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Catastrophic Antiphospholipid Syndrome Presenting with Extensive Iliac Vein Thrombosis and Subsequent Takotsubo Cardiomyopathy in a Young Woman

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Case Report

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Abstract

Background:

Catastrophic antiphospholipid syndrome (CAPS) is a life-threatening variant of antiphospholipid syndrome characterized by rapid multi-organ thrombosis. Its precipitation by progestogen therapy in young women with underlying thrombophilia remains underrecognized.

Case Presentation:

A 20-year-old woman with polycystic ovary syndrome (PCOS), treated with dydrogesterone 10 mg daily for two months, was admitted for extensive right iliac deep vein thrombosis extending to the inferior vena cava. After five days of anticoagulation, she re-presented with chest pain. Investigations revealed positive troponins, inferolateral ECG changes, apical akinesia on echocardiography (LVEF 59%), and patent coronary arteries on angiography. Left ventriculography was consistent with Takotsubo cardiomyopathy. Laboratory evaluation confirmed CAPS. The course was complicated by severe femoral puncture-site hemorrhage and epigastric artery bleeding in the context of extreme thrombocytopenia (platelets: 2,000/µL). The patient responded markedly to intravenous immunoglobulin (IVIG) therapy.

Conclusion:

Early recognition of CAPS is crucial, as prompt initiation of combined immunomodulatory and anticoagulant therapy significantly improves prognosis.

Background

Antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterized by recurrent arterial or venous thrombosis and/or pregnancy morbidity in the presence of persistent antiphospholipid antibodies. (1) It represents one of the most common acquired thrombophilias and can occur either as a primary condition or in association with other autoimmune diseases, particularly systemic lupus erythematosus.

Among these manifestations, catastrophic antiphospholipid syndrome (CAPS) represents the most severe and rare form of APS, occurring in less than 1% of patients with the disease. (2) CAPS is characterized by the rapid development of widespread thrombosis involving multiple vascular beds and leading to multiorgan failure over a short period of time, typically within days. Despite advances in recognition and management, CAPS

remains associated with high mortality rates, emphasizing the importance of early diagnosis and aggressive treatment. (3)

Cardiac involvement in APS is well documented and includes a variety of manifestations such as valvular heart disease, coronary artery thrombosis, intracardiac thrombi, and microvascular myocardial injury. However, stress-induced cardiomyopathy, also known as Takotsubo syndrome, has rarely been reported in association with antiphospholipid syndrome and even more exceptionally in the context of catastrophic APS.

Takotsubo cardiomyopathy is a transient form of left ventricular systolic dysfunction that mimics acute coronary syndrome but occurs in the absence of obstructive coronary artery disease. Although the exact mechanisms remain incompletely understood, catecholamine excess, microvascular dysfunction, and myocardial stunning are believed to play key roles in its pathophysiology. Systemic inflammatory or autoimmune conditions may act as triggering factors through endothelial dysfunction and intense physiological stress.

We report the case of a 20-year-old woman initially presenting with extensive iliac deep vein thrombosis who rapidly developed cardiac involvement mimicking acute coronary syndrome. Further investigations revealed normal coronary arteries with ventriculographic findings compatible with Takotsubo cardiomyopathy in the setting of catastrophic antiphospholipid syndrome. This case highlights the complex interaction between autoimmunity, thrombosis, and stress-related myocardial dysfunction.

Case report

A 20-year-old woman with a history of polycystic ovary syndrome (PCOS) presented to the emergency department with right lower limb pain, and swelling of four days duration. She had been prescribed dydrogesterone 10 mg daily two months prior for cycle regulation. She reported no personal or family history of thromboembolic disease, autoimmune disorder, or other chronic illness. She was not taking any other medications, and denied tobacco use, pregnancy, or prolonged immobilization. Physical examination revealed right lower extremity pitting edema extending to the thigh, with skin warmth and tenderness along the iliac vessels. Cardiorespiratory examination was unremarkable. Doppler ultrasonography and CT venography confirmed extensive right iliac deep vein thrombosis with proximal propagation to the junction with the inferior vena cava, without radiological evidence of pulmonary embolism at that time. Dydrogesterone was immediately discontinued. Therapeutic anticoagulation was initiated with low-molecular-weight heparin (LMWH), bridged to a direct oral anticoagulant (DOAC). A comprehensive thrombophilia workup was initiated before discharge, including screening for inherited and acquired prothrombotic conditions. The patient was discharged after five days of uneventful hospitalization with outpatient follow-up scheduled.

