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SPECIAL ARTICLE

Group 4 pulmonary hypertension due to choriocarcinoma after molar pregnancy: case report and review

Hipertensión pulmonar del grupo 4 por coriocarcinoma tras embarazo molar: reporte de caso y revisión

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Abstract

A 46-year-old Mexican woman developed type 4 pulmonary hypertension (PH) due to tumor embolism from choriocarcinoma (CC), which is an uncommon presentation of this malignancy. She presented with precordial pain, dyspnea, and rapid functional decline. Imaging revealed obstructive thrombi in the pulmonary arteries, initially suggestive of operable chronic thromboembolic PH (CTEPH). A bilateral subsegmental pulmonary thromboendarterectomy was performed, the standard treatment for CTEPH, aimed at removing obstructive material and restoring hemodynamic stability. However, histopathological examination of the surgical specimens showed malignant cells positive for human chorionic gonadotropin, confirming CC as the source of tumor emboli and leading to reclassification of her condition as type 4.2.2 PH. The patient died intraoperatively due to severe airway bleeding and inability to wean from cardiopulmonary bypass.

Keywords: *Choriocarcinoma. Pulmonary embolism. Thromboendarterectomy. Pulmonary hypertension. Thromboembolism.*

Resumen

Una mujer mexicana de 46 años desarrolló hipertensión pulmonar grupo 4 debido a una embolia tumoral por coriocarcinoma, una presentación poco común de esta malignidad. Se presentó con dolor precordial, disnea y rápido deterioro funcional. Las imágenes revelaron trombos obstructivos en las arterias pulmonares, inicialmente sugerentes de hipertensión pulmonar tromboembólica crónica operable. Se realizó una tromboendarterectomía pulmonar bilateral subsegmentaria, que es el tratamiento estándar, con el objetivo de eliminar el material obstructivo y restaurar la estabilidad hemodinámica. Sin embargo, el examen histopatológico de las muestras quirúrgicas mostró células malignas positivas para gonadotropina coriónica humana, confirmando el coriocarcinoma como fuente de la embolia tumoral y conduciendo a la reclasificación de su condición como hipertensión pulmonar grupo 4.2.2. La paciente falleció intraoperatoriamente debido a una hemorragia grave de las vías respiratorias e incapacidad para retirarla de la circulación extracorpórea.

Palabras clave: *Coriocarcinoma. Embolia pulmonar. Tromboendarterectomía. Hipertensión pulmonar. Tromboembolia.*

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Date of reception: 03-07-2025
Date of acceptance: 22-07-2025
DOI: 10.24875/ACM.25000142

Available online: 07-10-2025
Arch Cardiol Mex. 2026;96(1):62-68
www.archivoscardiologia.com

Introduction

Pulmonary hypertension (PH) is defined as a mean pulmonary arterial pressure (mPAP) ≥ 20 mmHg and is classified into five groups based on etiology[1-3]. Group 4 includes causes related to pulmonary artery obstruction. This category is further subdivided into two classes: chronic thromboembolic PH (CTEPH, Group 4.1) and other pulmonary artery obstructions (Group 4.2)[1,3]. Within the latter subgroup, a rare cause is pulmonary artery embolization due to choriocarcinoma (CC), a rare and aggressive trophoblastic tumor classified by its origin as either gestational or non-gestational. The gestational form occurs in approximately 2-7/100,000 pregnancies, with 25-50% of cases arising after a molar pregnancy[4]. The lungs are the most common site of metastasis;[4] however, presentation as a pulmonary artery embolism is rare; a review identified fewer than 15 cases reported in the literature[5,6] It is believed that pulmonary artery involvement by CC may result from the malignant transformation of trophoblastic cells that migrate during pregnancy[6].

In this article, we present the case of a patient with a history of molar pregnancy who developed group 4 PH. This is followed by a literature review that aims to describe the clinical presentation, demographic characteristics, and outcomes of CC as an uncommon cause of PH group 4.2.

