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Pulmonary embolism and acro-ischemia in a lung cancer patient with COVID-19



Tromboembolismo pulmonar y acro-isquemia en un paciente con cáncer de pulmón y COVID-19

Dear Editor:

Several authors have reported the association between COVID-19, acral dermo-vascular findings, pulmonary embolism (PE) and disseminated intravascular coagulation (DIC).^{1–5} Herein we report a case of a COVID-19 pneumonia in a lung cancer patient with solitary brain metastases, whose initial clinical findings were secondary acrocyanosis and PE.

A 59-year-old man diagnosed with bone metastasis and solitary brain metastasis secondary to lung adenocarcinoma in treatment with osimertinib came into Radiation Oncology Department to receive brain stereotactic radiation therapy. Several comorbidities were identified: atrial fibrillation anticoagulated with LMWH, arterial hypertension and hypercholesterolemia treated with medications. Previous neurologic symptoms were fully abolished with dexamethasone 12 mg/d and lumbar pain related with bone metastases was controlled with transdermic fentanyl. No respiratory distress was present upon the first visit.

On the first treatment day (day 0) the patient presented to the hospital with cushingoid face, cough, fatigue, shortness of breath beginning suddenly two days before, lower extremities edemas, and painful, discolored skin area surrounding small shallow ulcer on the right big toe. Vital signs on day 0 were T 37.0 °C, HR 110 bpm, BP 89/56 mm Hg, and SpO_2 88% on room air. Most prominent physical exam findings were dispersed crackles on lungs auscultation, leg edemas up to the knees, and a painful 5 mm in diameter clean shallow ulcer with sharp margins located in the plantar surface of the right big toe, surrounded by patches of violaceous skin extended to the second toe. The violaceous patches faded under pressure. The baseline EKG showed rapid atrial fibrillation.

Cardiac failure secondary to PE was suspected and treatment with digoxin was started. On CT pulmonary angiogram (CTPA) it was documented the presence of filling defects in several lobar arteries diagnostic for PE associated with extensive opacifications involving both lungs interpreted as lung infarctions. Furthermore, tumor progression in the primary site and mediastinum was observed. Based on these findings, the patient was hospitalized, the LMWH dose was increased, oxygen was supplied through nasal

cannula, and diuretics plus antibiotics (tazobactam and clindamycin) were started.

Vascular surgeons examined the patient on day 8, verifying popliteal and foot pulse and not recommending vascular radiological exams due to the apparent distal nature of the vascular compromise. On day 9, the violaceous discoloration was more extensive, involving the right aspect of the foot. More severe dyspnea than before prompted to a thorax X-ray showing an extensive and diffuse bilateral lung infiltrate raising the suspicion of COVID-19 pneumonia. The patient was tested with positive result on PCR for SARS-CoV-2.

Table 1 shows the most relevant analytical parameters in chronological order. The clotting profile was not impaired (aPTT normal and Prothrombin INR slightly increased above 1.2), but D-dimer levels were elevated above 0.6 mg/mL (normal level, <0.6 mg/mL) and low platelet count reached grade 2 thrombocytopenia. No DIC criteria were fulfilled.

After 22 days of hospitalization the patient died due to COVID-19 infection, Staph. Aureus bacteremia, bilateral pulmonary embolism, and progressive metastatic lung cancer.

Compared with COVID-19 patients without cancer, COVID-19 patients with cancer had higher risks in death, admission into an intensive care unit, development of severe/critical symptoms, and utilization of invasive mechanical ventilation.³ Patients with blood cancers, lung cancers, or with metastatic cancer (stage IV) had the highest frequency of severe events.¹

Cases of COVID-19 bilateral pneumonia and concomitant acute PE have been reported.^{2,3} The incidence of venous thrombo-embolism (VTE) in 81 patients with severe COVID-19 pneumonia is 25%.⁴ The VTE group had older age, lower lymphocytes count, longer APTT, and higher D-dimer.⁴ Among 184 COVID-19 patients in a Dutch ICU, 31% had thrombotic complications, PE being the most frequent thrombotic complication ($n = 25$, 81%).³

Central thromboembolic events are not the only vascular complications of COVID-19. Zhang et al. have reported 7 patients with critical COVID-19 pneumonia and acro-ischemia.⁵ All patients had finger/toe cyanosis, skin bulla and dry gangrene. D-Dimer, fibrinogen and fibrinogen degradation product (FDP) were significantly elevated in most patients.

