THE JOURNAL OF ACADEMIC EMERGENCY MEDICINE

Massive Pulmonary Embolism with Mobile Right Atrial Thrombus in a Pregnant Patient Using Valproic Acid

Valproik Asit Kullanan Bir Hamilede Sağ Atriyumdaki Mobil Trombusun Neden Olduğu Masif Pulmoner Emboli

Hatice Ender Soydinç[1], Murat Yüce[2], Emine Sarı[3], Sema Yavuz[2], İbrahim Sarı[2], Vedat Davutoğlu[2], Remzi Yiğiter[4], Murat Akçay[2]
[1]Department of Obstetrics and Gynecology, Faculty of Medicine, Dicle University, Diyarbakır, Turkey
[2] Department of Cardiology, Faculty of Medicine, Gaziantep University, Gaziantep, Turkey
[3] Department of Pediatrics, Zeynep Kamil Women and Children Hospital, Istanbul, Turkey
[4] Department of Neurology, Faculty of Medicine, Gaziantep University, Gaziantep, Turkey

Abstract

Pulmonary embolism is a life threatening condition. Pregnancy is among the risk factors of pulmonary embolism. There is reluctance about using thrombolytics s during pregnancy due to potential teratogenic effects. Valproic acid is one of the most commonly used antiepileptic agents, hovewer, its use during pregnancy is controversial because of the teratogenic potential. Among adverse effects of valproic acid use, elevated liver enzymes, thrombocytopenia have been reported. Moreover, product literature warns that pregnant women using valproic acid should be monitored for low fibrinogen and platelets and the potential for bleeding. The present case report describes successful treatment of a massive pulmonary embolism with tissue plasminogen activator (t-PA), caused by a mobile right atrial thrombus in a 30-year-old first trimester pregnant women using valproic acid. This has not been reported previously. During follow-ups, she was free of any signs or symptoms and gave birth to a baby by spontaneous vaginal delivery. The baby was completely healthy without any problem or deformity.

(JAEM 2012; 11: 52-4)

Key words: Pulmonary embolism, pregnant, valproic acid, right atrium, thrombolytic

Received: 13.10.2009 **Accepted:** 14.10.2009

Özet

Pulmoner emboli hayatı tehdit eden bir durumdur. Hamilelik pulmoner emboli için risk faktörleri arasındadır. Potansiyel teratojenik etkilerinden dolayı hamilelikte trombolitik kullanımında çekince vardır. Valproik asit, en çok kullanılan antiepileptik ilaçlardan olmakla beraber, teratojenik potansiyelinden dolayı hamilelikte kullanımı tartışmalıdır. Valproik asit kullanımının yan etkileri arasında karaciğer enzimlerinde artış ve trombositopeni bildirilmiştir. Üstelik, ürün bilgisi hamilelikte valproik asit kullanımı sırasında hastanın düşük fibrinojen ve trombosit seviyeleri ile kanama riski nedeniyle monitorize edilmesi konusunda uyarıda bulunmaktadır. Bu vaka takdimi valproik asit kullanan 30 yaşında ve ilk trimesterdeki bir hamilede sağ atriyumdaki mobil trombusun neden olduğu masif pulmoner embolinin doku plazminojen aktivatörü ile başarılı bir şekilde tedavi edildiğinden bahsetmektedir ve daha önce bildirilmemiştir. Takiplerde hastanın herhangi bir semptom ve bulgusu olmadı ve spontan vajinal doğum ile bir bebek dünyaya getirdi. Bebek tamamen sağlıklıydı ve herhangi bir problemi veya deformitesi mevcut değildi.