Two days after discharge, the patient returned with acute-onset central chest pain radiating to the left shoulder, associated with dyspnea and mild diaphoresis. She denied fever, palpitations, syncope, or any new stressor. Vital signs on arrival: blood pressure 105/68 mmHg, heart rate 102 bpm, respiratory rate 18/min, SpO2 96% on room air, temperature 37.2°C. A 12-lead EKG showed T-wave inversions with biphasic changes in the inferolateral leads. Serial high-sensitivity troponin measurements were elevated and rising. Transthoracic echocardiography (TTE) demonstrated apical akinesia with an otherwise preserved left ventricular ejection fraction (LVEF 59%), without significant pericardial effusion or valvular abnormality.

Urgent coronary angiography revealed entirely normal, smooth coronary arteries with no evidence of obstructive disease, dissection, spasm, or thrombosis. (Fig. 1)

Left ventriculography confirmed apical wall motion abnormality, a pattern consistent with a Takotsubo cardiomyopathy. (Fig. 2) Extensive laboratory investigations were conducted to identify an underlying systemic etiology for the recurrent thrombotic and cardiac events:

- Homocysteine: 23.3 µmol/L (elevated; normal < 15 µmol/L) — indicating hyperhomocysteinemia, a recognized pro-thrombotic condition associated with endothelial dysfunction
- Complement C1 IgG: elevated — indicating classical complement pathway engagement
- Circulating immune complexes (CIC): 11.4 (elevated) — consistent with immune complex-driven vascular injury
- Antinuclear antibodies (ANA): positive at titer 1/80
- Anti-double-stranded DNA antibodies (anti-dsDNA): 27 UI/L (elevated) — raising the possibility of an underlying lupus spectrum disorder
- Antiphospholipid antibodies: strongly positive (lupus anticoagulant and/or anticardiolipin antibodies confirmed; awaiting 12-week repeat confirmation)
- Platelet count: 2,000/µL — severe thrombocytopenia

The clinico-biological constellation fulfilled the diagnostic criteria for Catastrophic Antiphospholipid Syndrome (CAPS) as defined by the Asherson criteria: involvement of at least three organ systems (venous thrombotic, cardiac/Takotsubo, and hematologic), symptom development within less than one week, and laboratory confirmation of antiphospholipid antibodies. The positive ANA and anti-dsDNA serology further raised suspicion for a lupus-associated secondary APS.

Despite the predominant thrombotic background, the patient's clinical course was complicated by significant hemorrhagic events attributable to severe thrombocytopenia: Expanding femoral puncture-site hematoma with active arterial bleeding following

coronary angiography with epigastric artery hemorrhage identified on a contrast-enhanced computed tomography (CT) scan. (Fig. 3) Hemostasis was successfully achieved using a Femostop compression device. After multidisciplinary discussion with the vascular surgery team, no endovascular or surgical intervention was deemed necessary, as the bleeding had ceased and the patient remained hemodynamically stable.This dual thrombotic-hemorrhagic state, the typical feature of the most severe CAPS presentations, posed major management challenges. With platelet counts at 2,000/µL, maintaining therapeutic anticoagulation carried an unacceptable hemorrhagic risk. A multidisciplinary team including hematology, cardiology, rheumatology, and interventional radiology was convened. Platelet transfusions and local hemostatic measures were implemented, and anticoagulation was temporarily suspended. Following the diagnosis of CAPS, treatment was initiated in accordance with international guidelines. The therapeutic strategy included intravenous immunoglobulins (IVIG): 2 g/kg over five days with high-dose intravenous corticosteroids: methylprednisolone 1 g/day for three days, then tapering and careful anticoagulation management:dose-adjusted LMWH with close platelet monitoring and transfusion support. The patient demonstrated significant clinical improvement following IVIG therapy. Platelet counts progressively recovered over seven days. Repeat echocardiography at day 10 showed resolution of the apical akinesia, confirming the reversible nature of Takotsubo cardiomyopathy. Troponin levels normalized. Hemorrhagic complications were controlled. The patient was transferred to the internal medicine department for rheumatology evaluation, immunosuppressive therapy optimization, and long-term anticoagulation planning.

