SUDDEN DEATH IN THE FIRST TRIMESTER OF PREGNANCY

MUERTE SÚBITA EN EL PRIMER TRIMESTRE DEL EMBARAZO(*)

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Abstract: The venous thromboembolism and thromboembolic events remain the leading cause of death during pregnancy and post-partum in developed countries. Recent investigations have provided an important evidence of significantly increased risk of venous thromboembolism after in vitro fertilization (IVF) pregnancies. Nevertheless, there are few case reports showing these emergency situations. We report the case of a 40 years old woman, in her twelve week of a twin after IVF pregnancy, who dies after two weeks with dizziness, tachycardia and respiratory distress. Our objective is double: to highlight the risks of the pregnancy even in developed countries and, on the other hand, to enhance the role of the forensic pathologist and the forensic studies as epidemiological information gatherers.

Keywords: pregnancy, *in vitro* fertilization, pulmonary embolism, sudden death.

Resumen: como es sabido, entre las primeras causas de mortalidad materna durante el embarazo se encuentran los episodios de tromboembolismo venoso. Varios estudios poblacionales ya han demostrado que dicho riesgo se encuentra aumentado de manera muy significativa en caso de embarazos logrados mediante técnicas de Fertilización *in vitro* (FIV). Sin embargo, apenas existen casos en la literatura que ilustren estas situaciones de emergencia. Presentamos el caso de una mujer de 40 años, embarazada de mellizos mediante FIV, en su 12ª semana de gestación, que fallece tras dos días con clínica de mareos, taquicardia y ahogos. La finalidad de su publicación es doble: por un lado llamar la atención ante uno de los riesgos que acompañan la gestación y, por otro, poner en valor la función del médico forense y el estudio autópsico como fuente de recogida de información de salud pública.

Palabras clave: Embarazo; fecundación in vitro; tromboembolismo pulmonar; muerte súbita.

INTRODUCTION

Pregnancy and postpartum related death is a global health problem, mainly in developing countries. World Health Organization (WHO) estimates 230 maternal deaths per 100.000 live births. The 80% of these deaths are due to serious hemorrhages (mainly in the postpartum), infections, arterial hypertension (*preeclampsia* and *eclampsia*) and dangerous abortions (1).

In developed countries, the maternal mortality rate decrease to 16 maternal deaths per 100.000 live births. (2). In Spain, the Sociedad Española de Ginecología y Obstetricia (SEGO) reviewed the data collected between 2010 and 2012 and estimated 6 maternal deaths per 100.000 live births, although the underestimation rate is 48%, higher than the underestimation rate of France (20%) or EEUU (38%) (2). The main cause of maternal morbidity is the pulmonary embolism (PE); the second, gestational hypertension (*preeclampsia* and *eclampsia*) (3). Recent studies suggest that risk incidence of venous thromboembolism (VTE) considerably increases in after *in vitro* fertilization (IVF) pregnancies (4,5,6,7), due to ovarian hyperstimulation and the pro-coagulation state produced.

The pulmonary embolism is a clinical emergency, with known signs, symptoms and treatment. Nevertheless, these patients survival has not improved in the last years. A quarter of them suffer a sudden death (8), so we must focus all the efforts in the prevention and early diagnosis.

We report a case of a 40 years old woman, in the first trimester of pregnancy after *in vitro* fertilization, who suddenly died in her house.

CASE REPORT

A 40 years old woman died suddenly at home. She was in the 12th week of pregnancy after *in vitro* fertilization, in treatment with Meriestra® 1mg (estradiol) and Progeffik® 200mg (progesterone) until the day before the death. She was no resting to prevent a miscarriage. She felt dizziness and tachycardia days before the death, with two intense events two days before. She went to her General Practitioner, who studied the arterial pressure (apparently normal) and recommended sweet drinks like *Coke*. The forensic physician couldn´t collect more information about the protocol of fertilization or evolution of the pregnancy.