Case report

A 46-year-old Mexican woman presented to the emergency department of the Ignacio Chavez National Institute of Cardiology with progressive precordial pain radiating to the left arm and exertional dyspnea over the past 3 months. Recently, her functional class had deteriorated to NYHA class IV, which led her to seek medical attention. In addition, 2 months ago, she had a single episode of syncope with complete recovery. She had a history of 5 pregnancies, 4 deliveries, and a hysterectomy due to a molar pregnancy 4 years before evaluation. As it was performed elsewhere, the surgical report of hysterectomy and human chorionic gonadotropin hormone (β-HCG) follow-up records were unavailable.

In the emergency room, she was evaluated with an electrocardiogram that revealed an SIQIIITIII pattern and other signs of right ventricular (RV) systolic overload (Fig. 1). Respiratory alkalosis was noted on the blood gas analysis, and laboratory tests showed an elevated N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) level and a normal D-dimer (Table 1).

Table 1. Laboratory values

Parameter	p	Normal reference	Unit
D-dimer	0.269	0.2-0.56	µg/mL
NT-ProBNP	10,971	5-284	pg/mL
HB	16.6	11.7-16.3	g/dL
HTC	49.2	35.4-49.4	%
MCV	89.6	83.3-100	fL
MCH	30.1	26.8-33.2	pg
LEU	12.6	3.56-10.3	$\times 10^3/\mu L$
PLT	295	167-431	$\times 10^3/\mu L$
pH	7.506	7.35-7.45	-
pCO_2	21.2	31-35	mmHg
pO_2	61.7	> 60	mmHg
HCO_3^-	16.6	18-22	mEq/L
Lac	1.5	< 1.5	mmol/L
Anion Gap	15.6	< 12	mEq/L
Osm	277.3	275-295	mmol/kg
K^+	3.5	3.5-5	mEq/L
Na^+	135	135-145	mEq/L
Cl^-	107	98-107	mEq/L
Ca^{2+}	8.8	8.6-10	mEq/L
INR	1.02	0.8-1.2	-
Anti-dsDNA	0.1	< 20	U/mL
IgG ACL	2.6	< 10	GPL/mL
IgG anti-β2GPI	3.7	< 8	U/mL
PT	12.6	9.2-12.2	seconds
aPTT	28.9	27.8-36.3	seconds

NT-ProBNP: N-terminal pro-B-type natriuretic peptide; HB: hemoglobin; HTC: hematocrit; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; LEU: leukocytes; PLT: platelets; pCO_2: partial pressure of carbon dioxide; pO_2: partial pressure of oxygen; Anion Gap: anion gap; Lac: lactate; Osm: osmolality; INR: international normalized ratio; Anti-dsDNA: anti-double-stranded DNA antibodies; IgG ACL: immunoglobulin G anticardiolipin antibodies; IgG anti-β2GPI: immunoglobulin G anti-beta-2 glycoprotein I antibodies; PT: prothrombin time; aPTT: Activated partial thromboplastin time.

A transthoracic echocardiogram (TTEC) demonstrated a slightly dilated right ventricle, hypertrophy of the RV free wall, and paradoxical septal motion (Fig. 1). A lower limb ultrasound was also performed, showing no evidence of deep vein thrombosis. A computed tomography pulmonary angiogram (CTPA) was performed, revealing findings consistent with acute-on-chronic thromboembolism (Fig. 1). Findings included thrombus