Discussion

This case presents a clinically instructive example of CAPS triggered by dydrogesterone in a young woman with previously undiagnosed antiphospholipid syndrome, culminating in extensive veinous thrombosis, Takotsubo cardiomyopathy, thrombocytopenic hemorrhage, and a systemic autoimmune inflammatory cascade.

Catastrophic antiphospholipid syndrome represents the most severe and life-threatening manifestation of antiphospholipid syndrome, occurring in less than 1% of patients with APS but accounting for a disproportionately high mortality rate, estimated between 30% and 50% despite modern therapeutic strategies. CAPS is characterized by the rapid development of multiple thrombotic events affecting small, medium, and large vessels, leading to multiorgan failure within a short period of time, usually less than one week. (4) (5)

In the present case, the disease was initially revealed by extensive right iliac deep vein thrombosis extending to the confluence of the inferior vena cava in a 20-year-old woman. Venous thromboembolism remains the most common initial manifestation of APS,

particularly in young patients without conventional thrombotic risk factors. The presence of polycystic ovary syndrome (PCOS) and recent hormonal therapy with dydrogesterone may have contributed to a prothrombotic state, although progesterone derivatives are generally considered less thrombogenic than estrogen-containing therapies. Nevertheless, hormonal therapy may act as a precipitating factor in individuals with underlying thrombophilic conditions.

In the context of CAPS, several mechanisms could explain the occurrence of Takotsubo cardiomyopathy. First, the severe systemic inflammatory response and cytokine release associated with CAPS may induce endothelial dysfunction and microvascular impairment. Second, microthrombotic involvement of the coronary microcirculation could lead to transient myocardial ischemia. Finally, the intense physiological stress associated with a life-threatening autoimmune disorder may trigger catecholamine surges capable of inducing stress cardiomyopathy. (6) Another striking aspect of this case is the profound thrombocytopenia that developed during hospitalization, with platelet levels dropping to 2,000/mm□ and complicated by severe hemorrhage at the femoral puncture site involving the epigastric artery. Thrombocytopenia is frequently observed in APS and CAPS and may result from immune-mediated platelet destruction, platelet consumption during widespread thrombosis, or complement activation. The coexistence of thrombosis and bleeding complications represents a significant therapeutic challenge in these patients, particularly in the setting of mandatory anticoagulation. (7)

The immunological findings in this patient further support the diagnosis of a systemic autoimmune process. The presence of positive antinuclear antibodies, anti-double stranded DNA antibodies, circulating immune complexes, and complement abnormalities suggests an underlying autoimmune activation that may represent either primary APS or APS associated with an evolving systemic autoimmune disease such as systemic lupus erythematosus (SLE). In fact, APS may precede the clinical onset of SLE in a subset of patients. (8) The rapid evolution of the clinical picture in this patient, with the occurrence of cardiac involvement shortly after the initial thrombotic event, raises strong suspicion for catastrophic APS. CAPS is frequently triggered by identifiable precipitating factors such as infections, surgical procedures, pregnancy, or medication exposure. In approximately half of cases, however, no clear trigger is identified.

Cardiac involvement in APS is well documented and may include coronary thrombosis, valvular disease, myocardial microvascular thrombosis, and cardiomyopathy. However, the association between CAPS and Takotsubo cardiomyopathy remains extremely rare. (9) The Takotsubo diagnosis requires specific discussion. In the absence of a significant emotional or physical stressor, and in the context of a florid immune-thrombotic syndrome, the classic catecholamine-mediated mechanism is an insufficient explanation. aPL antibodies are capable of activating coronary endothelial cells, inducing microvascular spasm, and

promoting microthrombosis in small vessels, mechanisms that can produce regional wall motion abnormalities indistinguishable from stress cardiomyopathy on functional imaging.(10) The laboratory findings provide important mechanistic insights. Hyperhomocysteinemia independently amplifies thrombotic risk by promoting endothelial injury, enhancing oxidative stress, and activating platelet aggregation, acting synergistically with aPL antibodies in driving vascular occlusion. The elevation of complement factors along with elevated circulating immune complexes, suggests complement pathway activation as a critical effector mechanism in this patient's CAPS, consistent with experimental data demonstrating that aPL-mediated complement activation is required for thrombosis in APS. The presence of elevated anti-dsDNA antibodies alongside with elevated ANA raises the possibility of secondary APS in the context of systemic lupus erythematosus (SLE) or a lupus-like disorder, which will require longitudinal immunological follow-up.

