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Pulmonary Thromboembolism in a Soccer Player after COVID-19 Infection: Case Report

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Abstract: Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes COVID-19, is characterized by an increased risk of thromboembolic events. However, more than 80% of patients are asymptomatic or have only minor/mild symptoms. In addition, diagnosing thromboembolism in athletes is challenging, as symptoms can be confused with musculoskeletal complaints or physical deconditioning. Case presentation: Here we report the case of a previously healthy 34-year-old professional soccer player with COVID-19 infection and genetic predisposition to thrombosis. At baseline, he was fit, had no symptoms, did not require hospital admission due to a COVID-19 infection, and was started on a five-day course of azithromycin and dexamethasone therapy. After 10 days of returning to professional activity, he developed pulmonary embolism following a COVID-19 infection during a physical exercise session. Angiotomography showed positive acute and subacute pulmonary thromboembolism, being treated with rivaroxaban 20 mg/day continuously. The shared decision-making between the medical team and the athlete was not to return to professional soccer, given the quantifiable risk. Considerations: This case illustrates the potential risk of COVID-19-induced pulmonary thromboembolism, which can be affected by genetic predisposition and dexamethasone therapy or the consequences of COVID-19. In this clinical period, the athlete's condition may be overlooked due to the masking effects of other clinical conditions and physical abnormalities. The residual effects of COVID-19 disease can appear late, requiring caution and follow-up by the medical team before releasing the athlete into a training program.

Key words: COVID-19, SARS-CoV-2, pulmonary embolism, anticoagulation, athlete.

1. Introduction

COVID-19 (coronavirus disease 2019) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. Coagulation disorders are common in COVID-19 and appear to be associated with increased thrombotic events, including arterial thrombosis, pulmonary embolism, and deep vein thrombosis [1, 2]. However, the clinical manifestations of COVID-19 are varied, ranging from asymptomatic to severe, and usually associated with prolonged immobilization and known comorbidities.

On the other hand, the occurrence and severity of hidden sequelae that may occur after asymptomatic or symptomatic cases of COVID-19 are not fully known [3]. In the absence of good evidence to improve approaches to diagnosing and treating COVID-19, any complaint needs to be valued for functional risk stratification.

Based on this, in return to the competitive practice of professional athletes who COVID-19 has infected,

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a conservative approach to return to sport is recommended, especially for competitive athletes, mainly due to the possibility of cardiorespiratory diseases and muscle compromise due to the high demand for functional sport in competitions [4, 5].

Although most athletes after COVID-19 appear to regain respiratory function, it is not uncommon to report persistent coughing and dyspnea, particularly during strenuous exercise [4, 5]. The American College of Cardiology and European Heart Association recommends that all athletes who test positive for COVID-19 have a more careful assessment of cardiorespiratory conditions, due to frequent complaints of extreme tiredness and possible lung burning during high-intensity exercise [6, 7]. Besides, patients affected by COVID-19 have a 27%-31% prevalence of venous thromboembolic events [8]. Thus, the likelihood of deep vein thrombosis and pulmonary embolism before intensive exercise after COVID-19 should be considered [9].

The sequelae of COVID-19 disease are obscure, varied, and present challenges for clinicians [10]. For athletes preparing to return to play, even those who fall into the mild to moderate category, the residual effects of the disease may appear late, requiring caution and monitoring by medical staff before placing the athlete on a structured training program [4, 6, 7, 9].

In this case report, we describe a professional soccer athlete who developed pulmonary thromboembolism after COVID-19.

