)	60 (53–63)	78 (59–84)	.177
Male Sex - n (%)	8 (40)	6 (50)	2 (25)	.373
Comorbidity- n (%)				
Arterial Hypertension	11 (55)	6 (50)	5 (62)	.670
Atrial Fibrillation	2 (10)	0	2 (25)	.147
Cancer	2 (10)	2 (17)	0	.495
Diabetes Type II	3 (15)	1 (8)	2 (25)	.537
Obesity	5 (25)	2 (16)	3 (37)	.347
Chronic Kidney Failure	4 (20)	2 (17)	2 (25)	.999
COPD	1 (5)	0	1 (12)	.400
Signs and Symptoms around the time of Hospitalization - n (%)				
Fever	19 (95)	12 (100)	7 (87)	.400
Cough	11 (55)	6 (50)	5 (62)	.670
Dyspnea	9 (45)	5 (41)	4 (50)	.999
Chest X-ray positive for opacities	11 (55)	7 (58)	4 (50)	.999
Need of O2 therapy	16 (80)	10 (83)	6 (75)	.999
Laboratory Tests on Admission - median (IQR)				
WBC, cells/μL	5440 (3735–7995)	4485 (3570–7345)	7150 (4830–9825)	.164
Lymphocytes, %	20 (7–24)	22 (11–24)	7 (6–23)	.113
Platelets, cells/μL	181 (121–227)	181 (121–206)	164 (108–311)	.877
T CD4+, cells/μL	501 (301–860)	528 (429–802)	467 (234–1315)	.713
T CD4/CD8 ratio	1.92 (1.21–2.9)	2.04 (1.21–2.09)	1.62 (1.39–1.92)	.624
Creatininemia, mg/dL	0.85 (0.7–1.14)	0.8 (0.6–1.14)	0.88 (0.72–2.00)	.440
LDH, U/L	243 (188–377)	312 (178–399)	243 (213–264)	.643
C reactive protein, mg/dL (n.v. < 2.9)	90 (17–140)	93 (17–130)	76 (27–146)	.877
Interleukin- 6, pg/mL	56 (24–112)	32 (25–112)	68 (22–109)	.868
D-dimers, μg/L (v.n < 500)	895 (477–1692)	741 (381–921)	1692 (855–5430)	**.030**
NT-pro-BNP, pg/mL (v.n. < 166)	122 (104–521)	115 (104–353)	337 (105–5045)	.327

https://doi.org/10.1016/j.ijid.2020.06.066

Table 1 (*Continued*)

Characteristics	Total (N = 20)	Absence of Pulmonary Embolism (N = 12)	Pulmonary Embolism (N = 8)	p value
HS-Troponin I, ng/mL (v.n. < 71)	10 (5–21)	8.4 (6.4–11)	20 (5–34)	.266
Arterial gas analysis on admission - median (IQR)				
pH	7.46 (7.44–7.51)	7.46 (7.44–7.49)	7.47 (7.41–7.53)	.999
pO2	79 (64–89)	76 (67–85)	82 (64–91)	.699
pC02	33 (30–39)	34 (30–40)	32 (30–35)	.487
P/F ratio	343 (204–380)	343 (210–380)	328 (186–373)	.836
Antiviral Treatment - n (%)				
Lopinavir/r	9 (45)	7 (58)	2 (25)	.197
Hydroxycloroquine	13 (65)	9 (75)	4 (50)	.356
Azithromicin	11 (55)	7 (58)	4 (50)	.999
Days of Antiviral Treatment, median (IQR)	8 (5–9)	8 (6–12)	5 (5–9)	.101
Other Antibiotic treatment - n (%)	10 (50)	7 (58)	3 (37)	.650
Tocilizumab treatment (8 mg/Kg) - n (%)	5 (26)	4 (36)	1 (12)	.338
Enoxaparin Treatment - n (%)	17 (85)	10 (83)	7 (87)	.999
Enoxaparin, mg - median (IQR)	80 (80–120)	80 (80–120)	80 (40–120)	.337
Days of Enoxaparin - median (IQR)	11 (6–13)	11 (6–18)	9 (2–13)	.141
Days of Disease until CTPA, median (IQR)	25 (14–31)	25 (15–28)	23 (14–34)	.817
Need of 10 lt/min of O2 or NIV/IV - n (%)	8 (40)	6 (50)	2 (25)	.373
Need of ICU stay/mechanical ventilation - n (%)	6 (30)	4 (33)	2 (25)	.545
Heart rate >100 bpm when apiretic - n (%)	4 (20)	1 (8)	3 (37)	.255
Atypical chest pain - n (%)	2 (10)	1 (8)	1 (12)	.999
Revised Geneva Score - median (IQR)	1.5 (0–5.5)	0 (0–3)	1 (0–1)	**.025**
Well's Score - median (IQR)	1.25 (0–2.75)	0.5 (0–2.5)	5.5 (2–6)	.394
YEARS algorithm (PE not excluded) - n (%)	14 (70)	7 (58)	7 (87)	.325

