

Takotsubo cardiomyopathy as an atypical presentation of maternal heart disease in twin pregnancy. A case report

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Case Report

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ABSTRACT: We present the case of a woman of advanced age for pregnancy, multiparous, with assisted fertilization and dichorionic diamniotic twin pregnancy of 33.5 weeks with cardiovascular risk factors (sedentary lifestyle, smoking, high degree of work stress, chronic hypertension, hypertriglyceridemia) who developed gestational diabetes and peripartum hypertensive disease (severe preeclampsia). A cesarean section was performed due to an obstetric complication, during surgery, after birth, she presented hypertensive crisis and acute pulmonary edema that required coronary critical care. Biochemical markers and electrocardiographic, radiological, and angiographic studies were conclusive of Takotsubo syndrome. Her cardiovascular condition was complicated by a cerebral thrombosis resolved with an interventional catheterization. Recovery was satisfactory after a torpid evolution, cardiac function improved remarkably, blood pressure stabilized with drugs, and metabolic morbidities remained unaltered. Mild dysarthria was the only neurological sequelae. Obstetric aspects and the most important cardiovascular data of the case are discussed.

Keywords: Takotsubo syndrome; Acute coronary syndrome; Acute myocardial infarction; Maternal heart disease; Hypertensive crisis; High risk pregnancy.

Takotsubo syndrome is also known as Takotsubo cardiomyopathy, stress-induced cardiomyopathy, transient apical cardiomyopathy, and broken heart syndrome. First described in Japan,¹ the term Takotsubo has been borrowed from the Japanese word meaning octopus trap due to its similarity to the characteristic appearance of left ventricular apical bulge. Clinically, patients present with chest pain, dyspnea, ST-segment electrocardiographic changes, elevated blood concentrations of cardiac troponins, and contractility dysfunction or left ventricular apical hypokinesia with baseline hyperkinesis. In most cases, the regional left ventricular wall motion disturbance extends beyond the territory perfused by an epicardial coronary artery. The data simulate an acute myocardial infarction, but without the evidence of obstructive coronary artery disease.²

The pathophysiology is not fully understood; evidence indicates that disease mechanisms include myocardial "numbing" from coronary vasospasm secondary to high concentrations of catecholamines released into the blood from an acute state of physical or emotional stress with microvascular dysfunction, local increase in the products of the mechanism of inflammation and changes in the metabolism of cardiomyocytes.³

The incidence of Takotsubo syndrome has increased significantly. Minhas et al.⁴ reported a significant increase in cases from 2006 to 2012, probably due to better recognition of the disease. It usually occurs in men over 50 years of age, in postmenopausal women, or in younger patients of both genders with a wide variety of triggering factors, chronic morbidities, or drug-related. The list of potential triggers continues to grow, as do reviews to improve diagnosis and treatment.⁵

Arcari et al.⁶ studied gender differences, found that men with Takotsubo syndrome seem to have a different high-risk phenotype than women matched by age, comorbidities, and type of triggering factor. Evidence indicates that men require closer in-hospital surveillance and longer long-term follow-up. The authors concluded that gender differences favor women. However, they do not escape the manifestation of the syndrome.

The presentation of Takotsubo syndrome has been found to be extremely rare during pregnancy. Case reports are concentrated in the peripartum period, the difficulty to identify it increases because the clinical manifestations of Takotsubo syndrome are similar to those of acute coronary syndrome and because they overlap with gestational physiological changes, the cardiovascular response of labor

