Case Report

Deep Vein Thrombosis and Pulmonary Embolism in a Female Football Player with Calf Pain

Rodrigo Moreira Sales1,2,3, Ednei Costa Maia3, Rafael Moreira Sales4, Gustavo Gonçalves Arliani5, Carlos Tadeu Moreno1,5, Tathiana Rebizzi Parmigiano6

1Medical Department, Olympic Training and Research Center (COTP), Sao Paulo, Brazil
2Medical Department, Brazilian Paralympic Committee, Brasilia, Brazil
3Discipline of Sports Medicine and Physical Activity, Federal University of Sao Paulo (UNIFESP), Sao Paulo, Brazil
4Department of Physiotherapy, Estacio de Sa University, Recife, Brazil
5Department of Orthopedics and Traumatology, Federal University of Sao Paulo (UNIFESP), Sao Paulo, Brazil
6Department of Gynecology, Federal University of Sao Paulo (UNIFESP), Sao Paulo, Brazil

Email address: rodrigomedesport@yahoo.com.br (R. M. Sales)

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Abstract: Although many health professionals believe that exercise protects the athletes against thrombosis, it is discussed whether elite athletes are exposed to many thrombogenic acquired risk factors such as: dehydration, hemoconcentration, repeated microtraumas and extended periods of immobilization during travel or injury. Additionally, the use of combined oral contraceptive (COC) may increases the risk of venous thrombosis fourfold in healthy women. We report a case of a 21-years-old professional female football athlete who developed deep vein thrombosis (DVT) followed by pulmonary embolism (PE). The outpatient hypercoagulability workup was negative and the case was associated to the use of COC pills. The patient was treated with rivaroxaban for 5 months, with complete resolution of the symptoms. There are a few cases in the literature of venous thromboembolism (VTE) involving athletes. Cases of VTE attributable to the use of COC are extremely rare in this population. The diagnosis of VTE in athletes is a challenge for physicians, because the symptoms may erroneously be confused with musculoskeletal complaints. Team physicians who work with female athletes should be alert to modifiable risk factors for VTE, as well as able to perform the early diagnosis and initial clinical management of this condition. DVT should be considered as a differential diagnosis of calf pain in women, especially in athletes, due to the well-defined increase on the risk of thrombosis with the use of COC pills.

Keywords: Venous Thrombosis, Pulmonary Embolism, Combined Oral Contraceptives, Athletes, Football

1. Introduction

The venous thromboembolism (VTE) comprises deep vein thrombosis (DVT) and pulmonary embolism (PE) [1]. The incidence for the first episode of VTE is approximately 1.4 per 1000 persons/year, in accordance to a Norwegian population-based study. In this study, the incidence in women was slightly higher in comparison to men (respectively, 1.58 per 1000 person-years versus 1.28 per 1000 person-years) [2]. However, the real incidence of DVT is unknown. In fact, this is attributable to the occurrence of thrombosis with spontaneous resolution and cases of undefined diagnosis [3]. Acute PE is the most severe clinical presentation of the VTE and, in most cases, is a consequence of DVT [4]. Approximately one third of the patients with symptomatic VTE presents PE [5]. The incidence of PE, associated or not with DVT, was 34.2 per 100,000 person-years in a prospective cohort study...
conducted in the United Kingdom [6]. In patients with proximal DVT, PE may occur in up to 50% of the cases [7]. DVT should be considered as a possible diagnosis in young healthy athletes with symptoms of lower extremity pain or swelling [3].

2. Case Report

A 21-years-old professional female football athlete presented to the medical department with pain in the left calf after a routine training session. The athlete referred an insidiously beginning of a moderate intensity tightening pain in the left calf without any local trauma. There was no systemic complaints and the vital signs were stable in the initial clinical evaluation. Palpation revealed mild pain on the left popliteal region with no swellings, calf tenderness, hematomas or muscle gaps associated during the orthopedic physical examination. The main diagnostic hypothesis was acute muscle injury of the gastrocnemius muscle and she was moved away from training for two weeks. In addition, it was prescribed cryotherapy, physical therapy treatment and analgesic/muscle relaxant medication.