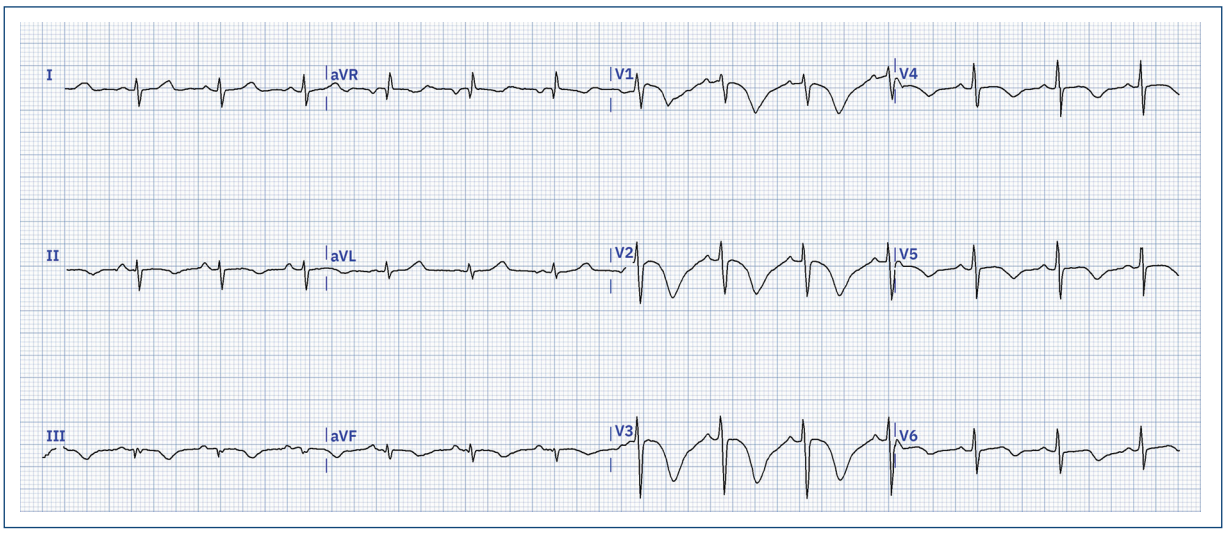

Figure 1. Emergency department electrocardiogram. Sinus rhythm. Dextrorotated and semi-horizontalized showing signs of right ventricular overload (SIQIIITIII pattern +inverted and asymmetrical T waves) and a prolonged QT interval.

occluding the lumen of the right pulmonary artery with lobar and segmental extension, absence of opacification of arterial branches in the right lung, and a partial thrombus in the lumen of the left pulmonary artery with multiple segmental and subsegmental filling defects in the upper and lower lobes (Fig. 2).

Due to evidence of RV dysfunction on TTEC, elevated NT-pro-BNP, and preserved normotension (systolic blood pressure > 90 mmHg), the patient was classified as having intermediate risk pulmonary thromboembolism. Heparin therapeutic anticoagulation was initiated, and she was considered a candidate for pulmonary endarterectomy (PEA) after right heart catheterization, which confirmed PH with acceptable upstream resistance and pulmonary vascular resistance for the procedure (Table 2). In the same catheterization, a pulmonary angiography was performed, revealing complete occlusion of the right pulmonary artery from its ostium (Supplementary Video 1).

PEA using cardiopulmonary bypass procedure was performed on both pulmonary arteries up to their segmental branches, and the retrieved thrombus was sent for analysis. Macroscopically, the thrombus appeared friable and easily fragmentable. Microscopic examination revealed malignant cells with large round nuclei and scant cytoplasm. Immunohistochemical staining was positive for HCG, consistent with CC (Fig. 3). Due to logistical issues, it was not possible to perform additional immunohistochemical markers to differentiate between primary and metastatic CC. However, based on the history of molar pregnancy and the cellular morphology, it is highly likely that this was a case of gestational CC. The patient died intraoperatively due to profuse airway bleeding and failure to wean off extracorporeal circulation.

Materials and methods

A literature search was conducted in Medline in June 2025 using the following keywords: “pulmonary embolism AND choriocarcinoma,” applying the filter for “case reports” and without time restrictions. For the case report, the 2024 CARE guidelines and checklist for case reports were utilized.

Results

A total of 50 cases were identified. These were further screened using the following inclusion criteria: (1) A hemodynamic diagnosis of PH (either 1.1 defined as a mPAP > 20 mmHg confirmed by right heart catheterization, or 1.2 a high probability of PH based on echocardiographic findings); (2) Imaging evidence of pulmonary embolism; and (3) Histological confirmation of the obstructing agent as CC. After applying these criteria, six cases were selected. Including the present case, a total of seven cases were analyzed and are summarized in table 2.

The average age was 32.7 (21-47) years, and all patients had a history of at least one pregnancy.