The external examination of the woman, 158cm high and slim, revealed intense pallor of acral areas and face, lip and nail cyanosis, strongly instituted *rigor*, fixed lividities on lower areas and cervical region and leg-pitting edema at the ankles. She had no varicose veins. Internal examination showed a 13x11x4 cm relaxed and flabby gravid uterus, with 4 leiomyoma and monochorionic biamniotic twin pregnancy, male and female. The ovaries were normal and no thrombi were found in the pelvic veins. Congestive lungs with increased weight and multiple thrombi at medium and high diameter vessels. Hepatic parenchyma with yellow dots. Thrombosis in the left popliteal vein was revealed. Histopathologically, the pulmonary cronic thromboembolic disease was confirmed, with recent and organized thrombi with recanalization at small, medium and high diameter vessels, and acute pulmonary edema. (Fig. 1).

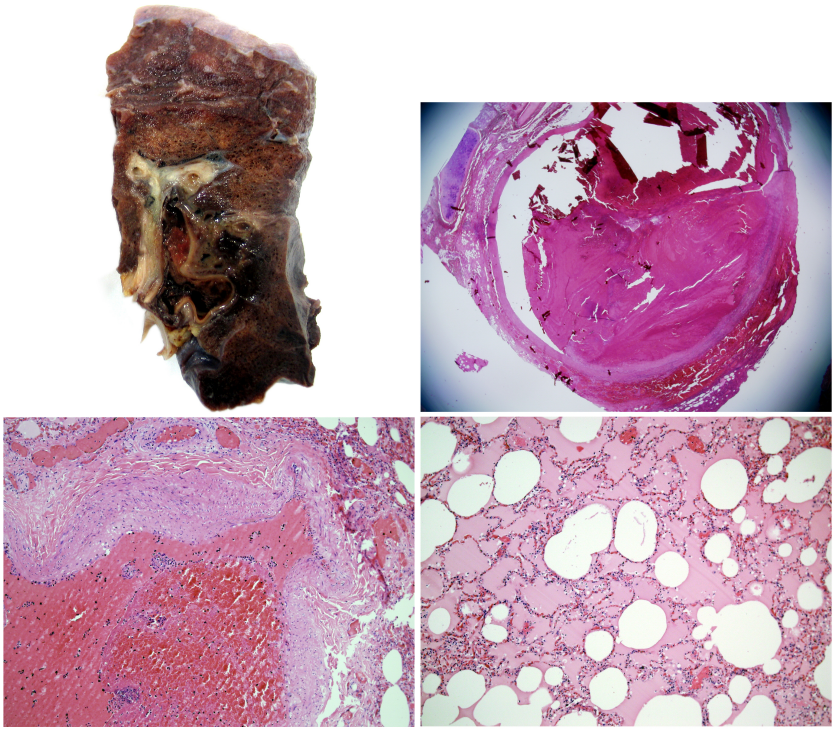

Fig.1. 1. Pulmonary thromboembolism.

Congestive lungs with multiple thrombi at medium and high diameter vessels (a). Pulmonary cronic thromboembolic disease (b), with recent and organized thrombi with recanalization (c) at small, medium and high diameter vessels, and acute pulmonary oedema. (d).

The left popliteal vein thrombosis was chronic, with recanalization. (Fig. 2).