After 12 days, the athlete returned with persistent complaint of pain in her left leg and dyspnoea of sudden beginning at rest about 6 hours earlier. She has denied other symptoms such as fever, cough, wheezing, lipothymia or syncope and reported no evident triggering factor for dyspnoea.

Her current medications included the use of combined oral contraceptive (COC) for the last 4 years (drosiprenone 3 mg and ethinylestradiol 0,03 mg). The patient had no significant medical history. She denied smoking and dietary supplements or illicit drug use. There was no family history of hypercoagulopathies, congenital heart disease or myocardiopathies, sudden death, family dyslipidemia and rheumatological diseases.

Physical examination showed a respiratory rate of 24 breaths per minute, heart rate of 84 bpm, blood pressure of 90/60 mmHg, oxygen saturation of 98% on room air, axillary temperature of 36.9 °C (98.4 °F) and BMI of 20,21 kg/m². On cardiovascular examination, she had a regular heart rhythm with regular symmetrical pulses and capillary refill was less than 2s. No murmurs, rubs, or gallops were detected. The lungs were clear on auscultation. In addition, there were no deformities, crackles, or abnormalities on thoracic palpation or percussion. There was no mass or hepatosplenomegaly in abdominal examination. Furthermore, the patient presented claudication on march, mild edema in the left calf, with tenderness and pain on palpation of the left popliteal region. The peripheral pulses of both lower limbs were preserved. Testing of strength, deep reflexes and sensation resulted negative.

The athlete was immediately referred to the emergency room of a nearby university hospital with the diagnostic hypothesis of DVT in the left leg with possible PE. Thus, a secondary investigation was performed with chest X-ray, 12-lead electrocardiogram (12-lead ECG), Doppler ultrasonography (US) and computed tomographic angiography (CT angiography).

Chest X-ray and 12-lead ECG studies were unremarkable. The US study revealed the presence of a thrombus located in the left femoral vein until the left popliteal vein (Fig. 1). The CT angiography indicated filling defects in the pulmonary arteries branches to the basal segments of both lower lobes, the right upper lobe and the lingula, consistent with PE (Fig. 2). In total, there were 6 thrombus distributed in described locations.

Figure 1. Doppler ultrasonography of the left lower limb demonstrating a thrombus in the left femoral vein.
Anticoagulation with rivaroxaban 30 mg/d was initiated and the use of COCs was immediately discontinued. After 12 hours of clinical observation, the patient was discharged with oral anticoagulation prescription. The team medical staff and a vascular surgeon developed the clinical follow up. Rivaroxaban was reduced to 20 mg/d after 3 weeks. The outpatient hypercoagulability workup was negative (Table 1).