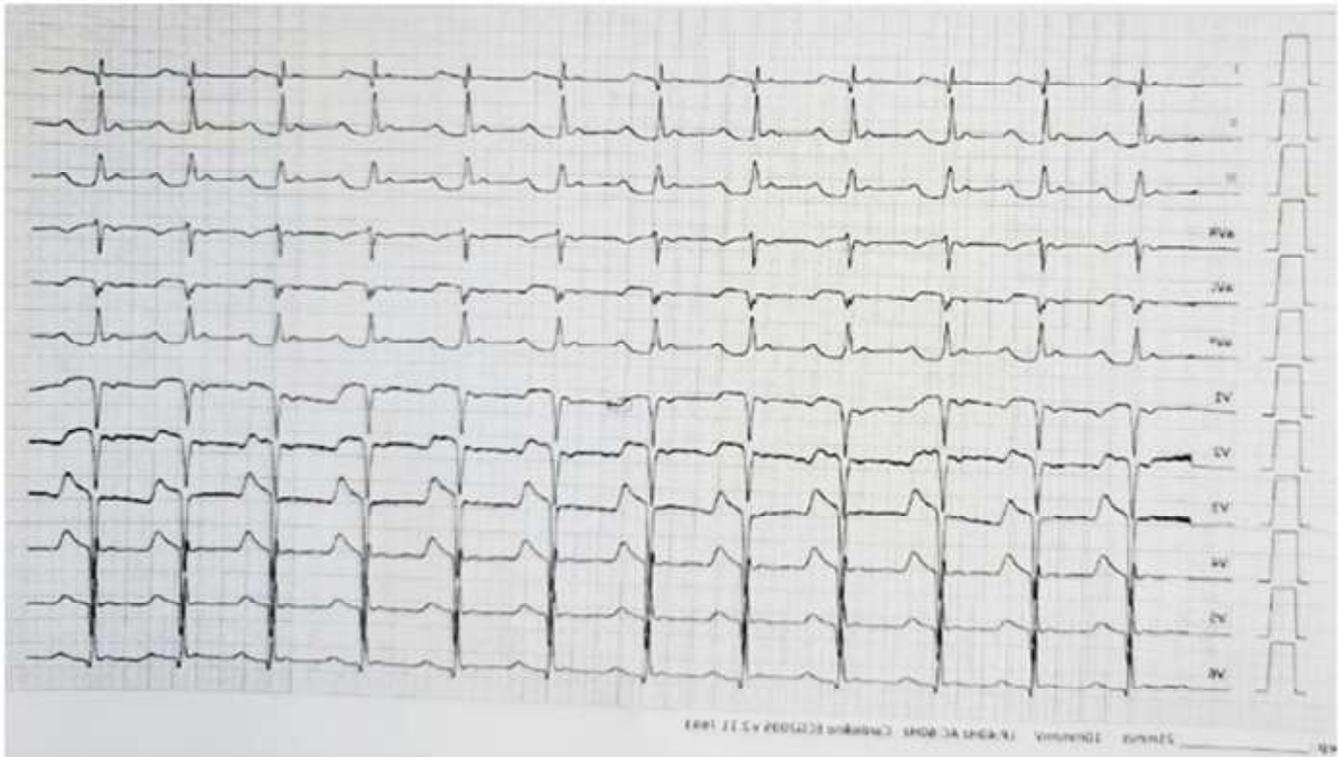


Figure 1. Electrocardiogram with ST elevation of 2 mm corresponding to the anteroseptal area.

childbirth, peripartum stress, anesthesia stress and the emotional response of the patient regarding the condition of the newborn and their family environment.

We present the case of a woman of advanced age for pregnancy, multiparous, with assisted fertilization and dichorionic diamniotic twin pregnancy of 33.5 weeks with cardiovascular risk factors, gestational diabetes and severe intrapartum preeclampsia who underwent cesarean section. After birth, she presented a hypertensive crisis and acute pulmonary edema that required coronary critical care. Biochemical markers and electrocardiographic, radiological, and angiographic studies were conclusive of Takotsubo syndrome. It was complicated by a cerebral thrombosis resolved with interventional catheterization. Recovery was satisfactory with minimal neurological sequelae.

Marker	Measurements				
	admission	6 hours	12 hours	24 hours	48 hours
Troponin I ng/ml	721	762	1450	827	253
Brain natriuretic peptide pg/ml	10	487	1025	928	400

Table 1. Blood concentrations of cardiac injury markers during the stay in the Coronary Intensive Care Unit.

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It was a 46-year-old woman with a history of sedentary lifestyle, executive business occupation with

a high level of work stress, smoking since the age of 22 with consumption of 12 cigarettes per day, chronic arterial hypertension of two years of evolution treated with oral valsartan 80 mg per day and hypertriglyceridemia of 5 years of detection without drug management. Surgical history: tonsillectomy at 4 years, surgery for chronic sinusitis at 23 years, cosmetic tummy tuck at 32 years, and placement of breast implants at 34 years. Obstetric history: two normal full-term pregnancies attended with vaginal delivery 18 and 16 years previously, without complications. Subsequently, she did not use a family planning method.

