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Case report Open Access

Pulmonary Embolism Secondary to Inappropriate use of Oral Contraceptive Therapy

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Abstract

Forty-one year old female admitted to the hospital due to a clinical presentation suggestive of pulmonary thromboembolism which was confirmed by CT angiography. There was no history of prior thromboembolic events, smoking, venous stasis or vascular lesion (negative lupus anticoagulant and anticardiolipins). The only documented hypercoagulability factor found was the use of an oral contraceptive containing drospirenone and ethinylestradiol for the last year. The patient was anticoagulated with enoxaparin recovered without sequelae, and is currently receiving outpatient treatment with warfarin. It is well known that the use of combined oral contraceptives is contraindicated in patients over the age of 35, in large part due to the increased risk of thromboembolic events associated with an increased hepatic synthesis of some coagulation factors. Therefore, this represents a case of a serious adverse reaction, potentially fatal, and completely preventable.

Background

Recently, the FDA issued an alert indicating the increased risk of thromboembolic disease associated with the use of drospirenone and other progestin and estrogen content in these medications. The FDA review indicates that the risk may be higher in patients older than 35 years, against the recommendations of the World Health Organization and the American College of Obstetricians and Gynecologists which advise the use of OCs in women over 40 years nonsmokers without arterial hypertension associated. Therefore, this case illustrates a potentially preventable serious adverse reaction to a medication and illustrates the importance of identifying possible cautions prior to begin hormonal contraception.

Case Presentation

Forty-one year old female who presents with sudden sharp chest pain for the past 20 minutes, with a 10/10 intensity on the visual analog scale (VAS). The pain radiated to the lumbar region and was associated with dyspnea. She did not present syncope or hemoptysis. No significant medical history, non-smoker, and using birth control with drospirenone-ethinylestradiol 3mg/0.02 mg as of a year ago.

The patient is admitted conscious, alert, and hydrated, with signs of respiratory difficulty: tachypnea and intercostal retractions. HR: 110 per minute, RR: 26 per minute, BP: 85/48 mmHg, T: 37.7°C, BMI: 24 kg/m^2, pulseox: 94% at 28% FIO_2.

Normochromic, moist oral mucosa, without jugular distension, neck masses or lymphadenopathies, tachycardic cardiac sounds, right basal hypoventilation and pain on superficial palpation of the right costal cage. Abdomen soft without masses or organomegaly. No edemas or signs of deep venous thrombosis and no motor or sensory neurological deficit. Glasgow coma scale 15/15.

Investigations

EKG: sinus tachycardia without signs of ischemia or necrosis.

The complete blood count showed mild leukocytosis and anaemia

Normal renal function and electrolytes.

Chest x-ray showed: right basal parenchymal opacity and increased vascular markings.

Arterial gases showed respiratory alkalosis with moderately altered oxygenation.

The CT angiogram showed: pulmonary thromboembolism with right basal parenchymal opacity related to pulmonary ischemia without tomographic signs of right ventricular dysfunction.

Lupus anticoagulant and anticardiolipins: negative.

Differential Diagnosis

Musculoskeletal pain, Pleuritis, Pericarditis, Hyperventilation, Acute Coronary Syndrome, Anxiety disorders, Cardiac tamponade, Pneumothorax, Pulmonary Edema, and Pulmonary Hypertension.

Treatment

She was treated with IV fluids, enoxaparin, morphine, omeprazole and oxygen by nasal cannula.

Outcome and Follow-up

Currently the patient is asymptomatic and without functional limitations. She is being treated with warfarin 5 mg qd during six months after out, INR 2.3

Discussion

Combined oral contraceptives (COC) are associated with an increased risk of venous thromboembolism (VTE) [1]. It has been reported that the risk is double that of non-users, but that the total risk is low [2].

The most probable mechanism is the estrogen induction of hepatic plasma proteins involved in coagulation [2].

The risk of thromboembolism varies according to the degree of exposure to estrogen and the type of progestin used. There has been

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documentation to the effect that oral contraceptives, especially those containing drospirenone or other third or fourth generation progestins, have been associated with an increased risk of VTE [2].

A review published by the FDA in 2011 entitled: "Combined Hormonal Contraceptives (CHCs) and the Risk of Cardiovascular Disease Endpoints" also found that the risk of VTE could be higher in women between 35 and 55 years old who take COCs containing drospirenone, (the age range of our patient) [3].

However, another FDA review published in 2012 found conflicting evidence regarding the risk of VTE associated with the use of COCs containing drospirenone. According to some epidemiological studies, the risk of VTE can be up to 3 times higher in women who take COCs containing this progestin, compared to users who take COCs with different progestins. However, other studies that were part of the FDA review did not confirm this association [4].

Likewise, one of the most important studies aimed at evaluating the safety of drospirenone versus levonorgestrel and other progestins included in COCs included 58,674 women who were followed for 142,475 women-years of observation, finding that the hazard ratio of VTE for drospirenone was 1.0 and 0.8 for levonorgestrel [5].

Along these lines, Martinez et al.´s systematic review published in 2012 confirmed a slight increase in risk in patients using COCs containing drospirenone compared to levonorgestrel (RR 1.26, 95% CI: 1.03–1.52) [6].

Other risk factors include age, thrombogenic mutations (women with a Factor V Leiden mutation may have a risk of VTE up to 35 times higher), personal or family history of VTE, pregnancy and postpartum (increased risk up to 3 to 6 weeks after giving birth), obesity, length of long trips, and travelling at high altitudes (more than one week at more than 4,500 meters above sea level) [1,2]. Other than age, none of these risk factors could be documented in this patient.

Although this adverse reaction is more frequent in the first four months of contraceptive use [6], it is remarkable that in our patient the event presented a year after having begun the medication.

Learning Points/Take Home Messages

- Always consider the possibility of thromboembolic events in patients using oral contraceptives.
- Evaluate very well the risk factors for thromboembolic events and weigh the benefit/risk ratio before prescribing oral contraceptives.
- Recognize that age over 40 years is a possible caution for the use of oral contraceptives.

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