**Table 1. Outpatient hypercoagulability workup.**

| Variable (unit)                      | Result         | Reference value          |
|--------------------------------------|----------------|--------------------------|
| Red blood cells (cels/mm³)           | 4.36 x 10⁶     | 4.2-5.4 x 10⁶            |
| Hemoglobin (g/dL)                    | 12.2           | 12-16                    |
| Hematocrit (%)                       | 36.9           | 37-45                    |
| White blood cells (cels/mm³)         | 3,968          | 3,500-11,000             |
| Platelets (cels/mm³)                 | 193,000        | 150,000-450,000          |
| APT/INR*                             | 1.41           | 0.9-1.3                  |
| Activated partial thromboplastin time ratio | 0.93          | < 1.30                  |
| Erythrocyte sedimentation rate (mm)  | 2              | < 20                    |
| Fibrinogen (g/dL)                    | 253            | 200-400                  |
| Homocysteine (µmol/L)                | 10.3           | 4.44-13.56               |
| Lactate dehydrogenase (U/L)          | 154            | 240-480                  |
| Functional protein C (%)             | 92             | 70-140                   |
| Free protein S (%)                   | 84.3           | 60.1-113.6               |
| Antithrombin III (%)                 | 118            | 75-125                   |
| Factor V Leiden mutation             | Negative       | Negative                 |
| Prothrombin gene mutation            | Negative       | Negative                 |
| Antinuclear antibody                 | Negative       | Negative                 |
| Anti-beta 2-glycoprotein I IgG       | 10             | Normal up to 15          |
| Anti-beta 2-glycoprotein I IgM       | < 1            | Normal up to 10          |
| Anti-cardiolipin IgA (APL †)         | 0.1 APL        | Normal up to 10 APL      |
| Anti-cardiolipin IgG (GPL ‡)         | 2.3 GPL        | Normal up to 15 GPL      |
| Anti-cardiolipin IgM (MPL §)         | 5.8 MPL        | Normal up to 12.5 MPL    |
| Total cholesterol                    | 207 mg/dL      | Borderline up to 239 mg/dL|
| LDL-cholesterol                      | 128 mg/dL      | Borderline up to 159 mg/dL|

* APT/INR: Activated prothrombin time/International Normalized Ratio; † APL: IgA phospholipid units; ‡ GPL: IgG phospholipid units; § MPL: IgM phospholipid units.
The use of anticoagulants was suspended after 5 months of the initial evaluation. During the entire period of follow-up, the patient remained asymptomatic. The athlete progressive returned to sport 1 week after the suspension of rivaroxaban. After 3 weeks, the athlete was released to play in official matches. After 1 year of diagnosis, the patient had not presented new complications or relapses.

3. Discussion

In this article, we report a case of DVT followed by PE in a professional female football player. A few cases of VTE involving athletes were described in the literature. A 33-years-old female triathlete, with no significant medical history, developed DVT and PE after finishing a half-Ironman Triathlon race. In this case, the athlete had driven a car on the morning after the race for about 5 hours and was using oral contraceptive regularly [3]. The case of a high school 16-years-old athlete with sudden onset of dyspnea and retrosternal pain during a routine training session was reported in male football. This patient reported increased fatigue, abdominal pain, muscle aches, and malaise for 2–3 d before the event and had history of recent use of naproxen sodium for 6 weeks. A Computed tomography (CT) scan of the chest showed bilateral pulmonary emboli [8].

In the women’s football, there is a case report of a collegiate 19-years-old athlete who presented bilateral PE with evidence of left lower lobe infarction. The athlete was using COCs for treatment of endometriosis and she had traveled for approximately 5 hours on the team bus. However, the genetic testing on further investigation revealed positive to the genetic mutation of the factor V Leiden, which is the most common cause of inherited coagulation disorders [9, 10]. There is no case report in the literature of DVT with PE in a professional athlete of women's football.

The prevalence of hereditary thrombophilias (HT) in elite athletes is similar to that observed in the general population (between 6% and 8%). Thus, the role of HT as a risk factor for VTE does not seem to be greater in athletes. Nevertheless, it is discussed whether elite athletes are exposed to many thrombogenic acquired risk factors such as dehydration, hemoconcentration, repeated microtraumas and extended periods of immobilization during travel or injury [11, 12].

The safety of broad prescription of COC pills between athletes is controversy, because of the known thrombogenic potential of oral contraceptives and since athletes are exposed to many acquired thrombogenic risk factors in elite sport [12]. The use of COCs may increases the risk of venous thrombosis fourfold in healthy women. All individual types of COCs increases thrombosis risk more than two-fold compared with non-use. This risk depends on the different types of combined pills and can be 50% to 80% higher with gestodene, desogestrel, cyproterone acetate and drospirenone compared to those pills containing the progestogen levonorgestrel. Therefore, it is reasonable prefer the use of COCs with the lowest possible dose of ethinylestradiol (30 mcg or less) in association to levonorgestrel as progestogen [13].