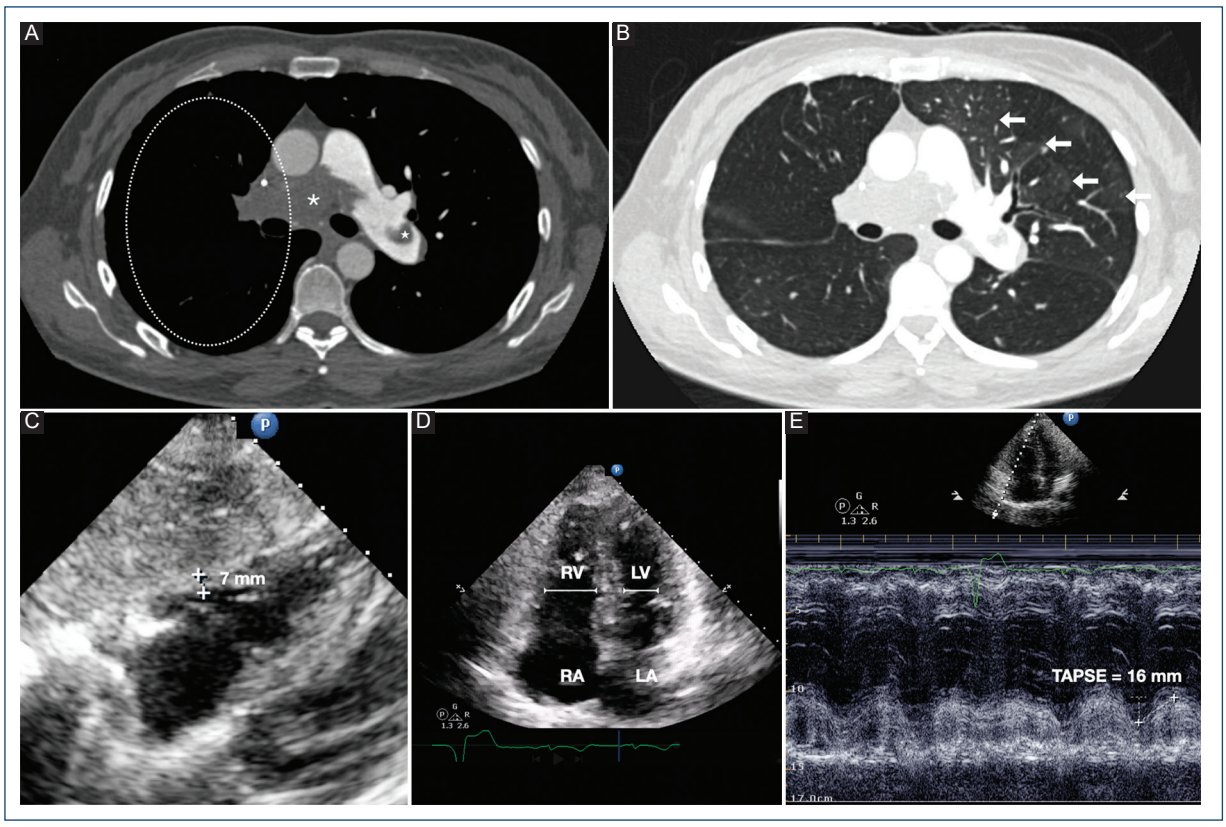

Figure 2. Computed tomography angiogram and transthoracic echocardiogram. **A:** axial section at the level of the pulmonary artery bifurcation in vascular window, demonstrates a thrombus completely occluding the lumen of the right pulmonary artery (asterisk), extending into the lobar and segmental branches. There is no opacification of the arterial branches within the ipsilateral lung (circle). Additionally, a partial thrombus is observed within the lumen of the left pulmonary artery (star). **B:** axial section at the level of the pulmonary artery bifurcation in lung parenchymal window, reveals a mosaic perfusion pattern on the left side (arrows), a finding suggestive of acute-on-chronic thromboembolism. The echocardiogram demonstrated evidence of right ventricular (RV) systolic dysfunction, a reduced fractional area change (FAC% = 27.7%), as well as dilatation and hypertrophy of the RV. **C:** subcostal four-chamber view, showing hypertrophy of the RV free wall measuring 7 mm. **D:** apical four-chamber view demonstrating, an RV/LV ratio of 1.43. **E:** M-mode in apical four-chamber view demonstrating, TAPSE of 16 mm. TAPSE: tricuspid annular plane systolic excursion; RV: right ventricle; LV: left ventricle; RA: right atrium; LA: left atrium.