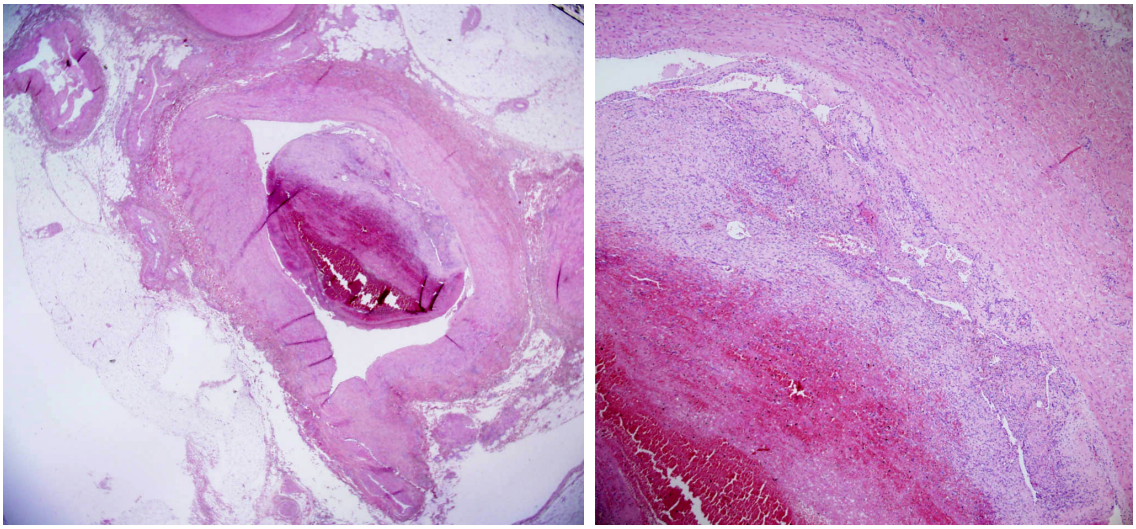

Fig.2. Left popliteal vein

Cronic thrombosis with recanalization. Panoramic view (a) and high power view.

Focal hepatic steatosis and congestion of the zone 3. The examination of the uterus and the fetuses showed funiculitis with perivascular damage and acute chorioamnionitis and villitis in both.

DISCUSSION

Women in reproductive age have an increased risk of venous thromboembolism (VTE), due to hormonal contraception, pregnancy and the profertility ovarian stimulation. All these situations alter the levels of pro-and anticoagulants as well the fibrinolytic system.(3,4).

For a time a similar risk was assumed for natural pregnancies and after *in vitro* fertilization pregnancies. However, some recent studies reveal a significantly increase of VTE and even pulmonary embolism during the first trimester after a IVF pregnancy. In 2012 Rova *et al*. found a 10-fold increase (100-fold in those pregnancies complicated with an ovarian hyperestimulation sindrome, a 6-7% of IVF pregnancies) (5). In 2013, Henriksson *et al*. reported a 7-fold in increase (6) and in 2014 Hansen *et al*. (7) supported these studies, with no significant differences in single or multiple IVF pregnancies. They also revealed an increased risk of VTE during the first 6 weeks post-partum. So, in this group of pregnancies the thromboprophylaxis is needed.

The risk of suffering a pulmonary embolism (PE) after a VTE is well known. Even so, the diagnosis is still difficult and nowadays a quarter of patients with PE die with sudden death (5). The suspicious signs (A) and symptoms (B) are (8):

A: **dyspnoea, pleuritic pain**, pain/ oedema in the legs, hemoptysis, palpitations, chest pain, heart attack.

B: **Tachypnea > 20/min, tachycardia >100/min**, crackles, intense S4/S2 cardiac sound, signs related with de VTE, temperature > 38º, right “gallop”.

Our patient felt dyspnoea and palpitations for two weeks, with apparent tachycardia in the two days before death. She showed some signs and symptoms of PE, although no evidence of venous thrombosis was clear. Probably these could be the reason the general practitioner didn´t suspect the PE. We don´t know if she told him her pregnancy was IVF mediated. The fetuses showed signs related with a fetal death (intrauterine), a time before of the mother´s, probably due to her cronic thromboembolic disease.

We have found no other VTE risk factors besides the *in vitro* fertilization, since the woman was slim, no smoker, without varicose veins or ovarian hyperstimulation syndrome´s signs. According to recent studies made by Rova, Heriksson and Hansen, *in vitro* fertilization could be the only risk factor (5,6,7). Even though some cases of VTE after

IVF pregnancies have been found in the bibliography reviewed, this is the first sudden death case due to pulmonary thromboembolism reported.

CONCLUSIONS

As Christiansen *et al.* (10) reported and the last SEGO (2) survey has corroborated, it is often difficult to identify the maternal deaths in the clinical practice. We must collect all the information about deaths among women of reproductive age, pregnancy status at or near the time of death and the medical cause of death. "The forensic works is crucial in identifying these cases and elucidating emerging trends" (10).

The objective of this case report is double: to highlight the risks of pregnancy even in developed countries and, on the other hand, to enhance the role of the forensic physicians and pathologists as epidemiological information gatherers.

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