(JAEM 2012; 11: 52-4)

Anahtar kelimeler: Pulmoner emboli, hamile, valproik asit, sağ atriyum, thrombolitik

Alındığı Tarih: 13.10.2009 **Kabul Tarihi:** 14.10.2009

Introduction

Pulmonary embolism is a life threatening condition (1-6). Pregnancy is among the risk factors for pulmonary embolism (4-14). There is reluctance about using thrombolytics during pregnany due to potential teratogenic effects. Valproic acid is one of the most commonly used antiepileptic agent however, its use during pregnancy is controversial because of its teratogenic potential (15, 16). Among adverse effects of valproic acid, elevated liver enzymes and thrombocytopenia have been reported (17). Moreover, product literature warns that pregnant women using valproic acid should be monitored for low fibrinogen and platelets and the potential for bleeding. The present case report describes successful treatment of massive pulmonary embolism with tissue plasminogen activator (t-PA), caused by mobile right atrial thrombus in a first trimester pregnant women using valproic acid, which has not been reported previously.

Correspondence to / Yazışma Adresi: İbrahim Sarı, Department of Cardiology, Faculty of Medicine, Gaziantep University, 27310 Gaziantep, Turkey
Phone: +90 505 355 67 97 Fax: +90 342 360 39 28 e.mail: drisari@yahoo.com
doi:10.5152/jaem.2011.048

Case Report

Eight months previously, a 30-year-old pregnant women presented to the emergency department with acute onset of dyspnea, presyncope, fatigue and palpitation. Her past medical history revealed that she had epilepsy and had been using valproic acid 500 mg/day for 15 years. She was in her 8th week of pregnancy. Her vital signs were as follows: blood pressure, 85/55 mm Hg; pulse rate, 116/min; respiratory rate, 23/min; temperature, 37.7°C and pulse oximetry, 88%. On electrocardiography, she had sinus tachycardia, incomplete right bundle branch block, and S wave in lead I and a Q wave and T wave in lead III. Physical examination revealed a. tricuspid regurgitation murmur, an accentuated P2, pale, cold and sweaty skin, and faint and filiform peripheral pulses. Transthoracic echocardiography revealed normal left ventricular and atrial chamber sizes and function However, there was a significant increase in right ventricular size with free wall hypokinesis sparing the apical region (McConnell sign). There was a semi-mobile worm-like thrombus in the right atrium, which was entering into the right ventricle at each diastole (Figure 1, left panel). There was moderate tricuspid regurgitation with pulmonary hypertension (estimated pulmonary artery pressure was approximately 50 mmHg) and the main pulmonary artery was dilated. Emergency obstetric examination of the patient was compatible with a 8 week pregnancy with normal fetal growth. She was then quickly transferred to the coronary care unit with the diagnosis of massive pulmonary embolism. Because she and her husband refused any surgical treatment option due to her pregnancy, we gave her 100 mg continuous t-PA infusion over 2 hours. We started unfractionated heparin after t-PA according to activated partial thromboplastin time measurements.

After t-PA, her signs and symptoms resolved completely. Transthoracic echocardiographic control revealed that the right atrial thrombus had disappeared and right ventricular size and function normalized (Figure 1, right panel). Estimated pulmonary artery pressure was 22 mmHg and there was only minimal tricuspid regurgitation. Her laboratory examinations and lower extremity ultrasound were within normal limits and were not in accordance with any possible association with vascular pathologies or hematological disorders.

She was discharged with enoxaparin 1mg/kg twice daily which was switched to unfractionated heparin in the 34th week of pregnancy and valproic acid 500 mg/day. During follow-ups, she was free of any signs or symptoms and gave birth to a healthy baby by spontaneous vaginal delivery. On her last visit, she was completely healthy and the baby was free of any problem and deformity.

Discussion

Pulmonary embolism is a life threatening condition (1-6). Pregnany is among the risk factors and the risk of deep venous thrombosis and pulmonary emboli is increased four to six times due to the procoagulant state of pregnancy (4-14). Treatment strategies of massive pulmonary embolism include thrombolysis and surgical/interventional embolectomy. T-PA is the recommended thrombolytic agent. There is reluctance about using thrombolytics during pregnany due to the potential teratogenic effects. Although not subject to randomized studies, there are successful reports of thrombolytic treatment with t-PA during pregnancy (4-14). Leonhardt et al. states that t-PA does not cross the placenta and complication rates of thrombolytic therapy in pregnants are not higher than in the large randomized trials in the non-pregnant population (3). Moreover, it is suggested that the risk of surgical embolectomy with cardiopulmonary bypass might outweigh the risk of thrombolytics for the mother and fetus.