However, only our patient had a history of molar pregnancy. mPAP showed a wide range from 24 to 105 mmHg. In most cases, β-hCG levels were elevated. The most common symptoms were dyspnea (6/7) and chest pain (5/7). Constitutional symptoms were also reported, including fever (2/7) and night sweats (1/7). Only one patient presented with gynecologic symptoms, specifically vaginal bleeding. The average latency period between the last pregnancy and the onset of symptoms was 21 (2-36) months.

Regarding the presumptive diagnoses before confirmation, 5 of the 7 cases were initially misdiagnosed as pulmonary thromboembolism. Of the patients who received chemotherapy, (2/7) both survived. In contrast, all patients who underwent alternative treatments (including PEA) died.

Discussion

The origin of CC as a neoplastic embolus is unclear, and it may be either primary or metastatic (often gestational in origin). Trophoblasts have been identified in the pulmonary arteries during autopsies of patients who died after childbirth or abortion. It is hypothesized that pulmonary artery CC may arise from malignant transformation of these trophoblasts over time[6].

In another literature review on pulmonary embolism due to CC, 10 out of 11 cases had a history of abortion, with a latency period of 24-72 months between the pregnancy and symptom onset, and no identifiable uterine primary tumor[5,6]. This is consistent with the findings of our review.

Table 2. Literature review

Year of report	References	Country of origin	Age (years)	Gravida	Abortions	Molar pregnancy	Hemodynamic parameters (mmHg)	β-hCG levels (IU/mL)	Clinical manifestations	Symptom onset interval (months)	Initial diagnosis	Treatment	Clinical outcome
1993	13	Japan	47	1	1	No	mPAP: 24 SBP: 42 DBP: 14	Not elevated	Chest pain, dyspnea	36	NA	PEA	Deceased
1997	14	Germany	33	2	1	No	PAP: 34	129,500	Dyspnea, chest pain, cough	5	PE	Methotrexate	Deceased
2016	6	China	25	3	3	No	mPAP: 105	> 1,000-1,000,000	Dyspnea, cough, orthopnea	6	Pneumonia, PE	PEA	Deceased
2016	15	Latvia	31	2	NM	No	ECOTT: HPHP mPAP: 30	2,690	Chest pain, cough, recurrent PE, severe dyspnea, hypoxemia, enlarged right ventricle	18	CTEPH	PEA + chemotherapy	Survived
2017	16	China	26	4	2	No	ECOTT: HPHP	128,575.77	Cough, sputum, night sweats, dyspnea, irregular vaginal bleeding, PE	32	Bronchitis, suspected pulmonary TB	Chemotherapy	Deceased
2023	5	China	21	1	1	No	mPAP 28	> 10,000	Chest pain, mild fever, massive pulmonary embolism	2	Pneumonia	Chemotherapy	Survived
Present case		Mexico	46	5	1	Yes	mPAP 45	Not performed	Dyspnea, chest pain, sumassive pulmonary embolism, syncope	48	CTEPH	PEA	Deceased

PAE: pulmonary endarterectomy; mPAP: mean pulmonary artery pressure; CTEPH: chronic thromboembolic pulmonary hypertension; β-hCG: beta human chorionic gonadotropin; NM: not mentioned; NP: not performed; HPHPE: high probability of pulmonary hypertension on echocardiography.