The thrombocytopenic hemorrhage paradox observed here, simultaneous macro- and microvascular thrombosis with life-threatening bleeding from platelet counts of 2,000/µL, represents the most complex therapeutic challenge in CAPS. Thrombocytopenia in CAPS is multifactorial, resulting from platelet consumption at sites of microvascular thrombosis, immune-mediated platelet destruction, and possible thrombotic microangiopathy (TMA) overlap. The extreme thrombocytopenia rendered standard anticoagulation hazardous, necessitating immunomodulation as the primary therapeutic modality. IVIG therapy proved highly effective in this case. Its mechanisms in CAPS include blockade of Fc receptors on macrophages (reducing platelet destruction), neutralization of pathogenic antibodies, complement inhibition, and modulation of B- and T-cell function. The rapid platelet recovery and clinical improvement observed align with published case series reporting IVIG efficacy in aPL-mediated thrombocytopenia and CAPS. This case supports IVIG as a first-line rescue therapy in CAPS patients where hemorrhagic risk precludes optimal anticoagulation.(11) Management of catastrophic antiphospholipid syndrome requires rapid initiation of aggressive combined therapy. The current standard of care typically includes therapeutic anticoagulation, high-dose corticosteroids, plasma exchange, and/or intravenous immunoglobulins (IVIG). The so-called “triple therapy” approach (anticoagulation, corticosteroids, and plasma exchange or IVIG) has been associated with improved survival compared with anticoagulation alone.

In our patient, treatment with intravenous immunoglobulins resulted in significant clinical and biological improvement. IVIG may exert beneficial effects by modulating autoantibody activity, inhibiting complement activation, and reducing immune complex-mediated vascular injury.

This case highlights several important aspects of catastrophic APS. First, the syndrome may present initially with large-vessel thrombosis before rapidly progressing to multiorgan

involvement. Second, cardiac manifestations may mimic acute coronary syndrome but can be related to stress cardiomyopathy in the absence of coronary artery disease. Finally, severe thrombocytopenia and hemorrhagic complications may occur even in the context of a highly prothrombotic state.

Conclusion

This case illustrates a rare and severe presentation of catastrophic antiphospholipid syndrome in a young woman initially presenting with extensive iliac deep vein thrombosis and subsequently developing Takotsubo cardiomyopathy. Early recognition and prompt immunomodulatory therapy are essential to improve outcomes in this life-threatening condition

Increased clinical awareness of CAPS as a differential diagnosis in young patients presenting with concurrent venous thromboembolism, unexplained cardiomyopathy, thrombocytopenia, and autoimmune serology is essential to reduce diagnostic delays and improve outcomes in this rare but devastating syndrome.

Abbreviations

aPL
Antiphospholipid antibodies
ANA
Antinuclear antibodies
anti-dsDNA
Anti–double stranded DNA antibodies
APS
Antiphospholipid syndrome
CAPS
Catastrophic antiphospholipid syndrome
CT
Computed tomography
DVT
Deep vein thrombosis
EKG
Electrocardiogram
IVC
Inferior vena cava
IVIG
Intravenous immunoglobulins
LVEF

Left ventricular ejection fraction
PCOS
Polycystic ovary syndrome

Declarations

Ethics approval and consent to participate

Written informed consent was obtained from the patient.

Consent for publication

Written informed consent for publication of clinical details and images was obtained from the patient.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

A.M. collected the clinical data and drafted the manuscript. A.H. and Z.M. contributed to the interpretation of clinical and imaging findings. A.M. supervised the work and critically revised the manuscript. All authors read and approved the final manuscript.

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References

1. Asherson RA. The catastrophic antiphospholipid (Asherson's) syndrome. Autoimmun Rev déc. 2006;6(2):64–7. 10.1016/j.autrev.2006. 06.005 PubMed PMID: 17138244.
2. Cervera R, Rodríguez-Pintó I, Colafrancesco S, Conti F, Valesini G, Rosário C, et al. 14th International Congress on Antiphospholipid Antibodies Task Force Report on Catastrophic Antiphospholipid Syndrome. Autoimmun Rev juill. 2014;13(7):699–707. .002 PubMed PMID: 24657970.