Valproic acid is one of the most commonly used antiepileptic agent. During pregnancy, use of valproic acid is controversial because it is difficult to balance the loss of seizure control and an elevated risk of major congenital malformations (15, 16). When used during pregnancy, use of the lowest possible effective dose of (<1000 mg/day) is recommended with close antenatal monitoring (15, 16). Among adverse effects of valproic acid use, elevated liver enzymes and thrombocytopenia have been reported (17). Moreover, product literature warns that pregnant women using valproic acid should be

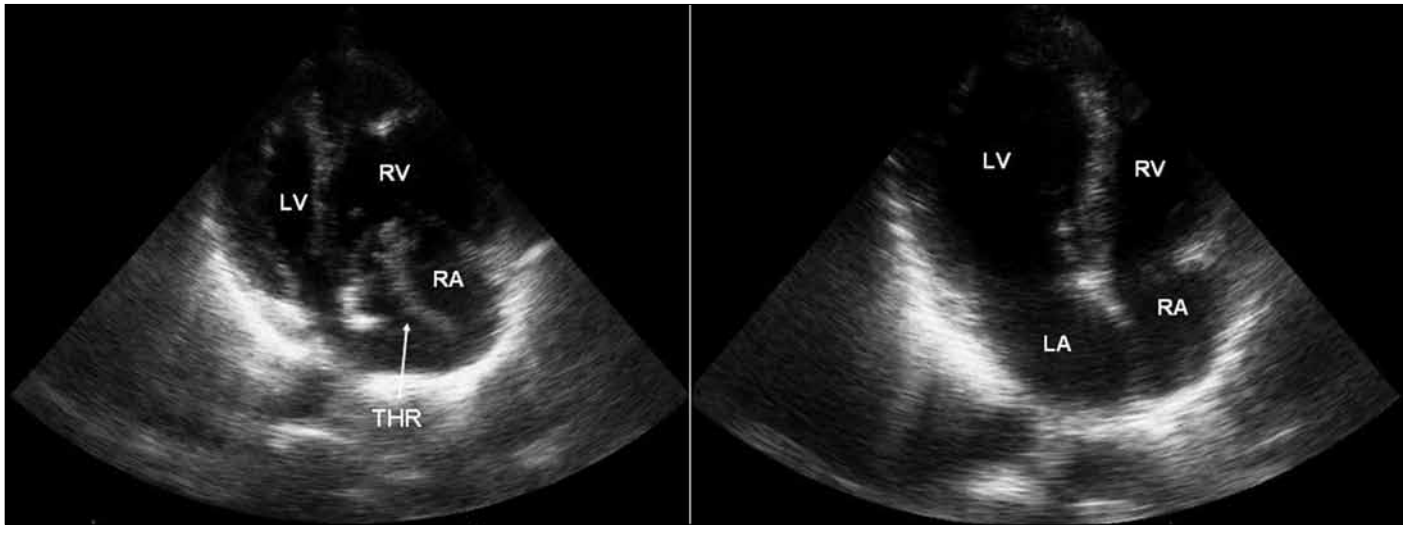

Figure 1. *Left Panel:* Transthoracic echocardiography revealing significant increase in right ventricular size and a semi-mobile worm-like thrombus in the right atrium, which was entering the right ventricle at diastole. Note that the interventricular septum is shifted towards the left ventricle. *Right Panel:* After 100 mg continuous tissue plasminogen activator infusion over 2 hours, the thrombus dissolved completely. Note that right ventricular size and interventricular septum position are normal

LV; left ventricle, RV; right ventricle, RA; right atrium, LA; left atrium, THR; thrombus

monitored for low fibrinogen and platelets and the potential for bleeding. However, thromboembolic events such as pulmonary embolism have not been reported during valproic acid usage.