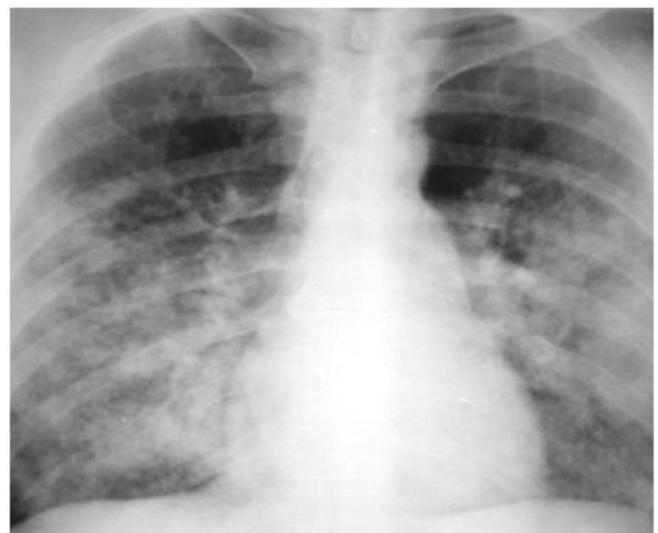


Figure 2. Diffuse mottled infiltrates with poor borders defined secondary to acute pulmonary edema whose distribution is known as a “butterfly-wing” image.