3. de Groot PG, Derksen RHWM. Pathophysiology of the antiphospholipid syndrome. J Thromb Haemost JTH août. 2005;3(8):1854–60. 10.1111/j.1538-7836.2005. 01359.x PubMed PMID: 16102052.
4. Espinosa G, Rodríguez-Pintó I, Cervera R. Catastrophic antiphospholipid syndrome: an update. Panminerva Med sept. 2017;59(3):254–68. 10.23736/S0031-0808.17.03324-9. PubMed PMID: 28488841.
5. Erkan D, Asherson RA, Espinosa G, Cervera R, Font J, Piette JC, et al. Long term outcome of catastrophic antiphospholipid syndrome survivors. Ann Rheum Dis juin. 2003;62(6):530–3. 10.1136/ard.62.6.530. PubMed PMID: 12759289; PubMed Central PMCID: PMC1754574.
6. Meroni PL, Borghi MO, Raschi E, Tedesco F. Pathogenesis of antiphospholipid syndrome: understanding the antibodies. Nat Rev Rheumatol juin. 2011;7(6):330–9. 10.1038/nrrheum.2011.52. PubMed PMID: 21556027.
7. Bucciarelli S, Cervera R, Espinosa G, Gómez-Puerta JA, Ramos-Casals M, Font J. Mortality in the catastrophic antiphospholipid syndrome: causes of death and prognostic factors. Autoimmun Rev déc. 2006;6(2):72–5. 10.1016/j.autrev.2006.06.007. PubMed PMID: 17138246.
8. Cervera R, Rodríguez-Pintó I, Espinosa G. The diagnosis and clinical management of the catastrophic antiphospholipid syndrome: A comprehensive review. J Autoimmun août. 2018;92:1–11. 10.1016/j.jaut.2018.05.007. PubMed PMID: 29779928.
9. Cervera R, Bucciarelli S, Plasín MA, Gómez-Puerta JA, Plaza J, Pons-Estel G, et al. Catastrophic antiphospholipid syndrome (CAPS): descriptive analysis of a series of 280 patients from the « CAPS Registry ». J Autoimmun. 2009;32(3–4):240–5. .008 PubMed PMID: 19324520.
10. Lyon AR, Citro R, Schneider B, Morel O, Ghadri JR, Templin C, et al. Pathophysiology of Takotsubo Syndrome: JACC State-of-the-Art Review. J Am Coll Cardiol 23 févr. 2021;77(7):902–21. 10.1016/j.jacc.2020.10.060. PubMed PMID: 33602474.
11. Tektonidou MG, Andreoli L, Limper M, Amoura Z, Cervera R, Costedoat-Chalumeau N, et al. EULAR recommendations for the management of antiphospholipid syndrome in adults. Ann Rheum Dis oct. 2019;78(10):1296–304. 10.1136/annrheumdis-2019-215213. PubMed PMID: 31092409; PubMed Central PMCID: PMC11034817.