In conclusion, the present case report describes successful treatment of massive pulmonary embolism with t-PA, caused by mobile right atrial thrombus in a first trimester pregnant women using valproic acid, which has not been reported previously.

Conflict of Interest

No conflict of interest was declared by the authors.

References

1. Chan L, Cutler A. Thrombolytic therapy and prophylactic anticoagulation in pregnant patients. Am J Emerg Med 1999; 17: 106-7.[CrossRef]
2. Huang SL, Chien CH, Chang YC. A floating thrombus of the right ventricle in severe massive pulmonary embolism. Am J Emerg Med 2008; 26: 1071. [CrossRef]
3. Goldhaber SZ, Visani L, De Rosa M. Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER). Lancet 1999; 353: 1386-9.[CrossRef]
4. Torbicki A, Tramarin R, Morpurgo M. Role of echo/Doppler in the diagnosis of pulmonary embolism. Clin Cardiol 1992; 15: 805-10. [CrossRef]
5. Kasper W, Geibel A, Tiede N, Bassenge D, Kauder E, Konstantinides S, et al. Distinguishing between acute and subacute massive pulmonary embolism by conventional and Doppler echocardiography. Br Heart J 1993; 70: 352-6.[CrossRef]
6. Guidelines on diagnosis and management of acute pulmonary embolism. Task Force on Pulmonary Embolism, European Society of Cardiology. Eur Heart J 2000; 21: 1301-36.[CrossRef]
7. Ahearn GS, Hadjiliadis D, Govert JA, Tapson VF. Massive pulmonary embolism during pregnancy successfully treated with recombinant tissue plasminogen activator: a case report and review of treatment options. Arch Intern Med 2002; 162: 1221-7.[CrossRef]
8. Flossdorf T, Breulmann M, Hopf HB. Successful treatment of massive pulmonary embolism with recombinant tissue type plasminogen activator (rt-PA) in a pregnant woman with intact gravidity and preterm labour. Intensive Care Med 1990; 16: 454-6.[CrossRef]
9. Patel RK, Fasan O, Arya R. Thrombolysis in pregnancy. Thromb Haemost 2003; 90: 1216-7.
10. Seifried E, Gabelmann A, Ellbruck D, Schmidt A. Thrombolytic therapy of pulmonary artery embolism in early pregnancy with recombinant tissue-type plasminogen activator. Geburtshilfe Frauenheilkd 1991; 51: 655-8. [CrossRef]
11. Yap LB, Alp NJ, Forfar JC. Thrombolysis for acute massive pulmonary embolism during pregnancy. Int J Cardiol 2002; 82: 193-4.[CrossRef]
12. Sofocleous CT, Hinrichs C, Bahramipour P, Barone A, Abujudeh H, Contractor D. Percutaneous management of lifethreatening pulmonary embolism complicating early pregnancy. J Vasc Interv Radiol 2001; 12: 1355-6. [CrossRef]
13. Baudo F, Caimi TM, Redaelli R, Nosari AM, Mauri M, Leonardi G, et al. Emergency treatment with recombinant tissue plasminogen activator of pulmonary embolism in a pregnant woman with antithrombin III deficiency. Am J Obstet Gynecol 1990; 163: 1274-5.
14. Leonhardt G, Gaul C, Nietsch HH, Buerke M, Schleussner E. Thrombolytic therapy in pregnancy. J Thromb Thrombolysis 2006; 21: 271-6.[CrossRef]
15. Ornoy A. Valproic acid in pregnancy: How much are we endangering the embryo and fetus? Reproduct Toxicol 2009; 28: 1-10.[CrossRef]
16. Genton P, Semah F, Trinka E. Valproic acid in epilepsy: pregnancy-related issues. Drug Saf 2006; 29: 1-21.[CrossRef]
17. Manoguerra AS, Erdman AR, Woolf AD, Chyka PA, Caravati EM, Scharman EJ, et al. Valproic acid poisoning: An evidence-based consensus guideline for out-of-hospital management. Clin Toxicol 2008; 46: 661-76. [CrossRef]