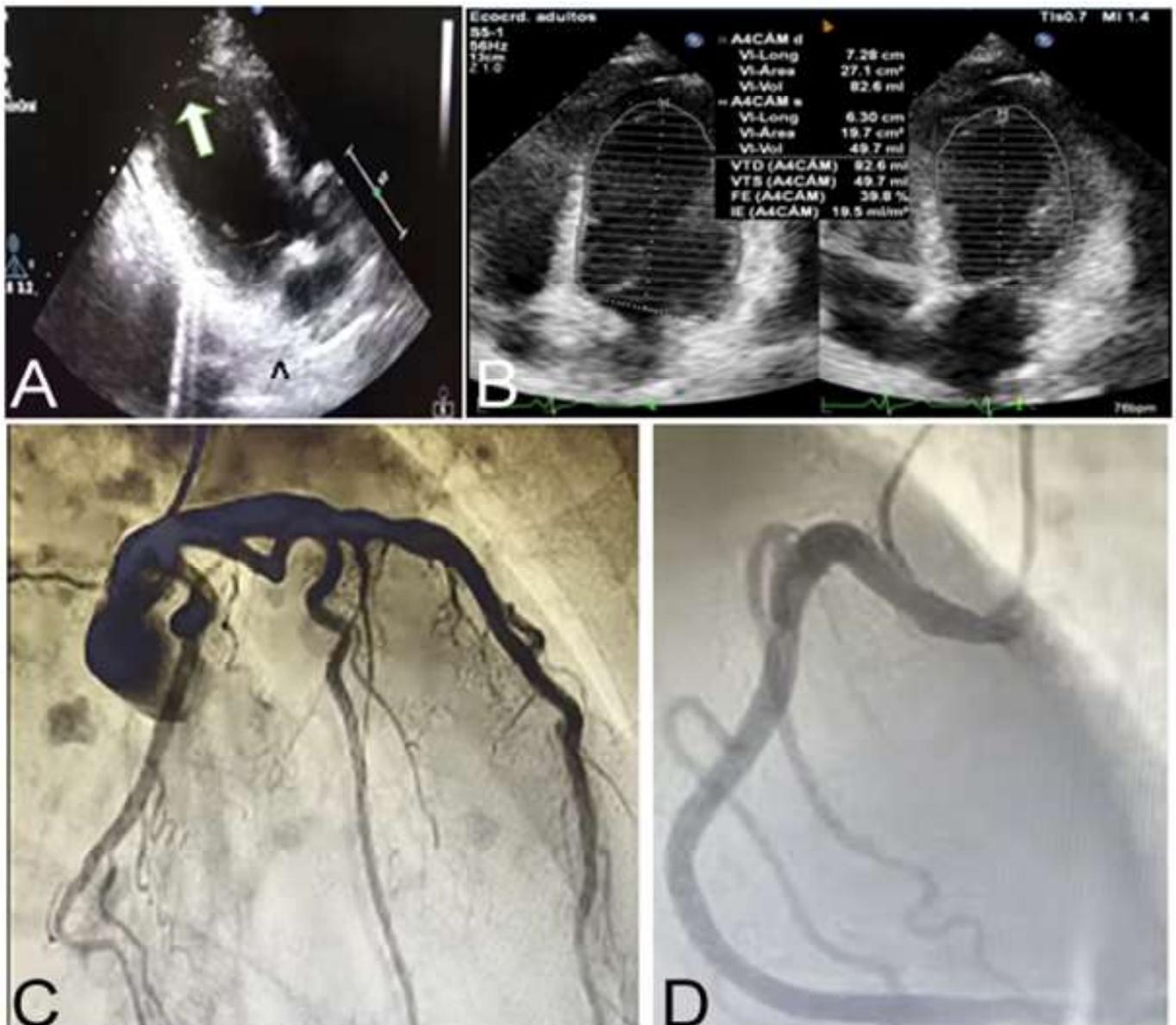


Figure 3. A. Two-dimensional echocardiogram. Apex hypokinesia, inferolateral apical (arrow) and septo-apical. B. Left ventricular ejection fraction 39.8%. C. Diagnostic coronary angiography. The trunk of the left coronary artery and the entire left system are observed without significant lesions, D. Right coronary artery without significant lesions.

For personal reasons (change of partner) she requested professional advice because she wanted a third pregnancy through an assisted technique in a private hospital. After concluding her study protocol, the patient was considered a candidate for in vitro fertilization, her studies did not include a cardiological assessment.

In vitro fertilization was carried out without complications. A dichorionic and diamniotic twin pregnancy was achieved that was complicated by gestational diabetes mellitus detected at 22 weeks controlled with diet and isthmic-cervical incompetence detected at 24 weeks that required successful cerclage. From the beginning and throughout the pregnancy, she received long-acting oral nifedipine 30 mg every 24 hours and oral methyldopa 250 mg every 8 hours with good blood pressure control and oral metformin 850 mg every 12 hours with good glycemic control.

On June 21, 2022, she went to the emergency department with spontaneous labor when she was 33.5 weeks gestational. The decision was to admit her to the hospital to remove the cervical cerclage and terminate the pregnancy by caesarean section. The cervical cerclage was removed and then the cesarean section was performed under the effect of a successful neuraxial block. Two live preterm fetuses were obtained with an age calculated by the Capurro method according to 33-34 weeks with an Apgar score of 8-9 and 8-9 at one and five minutes after birth. The review by the pediatrician in the operating room reported that both newborns were healthy and did not require intensive care. Intraoperative bleeding was estimated at 750 ml.

During the cesarean section and after the birth of the twins, the patient presented a hypertensive crisis 200/100 mmHg and the non-invasive monitor showed

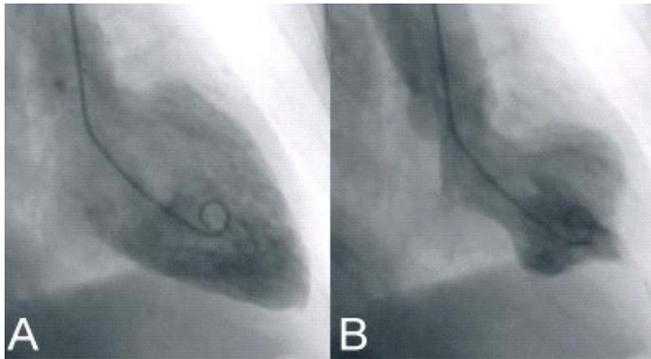


Figure 4. Ventriculography A. Apical hypokinesia and hypercontractility of the basal segments, B. The classic “octopus trap” image.

monomorphic ventricular tachycardia with a pulse. A 150 mg intravenous bolus of amiodarone was administered and intravenous sodium nitroprusside infusion was started at a dose of 0.5 mcg/K calculated weight/minute, with which the data disappeared. Bilateral tubal occlusion was performed. The surgery ended without technical or anesthetic complications. In the following minutes, he presented data suggestive of acute pulmonary edema and acute respiratory failure that required orotracheal intubation for advanced management of the airway with mechanical ventilatory assistance.