Legend: IQR = interquartile range; yr = years; COPD = chronic obstructive pulmonary disease; CTPA = Computed Tomography Pulmonary Angiography; NIV = non-invasive ventilation; IV = invasive ventilation; ICU = intensive care unit; PE = pulmonary embolism.

While thrombotic complications in the course of COVID-19 pneumonia are well documented, more needs to be known about the exact mechanism behind the coagulopathy, which could possibly be a result of direct viral damage to endothelial cells, but also could relate to the disseminated intravascular coagulation (DIC) activated in the course of viral sepsis (Li et al., 2020).

As APE diagnosis is essential for establishing the appropriate dosage and length of anticoagulant treatment, the identification of specific COVID-related predictors is warranted.

Conflict of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript; this includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Ethical approval

According to Italian law, the research did not require formal approval from the ethics committee since it was performed as an observational retrospective study in the context of normal clinical routines (art.1, leg. decree 211/2003). However, the study was conducted following the Declaration of Helsinki as well as national and institutional standards. All patients provided informed consent for the use of their data for research purposes. In any case, data were previously anonymized according to the requirements set by the Italian Data Protection Code (leg. Decree 196/2003).

Funding

This paper was not funded.

References

Casey K, Iteen A, Nicolini R, Auten J. COVID-19 pneumonia with hemoptysis: acute segmental pulmonary emboli associated with novel coronavirus infection [published online ahead of print, 2020 Apr 8]. Am J Emerg Med 2020;, doi: http://dx.doi.org/10.1016/j.ajem.2020.04.011.

Danzi GB, Loffi M, Galeazzi G, et al. Acute Pulmonary Embolism and COVID-19 pneumonia: a random association?. Eur Heart J 2020;(March) pii: ehaa254.

Li Hui, Liu Liang, Zhang Dingyu, et al. SARS-CoV-2 and viral sepsis: observations and hypotheses. Lancet 2020;(April) pii: S0140-6736(20)30920-X.

Tang N, Li D, Wang X, et al. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost 2020;18(April (4)):844–7.

Davide Fiore Bavaro[1,*]
Mariacristina Poliseno[1]
Department of Biomedical Sciences and Human Oncology, Section of Infectious Diseases, University of Bari, Bari, Italy

Arnaldo Scardapane
Interdisciplinary Department of Medicine, Section of Radiology and Radiation Oncology, University of Bari, Bari, Italy

Alessandra Belati
Nicolò De Gennaro
Department of Biomedical Sciences and Human Oncology, Section of Infectious Diseases, University of Bari, Bari, Italy

Amato Antonio Stabile Ianora
Interdisciplinary Department of Medicine, Section of Radiology and Radiation Oncology, University of Bari, Bari, Italy

Giacchino Angarano
Annalisa Saracino
Department of Biomedical Sciences and Human Oncology, Section of Infectious Diseases, University of Bari, Bari, Italy
[1]*Bavaro DF and Poliseno M equally contributed to this work.*

* Corresponding author at: Clinic of Infectious Diseases, University of Bari, Piazza G. Cesare, 11 - 70124 Bari, Italy.
E-mail address: davidebavaro@gmail.com (D. Bavaro).

Received 25 April 2020