Figures

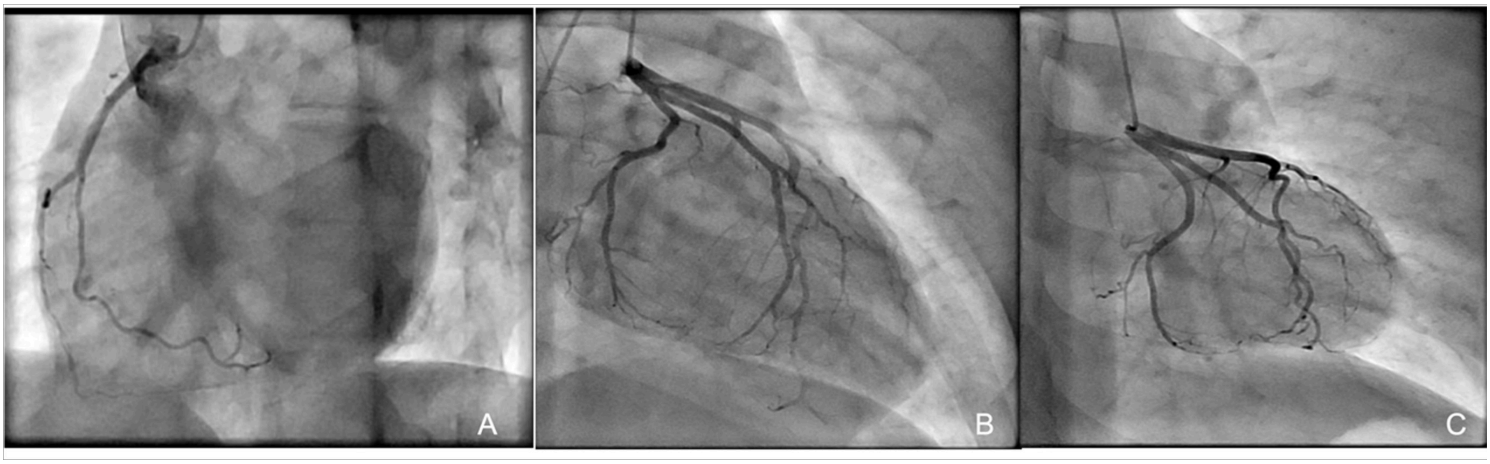


Figure 1

Coronary angiography demonstrating normal coronary arteries without evidence of obstructive coronary artery disease

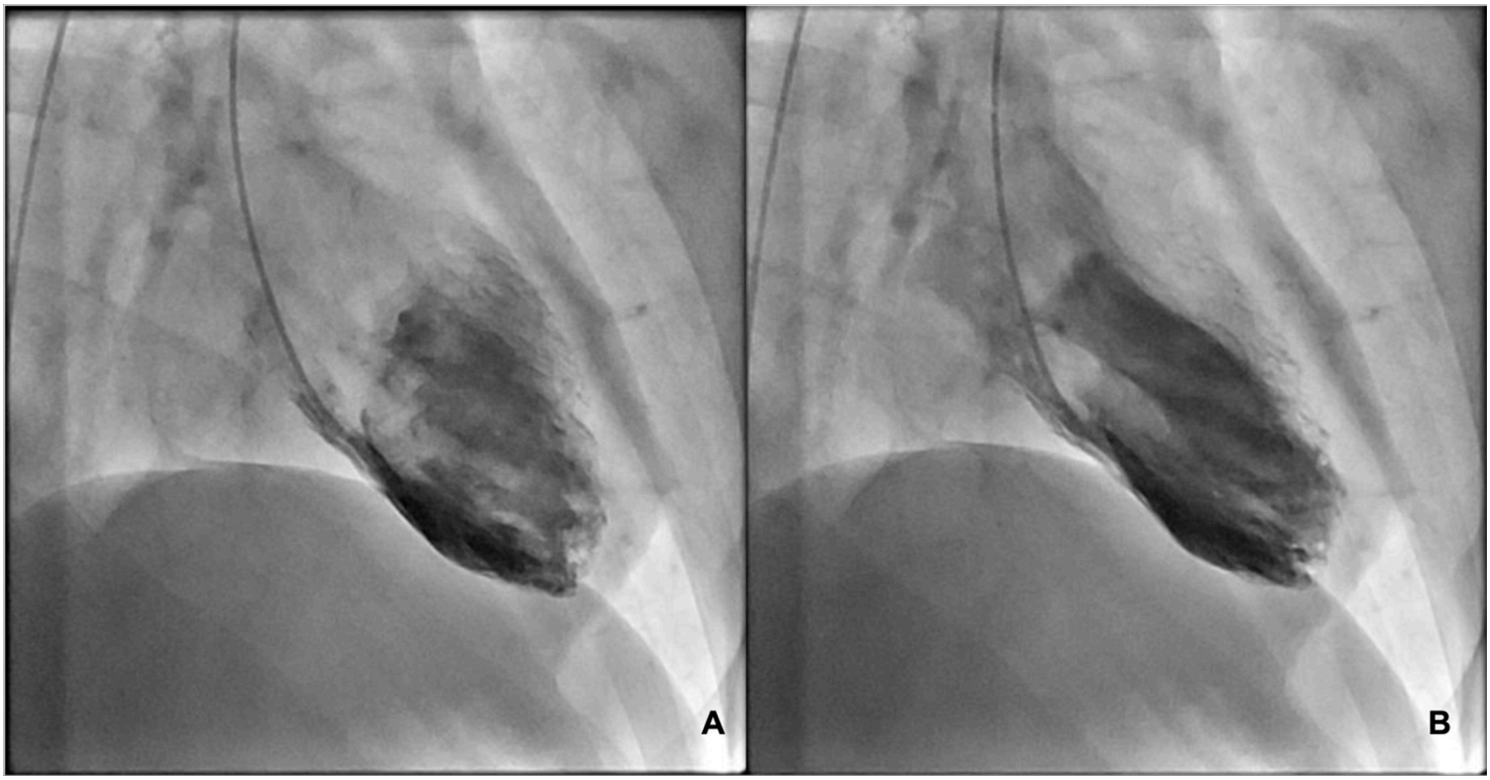


Figure 2

Left ventriculography. (A) End-diastolic frame and (B) end-systolic frame demonstrating apical akinesia consistent with stress-induced cardiomyopathy (Takotsubo syndrome)