The patient was admitted to the coronary intensive care unit (CICU). The electrocardiogram on admission showed sinus rhythm with a mean ventricular rate of 75 per minute and ST-segment elevation of 2 mm in the leads corresponding to the anteroseptal area (**Figure 1**) A peripheral blood sample for the determination of Troponin I reported elevated concentrations 721 ng/ml, the brain natriuretic peptide concentration was 10 pg/ml. Subsequent determinations of both markers showed maximum concentrations at 12 hours and then their decrease (**Table 1**). The clinical laboratory reported normal blood

count, serum electrolytes and coagulation tests, glucose 83 mg/dL, creatinine 0.7 mg/dL, BUN 18 mg/dL, lactic dehydrogenase enzyme 567 U/L, aspartate aminotransferase enzyme 14 U. /L, alanine aminotransferase enzyme 16 U/L and creatine phosphokinase enzyme 42 ng/mL with MB fraction 28 ng/mL. The rheumatology study profile reported anti-Ro, anti-SM, anti-La, double-chain NAA, ANCA, anticardiolipins, and lupus anticoagulant, all negative. Viral panel: HCV, HBV and HIV negative. Protein C and protein S negative.

Portable chest X-ray showed data consistent with unresolved acute pulmonary edema, without cardiomegaly (**Figure 2**).

The two-dimensional transthoracic echocardiogram on admission to the CICU reported decreased mobility of the apex and of the inferolateral-apical and septo-apical zones with the left ventricular ejection fraction of 39.8%, without intracavitary thrombi (**Figure 3A,B**). A scheduled coronary angiography was performed, which reported the absence of coronary lesions with generalized TIMI 3 flow (**Figure 3C,D**). Ventriculography showed atypical mobility of the left ventricle characterized by apical hypokinesia and hypercontractility in the basal segments (**Figure 4**). Pharmacological management was established with subcutaneous enoxaparin 60 mg every 12 hours, intravenous furosemide 40 mg every 12 hours, oral sacubitril/valsartan 50/160 mg every 12 hours, and intravenous infusion levosimendan at a dose of 0.2 mcg/K weight/minute as inotropic agent consistent with acute heart failure (acute pulmonary edema) and measurement of left ventricular ejection fraction with a critical value. Levosimendan was used for the first 24 hours only.

During the 24 hours after the cesarean section, mechanical ventilation assistance and the orotracheal cannula were withdrawn. During this period, the

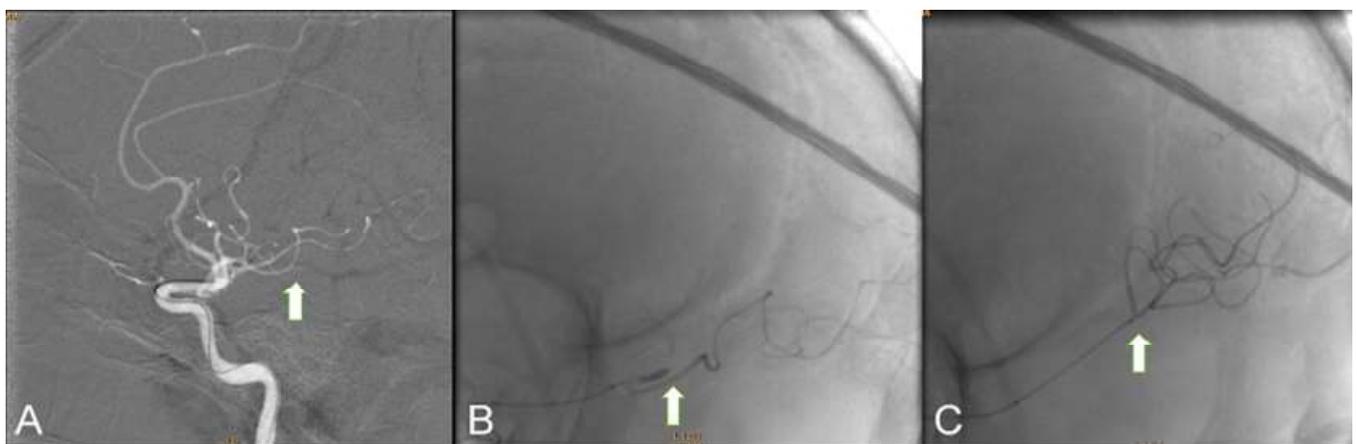


Figure 5. A. Thrombus in the M3 segment of the left middle cerebral artery (arrow). B. Identification of the lesion site and the position of an open stent (arrow). C. Control angiography showing adequate flow (arrow).

patient presented dysarthria and right hemiparesis. The magnetic resonance image showed a thrombus in the M3 segment in the territory of the left middle cerebral artery, with no evidence of intracranial hemorrhage. A 25 mg intravenous bolus dose of alteplase was immediately administered, this is a low dose due to the history of recent surgery. However, he did not present clinical data on reperfusion. A catheterization was performed to perform a thrombectomy through an open stent with successful results (**Figure 5**). The procedure ended without complications.