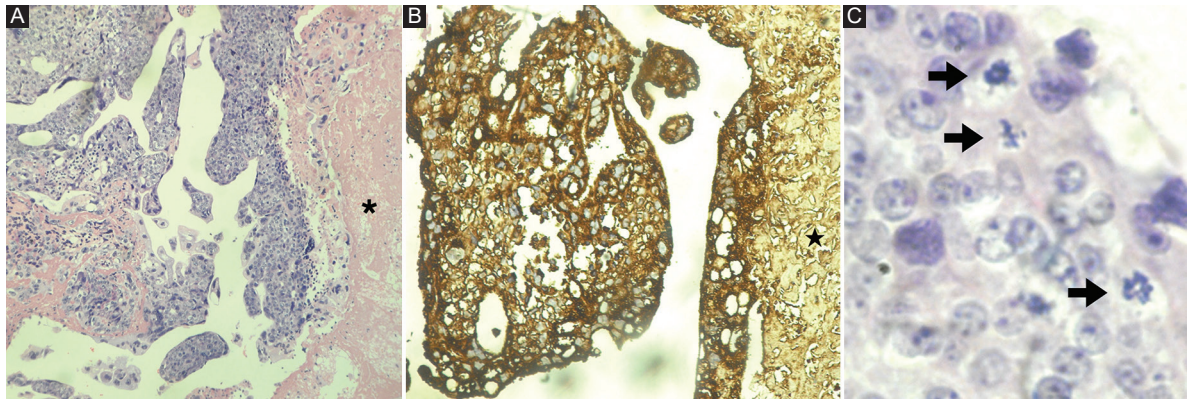

Figure 3. Histological sections of the thrombus. **A:** micrograph of an embolus extracted from the pulmonary artery hematoxylin and eosin (H&E) × 20, showing a malignant neoplasm composed of cells with large, round nuclei and scant cytoplasm, arranged in a solid histological pattern forming irregular projections. Thrombi accompanying the neoplasm are observed (asterisk). **B:** micrograph using immunohistochemistry with the human chorionic gonadotropin hormone (HGC) marker × 20, showing dark brown positive staining in malignant neoplastic cells, while the thrombus (star) is negative. **C:** higher magnification micrograph of the malignant neoplasm H&E × 40, showing cells with large, round nuclei and multiple nucleoli. In this field, three atypical mitoses (arrows).

As previously noted, the most frequent symptoms-dyspnea and chest pain-are nonspecific and can lead to misdiagnosis. Dyspnea and chest pain are typically attributable to pulmonary embolism, whereas syncope, which is strongly associated with PH[2,7], was observed only in the present case.

One of the most common initial presumptive diagnoses in pulmonary artery embolism due to CC was pulmonary thromboembolism, which in chronic form can cause group 4 PH, also known as CTEPH. Diagnosing CTEPH is complex, and current exclusion algorithms lack specificity[2,8]. According to the European Society of Cardiology guidelines, diagnosis should be based on findings obtained after at least 3 months of effective anticoagulation. These include a mPAP ≥ 20 mmHg, a pulmonary artery wedge pressure ≤ 15 mmHg, and the presence of vascular lesions identified via CTPA, or magnetic resonance imaging[1,2,9]. Furthermore, pulmonary angiography may reveal findings such as pouch defects, bands, webs, and occlusions, which are indicative of CTEPH[10].

PEA remains the treatment of choice for patients with operable CTEPH[10-12]. This procedure involves the surgical removal of obstructive fibrotic tissue from the pulmonary arteries[12]. The benefits of this intervention include the potential cure of CTEPH, improved survival, better quality of life, and long-term functional class[10,11]. The restoration of pulmonary hemodynamics occurs in 68.8-91.8% of the cases[12]. However, some of the complications include reperfusion pulmonary edema, persistent PH after procedure, and, in severe cases, pulmonary hemorrhage[10-12].

Despite its aggressive nature, CC responds well to chemotherapy[4,6]. One case report described a patient with pulmonary embolism secondary to gestational CC who had a favorable clinical outcome following chemotherapy. In that case, the diagnostic process began after identifying a history of medical abortion and incomplete follow-up of β-hCG levels. Further diagnostic workup revealed increased uptake in the pulmonary arteries on positron emission tomography (PET) scan, and a pelvic ultrasound showed findings consistent with uterine CC[5].

In the present case, the initial diagnosis was CTEPH, for which the patient underwent PEA. However, the diagnosis of pulmonary embolism due to CC -which was causing the PH-was not established until the histopathological analysis of the neoplastic embolus. During the diagnostic workup, a PET-computed tomography scan could have been beneficial given the favorable uptake of CC on this imaging modality.

Conclusion

Pulmonary artery embolization due to CC is a rare but potentially fatal condition that can lead to Group 4.2 PH as a result of intraluminal arterial obstruction. This etiology should be considered in the differential

diagnosis of CTEPH. Before pursuing PEA, we suggest including serum β-hCG level assessment in the diagnostic workup for patients with CTEPH and compatible clinical background. Particularly in women with relevant risk factors such as a history of abortion or, notably, molar pregnancy. In the present case, earlier recognition of CC might have significantly altered the clinical course, given the tumor's well-documented sensitivity to chemotherapy.

Further research is needed to improve our understanding of the pathophysiological mechanisms, latency period, and risk factors associated with CC-related PH, with the ultimate goal of enhancing early recognition and guiding optimal management strategies.