In summary, we now report one COVID-19 case with lung cancer and atrial fibrillation presenting central and peripheral intravascular complications highlighting the importance of hypercoagulation status in the pathogenesis, clinical presentation and prognosis of the disease.

Table 1
Analytical parameters in chronological order.

	Units	Day 0	Day 2	Day 5	Day 7	Day 9	Day 12	Day 14	Day 16
Fibrinogen	mg/dL			744				574	637
aPTT	s			31.6	27.9	28.9		34.0	33.8
Prothrombin INR				1.31	1.20	1.15		1.21	1.09
D-Dimer	μg/mL	28.7	–	–	–	–	–	1.3	1.7
Platelets	$\times 10^3/\mu\text{L}$	96.0	57.0	76.0	82.0	100.0	117.0	147.0	–
Lymphocytes	$\times 10^3/\mu\text{L}$	0.52	0.33	0.91	1.43	1.64	1.08	1.22	–
CRP	mg/dL	34.54	18.62	7.55	3.34	2.94	15.55	6.03	1.57

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Terapia antiagregante en el traumatismo craneoencefálico leve



Antiplatelet therapy in mild head trauma

Sr. Editor:

Hemos leído con interés el artículo de Gebenat González M et al.¹ sobre «Papel de la terapia antiagregante en el desarrollo de hemorragia intracraneal tras traumatismo craneal leve», y que es de sumo interés para la medicina de urgencias y emergencias.

Tras su lectura, nos gustaría comentar algunos aspectos que creemos que serían de interés. Aunque son varios los autores que han sugerido una asociación del tratamiento antiagregante en pacientes con traumatismo craneoencefálico (TCE) y mortalidad, otros, sin embargo, no han mostrado incremento de resultados desfavorables. En un metaanálisis reciente, solo se observa un discreto riesgo aumentado de fallecer entre el uso de tratamiento antiagregante y el TCE, sin significación estadística, y que probablemente haya que contemplar este factor de riesgo junto a la edad del paciente (mayores de 65 años) y no de forma aislada². Como vemos en el presente estudio ambos grupos de pacientes tienen edades menores de 65 años: 54 en el grupo de tomografía computarizada normal (TC) y 62 años con TC patológica, con lo que probablemente la edad es una variable de confusión importante.

Los autores eligen dentro de su estudio como comorbilidad la diabetes e hipertensión, creemos que se hubieran tenido que tener en cuenta dentro del estudio otras enfermedades crónicas como por ejemplo la enfermedad renal crónica por su alto riesgo de sangrado debido a múltiples factores (disfunción plaquetaria, anemia, fármacos concomitantes, etc.) u otras como la fibrilación auricular, antecedentes trombo-embólicos, insuficiencia cardíaca o ciertos tipos de demencia.

Los síntomas característicos de un TCE puro son los vómitos, confusión y amnesia con o sin pérdida previa de conciencia, sin embargo los autores no recogieron estas variables que se han relacionado con la gravedad y el pronóstico del cuadro^{3,4}. Añadir que existen también otros factores de riesgo asociados y que se han relacionado con complicaciones como son la presencia de déficits neurológicos, fracturas craneales, consumo de alcohol u

otras drogas, y los portadores de *shunt* para el tratamiento de la hidrocefalia, que tampoco se recogieron en este estudio⁵. En cuanto al concepto mecanismo lesional de alta energía no ha sido descrito por los autores, y es un concepto relativo, en ocasiones correlacionado con la edad, así en ancianos una caída desde su propia altura puede determinar lesiones graves, y ser considerada de alta energía, por lo que creemos importante y de relevancia su descripción en el estudio.

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