Drug management included oral clopidogrel 75 mg every 24 hours, oral acetylsalicylic acid 100 mg every 24 hours, and oral sacubitril/valsartan 50/160 mg every 12 hours. Phase I and II cardiac and neurological rehabilitation was started because his neurological condition improved and the two-dimensional transthoracic echocardiogram reported a left ventricular ejection fraction of 55%.

During the 48 hours after the cerebrovascular procedure, the patient recovered from the right hemiparesis, but she persisted with mild dysarthria. The stay in the CCU was 7 days, no neurological, cardiac, surgical or cerebral bleeding complications related to the invasive procedures or the use of drugs (enoxaparin, alteplase, clopidogrel, acetylsalicylic acid) were reported.

Additionally, the patient was managed in a general ward for 4 days and then sent home due to her stable clinical condition, without surgical complications and because her blood pressure was controlled (120/70 mmHg) and dysarthria had improved. Mild dysarthria was the only neurological sequelae. Outpatient pharmacological management included oral clopidogrel 75 mg every 24 hours, oral acetylsalicylic acid 100 mg every 24 hours, oral sacubitril/valsartan 50/160 mg every 12 hours, and oral atorvastatin 20 mg every 24 hours. Cardiac and neurological rehabilitation were indicated to continue at home. Breastfeeding was not authorized.

Discussion

The frequency of Takotsubo syndrome during pregnancy is extremely low.⁷ It has been reported in patients during the peripartum period attended in the hospital,⁸ without cardiovascular risk factors,⁹ with severe preeclampsia,^{10,11} with HELLP syndrome,¹² during lactation¹³ and after a normal vaginal delivery.^{14,15}

Here we present the case of a patient of advanced age for pregnancy, prenatal risk factors, gestational complications, with a twin pregnancy terminated with surgery and anesthesia, and intraoperative complications suggestive of acute coronary syndrome. Takotsubo syndrome was documented with a cerebral thrombosis that

complicated postpartum recovery. Coronary critical care and multidisciplinary management were necessary for a successful outcome.

Advanced maternal age for pregnancy, defined as pregnancy in a patient 35 years of age or older, is an independent risk factor widely associated with serious maternal and fetal adverse effects compared with the population of younger pregnant women.¹⁶ In this type of women of advanced age for pregnancy, the frequency of maternal-fetal complications increases in the presence of cardiovascular, metabolic, and immunological morbidities, and degenerative diseases, despite the fact that they remain stable at the time of conception. The lifestyle with a high degree of emotional, family and work stress contribute to the problem. The reported case met these adverse characteristics.

The novelty of the report is the twin pregnancy achieved through an assisted fertilization technique with gestational diabetes and severe preeclampsia as factors that may favor the appearance of Takotsubo syndrome. Possibly the triggers were surgical and anesthetic stress, as well as the patient's emotional response to the negative news of two premature twins with a high risk of complications who ultimately survived.

The intervention of the cardiologist during the cesarean section served to establish the management of ventricular tachyarrhythmia, hypertensive crisis, and heart failure with the initial diagnosis of acute coronary syndrome. The follow-up of the case in the CICU and the special studies served to stabilize the cardiovascular, hemodynamic and metabolic conditions and to accurately identify that it was Takotsubo syndrome. The choice of drugs based on cardiology criteria was satisfactory with no adverse effects, and the cerebral thrombosis was resolved with the appropriate technique with no evidence of bleeding.

At the end of her hospital stay, the account of the damage was favorable because the blood pressure was controlled within safe limits, as were the metabolic alterations, the contractile function of the myocardium was recovered and cardiac and neurological rehabilitation of the patient was possible in the hospital and its continuation at home. Mild dysarthria was the only neurological sequelae with a real possibility of complete recovery.

Conclusion

The study protocol for in vitro fertilization did not include cardiological assessment. The decision making of the medical team specialized in human reproduction techniques and the patient's decision to achieve a pregnancy must include the professional opinion of the cardiologist before conception because

in patients with cardiovascular risk factors and with high risk factors fetal pregnancy can have catastrophic consequences.¹⁷ The cardiologist should accompany the patient during pregnancy and in the peripartum period as a member of the multidisciplinary team.

Conflicts of interest

No conflicts of interests.

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