Acknowledgments

We would like to express our sincere gratitude to the department of clinical archives and informatics for their assistance in facilitating access to the patient's imaging studies. Our sincere thanks also go to the medical staff on the eighth-floor hospital ward at the Ignacio Chávez National Institute of Cardiology for their invaluable guidance and support throughout the course of this work.

Funding

This research has not received any specific grant from public, commercial, or not-for-profit funding agencies.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely collected and anonymized clinical data; therefore, individual informed consent was not required. Relevant ethical recommendations have been followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

Supplementary data

Supplementary data is available at DOI: 10.24875/ACM.25000142. This data is provided by the corresponding author and is published online for the benefit of the reader. The content of the supplementary data is the sole responsibility of the authors.

References

1. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RM, Brida M, et al. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Heart J. 2022;43:3618-731.
2. Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing GJ, Harjola VP, et al. 2019 ESC guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European respiratory society (ERS). Eur Heart J. 2020;41:543-603.
3. Simonneau G, Montani D, Celermajer DS, Denton CP, Gatzoulis MA, Krowka M, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J. 2019;53:1801913.
4. Bogani G, Ray-Coquard I, Mutch D, Vergote I, Ramirez PT, Prat J, et al. Gestational choriocarcinoma. Int J Gynecol Cancer. 2023;33:1504-14.
5. Wang P, Ren D, Guo C, Ding X, Cao Y, Zhao P, et al. A rare case of pulmonary artery embolism with choriocarcinoma: a case report and literature review. Oncol Lett. 2023;26:490.
6. Yan Z, Meining Y, Luyao M, Hai X, Li FR. Choriocarcinoma-associated pulmonary thromboembolism and pulmonary hypertension: a case report. J Biomed Res. 2016;30:243-7.
7. Pepke-Zaba J, Jansa P, Kim NH, Naeije R, Simonneau G. Chronic thromboembolic pulmonary hypertension: role of medical therapy. Eur Respir J. 2013;41:985-90.
8. Klok FA, Dzikowska-Diduch O, Kostrubiec M, Vliegen HW, Pruszczyk P, Hasenfuß G, et al. Derivation of a clinical prediction score for chronic thromboembolic pulmonary hypertension after acute pulmonary embolism. J Thromb Haemost. 2016;14:121-8.
9. Lang IM, Campean IA, Sadushi-Kolici R, Badr-Eslam R, Gerges C, Skoro-Sajer N. Chronic thromboembolic disease and chronic thromboembolic pulmonary hypertension. Clin Chest Med. 2021;42:81-90.
10. Yang J, Madani MM, Mahmud E, Kim NH. Evaluation and management of chronic thromboembolic pulmonary hypertension. Chest. 2023;164:490-502.
11. Goldberg JB, Giri J, Kobayashi T, Ruel M, Mittnacht AJ, Rivera-Lebron B, et al. Surgical management and mechanical circulatory support in high-risk pulmonary embolisms: historical context, current status, and future directions: a scientific statement from the American heart association. Circulation. 2023;147:e628-47.
12. Mangukia C, Rali P, Desai P, Ku TS, Brann S, Patel S, et al. Pulmonary endarterectomy. Indian J Thorac Cardiovasc Surg. 2021;37:662-72.
13. Yutani C, Imakita M, Ishibashi-Ueda H, Katsuragi M, Yoshioka T, Kunieda T. Pulmonary hypertension due to tumor emboli: a report of three autopsy cases with morphological correlations to radiological findings. Acta Pathol Jpn. 1993;43:135-41.
14. Trübenbach J, Pereira PL, Huppert PE, Farnsworth C, Mayer R, Feine U, et al. Primary choriocarcinoma of the pulmonary artery mimicking pulmonary embolism. Br J Radiol. 1997;70:843-5.
15. Skride A, Sablinskis K, Klepetko W, Lang I. Choriocarcinoma mimicking chronic thromboembolic pulmonary hypertension. Eur Heart J. 2016;37:1480.
16. Yang M, Peng L. Role of chemotherapy and thrombolysis in treatment of choriocarcinoma accompanied with pulmonary embolism: a case report with literature review. Medicine (Baltimore). 2017;96:e7866.