Alternatively, for birth control, other contraceptive methods can be used, such as progestogen-only contraceptives (injectable, oral and patches), the intrauterine device or IUDs (copper-bearing IUDs and levonorgestrel-releasing IUDs), or condoms (male and female) [14]. In the case reported, the athlete was using a COC containing drospirenone and she could have been benefited by the choice of a less thrombogenic progestogen or even another contraceptive method. Thus, the clinical outcome could have been different.

Many health professionals believe that exercise protects the athletes against thrombosis, but this cannot be true. The diagnosis of VTE in athletes is a challenge for physicians, especially because the symptoms may erroneously be confused with musculoskeletal complaints. In addition, elite athletes may not exhibit marked changes in vital signs due to physiological adaptations to exercise, such as their propensity to bradycardia at baseline [3].

The Virchow triad consists of venous stasis, endothelial injury, and hypercoagulability [15]. This conditions may not uncommonly be seen among athletes, who frequently perform strenuous exercise and expose themselves to several risk factors for VTE, such as dehydration, trauma, immobilization, extended trips, hemoconcentration, and polycythemia. Female athletes who use oral contraceptives have an additional risk for thrombosis. Therefore, it seems prudent to recommend that athletes keep always a good hydration status, avoid tight clothing and prolonged periods of immobilization, as well as use compression stockings during long trips [12, 16].

The Wells' criteria are a diagnostic tool widely used for clinical investigation of patients with suspected thrombosis and PE. This tool stratifies the patients into low, moderate or high risk in order to guide the initial approach of the medical staff. In low clinical suspicion cases, the dosage of D-dimer is indicated due to its high sensitivity. In contrast, a CT angiography should be performed if there is a strong clinical suspicion of PE, because of its high accuracy. Anticoagulation may be initiated even before diagnostic confirmation of PE in cases of high probability [17].

In hemodynamic stable patients, a reasonable treatment algorithm of VTE could initiate the anticoagulation with low-molecular-weight heparin or unfractionated heparin. The vitamin K antagonists could be used to maintenance of anticoagulation. Alternatively, oral anticoagulation can be initiated with Rivaroxaban, with no worsening prognosis and the advantage of no mandatory coagulation monitoring. In our case, rivaroxaban was also chosen because of the possibility of early discharge from the emergency room and outpatient follow-up, since the patient was stable. In addition, the reversible or transient risk factors for thromboembolism, such as oral contraceptives, should be immediately removed [17, 18].

Regarding the return to sport, we find no high-level of evidence-based recommendation for athletes about the time to return to sport. However, the general recommendation in cases of the first episode of proximal DVT or PE, related to non-surgical transitory risk factors, is that treatment with anticoagulants lasts 3 months [18]. In the case reported, we
decided to extend the anticoagulation period due to the lack of evidence on how to treat the first episode of proximal DVT or PE in female athletes. It is important to emphasize that athletes receiving anticoagulation therapy, should not engage in any competitive sports, such as football, due to the considerable risk for bodily contact, bleeding and intracranial hemorrhage [19]. For this reason, we decided to release the athlete to return to play only 1 week after rivaroxaban was suspended.

4. Conclusion

Team physicians who work with female athletes should be alert to modifiable risk factors for VTE, as well as able to perform the early diagnosis and initial clinical management of this condition. In fact, DVT should be considered as a differential diagnosis of calf pain in female, especially in athletes, because of the well-defined increase on the risk of thrombosis with the use of COC pills. The appropriate choice of hormone combinations and concentrations of oral contraceptive pills is essential in order to reduce the occurrence of thrombosis in athletes. Furthermore, the prophylactic use of anticoagulants in specific situations of prolonged trips, in athletes with increased risk factors, might be prudent. The general recommendations on maintenance of a good hydration status, avoid tight clothing, prevent prolonged periods of immobilization and the use of compression stockings on long trips seem to be relevant.

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