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Transfusion Medicine | LETTER TO THE EDITOR

Pulmonary embolism after blood donation in a healthy young female

Dear Sir,

A healthy 18-year-old woman presented for her second blood donation at our mobile blood collection unit. The venipuncture was non-traumatic with normal flow. Bruising, hematoma or arm soreness was not reported. Upon rising up after the blood collection, the donor felt dizzy. As she started biking home, she noted that she was much more out of breath than usual. The next morning, severe shortness of breath persisted. Telephonic contact to the blood bank's doctor on call, who noted that she had marked difficulty speaking, resulted in a quick referral to the emergency department.

Her vital signs upon arrival at the Emergency Department were temperature 37·6 °C, pulse 69 min^{-1}, respiratory rate 14 min^{-1}, blood pressure 116/64 and 100% O_2 saturation on room air. Her blood sugar was 7·1 mmol L^{-1}. Arterial blood gas showed pH 7·47, pCO_2 4·1(kPa), pO_2 16(kPa). C-reactive protein and complete blood count were normal. D-dimers were increased to 0·87 mg L^{-1} (reference range: <0·50 mg L^{-1}). Echocardiogram showed no findings consistent with a pulmonary embolism (PE) – normal ejection fraction and right ventricle function. Anticoagulant therapy was initiated and she underwent a ventilation/perfusion (V/Q) scan which showed bilateral small peripheral embolism (day 2 after blood donation). She was discharged home on anticoagulant therapy for 6 months. A repeat V/Q scan showed near-normalisation of the initial defects. Laboratory workup showed normal levels of antithrombin, cardiolipin antibodies, protein C and S, and no specific Factor V Leiden or Factor 2 gene mutation. Clinical history revealed no genetic or familial predisposition to thrombophilia.

Our patient was a physically active non-smoking high school student. She had a body mass index of 19·8. Her only medication was a third generation combined oral contraceptive (COC) containing gestodene and ethinyl estradiol (75 + 20 μg, once daily), which she had been taking for over a year. Thromboemboli development is dependent on three essential core factors, as described by Virchow's triad: (i) hypercoagulability (ii) venous stasis and (iii) endothelial injury. Hypercoagulability, due to a third generation COC she had been taking for over 1 year, was the one known risk factor in our patient. A randomised cross-over study measured the effects of third generation COCs on the anticoagulant pathways. The study showed significant changes that favoured thrombus formation including increase in factors II, VII, X and fibrinogen, as well as decrease in protein S and antithrombin (Middeldorp *et al.*, 2000; Tans *et al.*, 2000). However, the pro-thrombotic risk associated with COC was most pronounced in the first 3 months of use, and dropped significantly after the first year (van Hylckama Vlieg *et al.*, 2009). Our patient was taking a COC with the lowest dose of oestrogen (20 μg), documented to have a significantly lower risk of thrombosis compared to the higher dose (30 μg) preparations (van Hylckama Vlieg *et al.*, 2009). Collectively, the background thrombosis risk in our patient was low. One study reported an incidence of non-fatal PE associated with COC to be 1·72 cases per 100 000 treatment years (Hedenmalm *et al.*, 2004). Her age group (0–19 years) also, has shown to carry the lowest risk of thrombosis (Rosendaal, 2005). Venipuncture in association with blood donation causes local endothelial injury, subsequently exposing tissue factor and activating clotting factors in the coagulation pathway resulting in a local clot (Previtali *et al.*, 2011). Rosendaal (1999) suggests in his article that thrombosis is a multi-causal disease. He proposes that a synergism between different variable risk factors and events may contribute to increasing an individual's thrombosis potential sufficient to overcome a definite threshold leading to thrombosis. Borrowing from his synergy model, we hypothesise how our patient's increase in thrombosis potential, associated with her use of COC, was exacerbated by the endothelial injury and volume loss associated with blood donation, thereby exceeding her 'thrombosis threshold' and causing her respiratory distress. There have been earlier case reports of thrombosis complicating blood donation; specifically, two cases of deep vein thrombosis in the upper extremity after blood donation (Featherstone & Bayliss, 1987; Covin *et al.*, 2004). In the first donor, there were no prior risk factors, including use of COC. In the second donor, the only known risk factor was use of COC. In our patient, the temporality of events, the patient's young age, and absence of any known risk factors other than COC use, makes the blood collection more a high suspect rather than a coincidental factor in contributing to our patient's PE. However, it cannot be ruled out that our patient developed a PE after blood donation due to simple coincidence. According to ISBT Working Party on Haemovigilance grading guidelines from the International Haemovigilance Network, the authors believe that this case, presenting with clinical, laboratory and radiographic signs of pulmonary embolism, falls under the imputability grade of possible, and that our patient's low background risk of PE makes for a strong case that the donation was directly related to her complication. In summary, we present the first case of PE associated with blood

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donation occurring in a previously healthy young woman, whose sole risk factor was use of oral contraception. A 2010 survey from the Centers of Disease Control and Prevention showed that 10·7 million women aged 15–44 years were currently using oral contraceptive pills. The percentages listed ranged from 21% in the United States to up to 45% in Belgium and Portugal. These numbers translate to no insignificant numbers in the blood donor population of healthy women, even with such a low background incidence of PE. Because the associated mortality risk is high, one should have a high index of suspicion if a donor presents with respiratory difficulty for a favourable outcome in these rare instances.

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CONFLICT OF INTEREST

The authors have no competing interests.

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