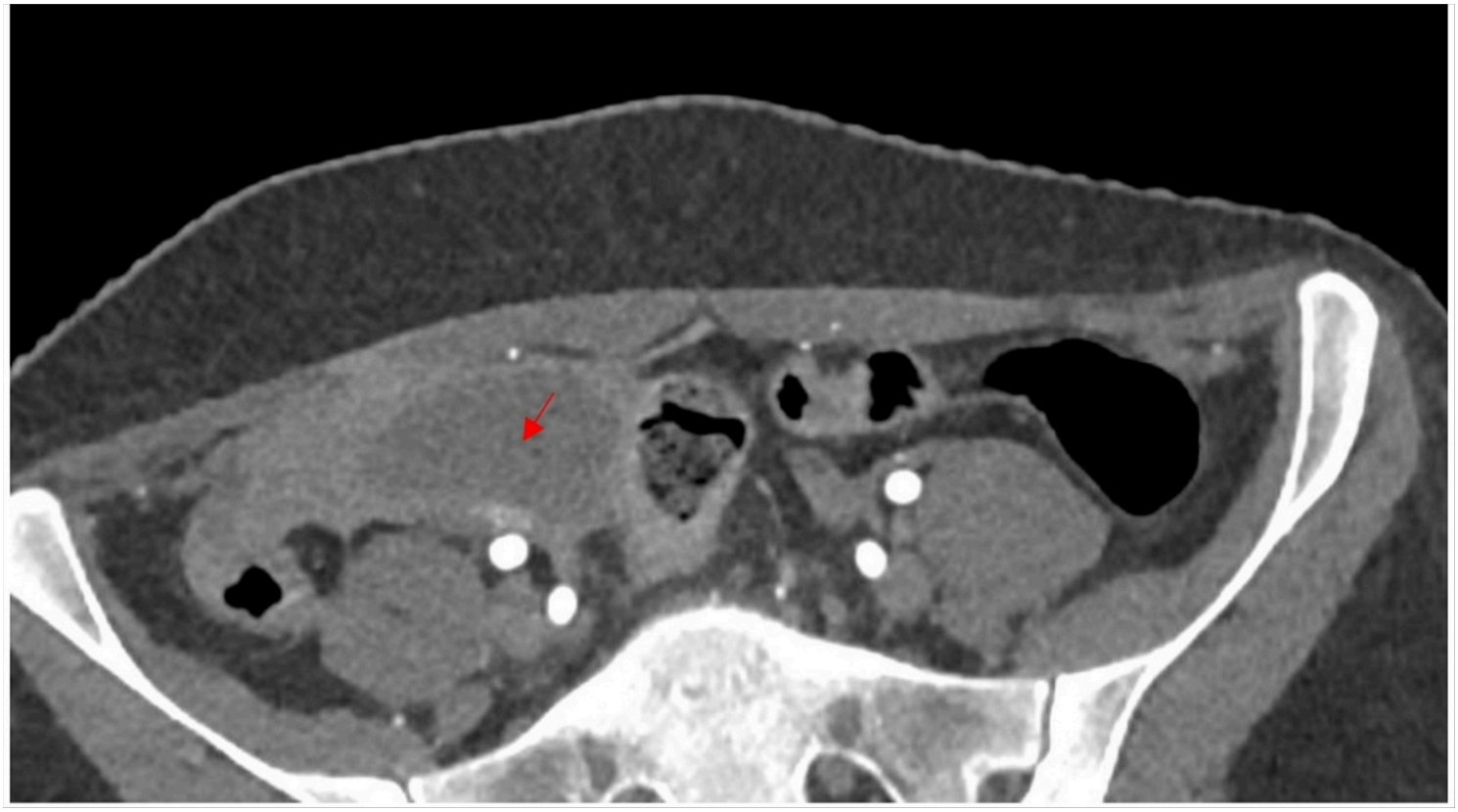


Figure 3

Contrast-enhanced CT scan of the lower limbs demonstrating a hemorrhagic suffusion in the right inguinal region related to bleeding from the inferior epigastric artery