2. Case Presentation

A 34-years-old Caucasian man, a professional soccer athlete, asymptomatic, was diagnosed with a positive PCR (polymerase chain reaction) test of a nasopharyngeal sample for SARS-CoV-2 in February/2021. He had non-diabetes Mellitus and did not have a history of pulmonary disease. He never smoked, did not drink alcohol, and did not use illicit drugs. However, he had a family history of deep vein thrombosis in the lower limb. The drug therapy was according to the clinical staff: azithromycin 500 mg/day for 5 days; (2) dexamethasone 4 mg/day for 5 days, (3) loratadine (syrup) 10 mg 12/12 h for 5 days, and (4) dipyrone 500 mg every 6 h. His body mass index was 23.6 kg/m^2 and his resting blood pressure was 90/60 mmHg. ECG (rest electrocardiogram) showed sinus rhythm with an average heart rate of 65 bpm. A physical examination revealed a body temperature of 36.7 ℃ and oxygen saturation of 96%. Laboratory tests showed normal hepatic and renal function and normal coagulation. Computed tomography of the thorax did not show any abnormality. After a quarantine period (14 days) he was reinstated to the soccer department, and he returned to regular physical training. Following the 10th day of training, he manifested symptoms of pulmonary burning with intense dyspnea and tiredness when walking. He was not taking any medication and was referred for evaluation of the symptoms. Rest spirometry showed a normal ventilatory function (Table 1). He underwent cardiopulmonary exercise testing on a treadmill, and he stopped exercising because of dyspnea (Table 1). Cardiac function showed normal-sized cardiac chambers (Table 1). Pulmonary artery systolic pressure was not estimated due to faint signs of tricuspid reflux. Laboratory tests showed coagulation abnormalities (Table 2). He underwent pulmonary angiotomography, which was positive for acute and subacute pulmonary thromboembolism. Branch filling failures were observed in the medial segment of the middle lobe and the segmental and subsegmental branches of the lower lobes, especially the right, consistent with the confirmed diagnosis of acute and subacute pulmonary thromboembolism (Fig. 1). He received a diagnosis of pulmonary thromboembolism and was treated with continuous use of rivaroxaban (20 mg/day). After that, there was a shared decision between the medical team and the athlete to define whether or not to return to professional soccer, based on consensus on cardiovascular risk stratification. Shared decision-making was not

Table 1 Baseline characteristics.

Cardiopulmonary exercise test		% predict
Heart rate (bpm)		
rest	66	
maximum	154	102%
Systolic blood pressure (mmHg)		
rest		
peak		
Diastolic blood pressure (mmHg)		
rest		
peak		
VO_2 pico (ml/kg/min)	35.3	95%
VE (L/min)	151	
$PETO_2$ (mmHg)	111	
$PETCO_2$ (mmHg)	28	
VD/VT	0.25	
Spirometry		
FVC	5.59	96%
FEV1	4.97	106%
FEV1/FVC	89%	109%
Echocardiogram		
Left atrium (cm)	3.2	
Left atrium indexed volume (ml/m2)	26	
Right ventricle (cm)	3.7	
Left ventricular diastolic diameter (cm)	4.9	
Left ventricular systolic diameter (cm)	3.0	
Ejection fraction (%)	69	

VE, pulmonary ventilation; VO_2, oxygen consumption; $PETO_2$, final expired pressure at alveolar oxygen level; $PETCO_2$, final expired pressure at the carbon dioxide alveolar level; VD/VT, estimated dead space; FVC, expiratory forced vital capacity and FEV1, forced expiratory volume in one second.

Table 2 Baseline laboratory tests.

	results	reference value
Prothrombin Time (TP) (sec)	15.8	13.1
Activity (%)	69.9	>70.0
Time report (TP/TR)	1.21	0.0 a 1.2
Thrombin Time (TT) (sec)	17.1	17.0
T Tromb Parc Ativ (APTT) (sec)	32.9	33.5
Time Report (APTT/TR)	0.98	1.00 a 1.21
Antithrombin III (%)	42	80 a 120
Platelets count (cells/mm^3)	210000	150000 a 450000
Red blood cells (cells/mm^3)	5.8	4.3 a 5.7
Hemoglobin (g/dL)	17.6	13.5 a 17.5
Functional protein C (%)	94	70 a 130
Free protein S (%)	104	70 a 148
Anti-cardiolipin (IgG) antibodies (GPL/mL)	19	10 – 40
Lupic anticoagulant research	Negative	Negative
Factor V Leiden mutation	Negative	Negative
Prothrombin gene mutation	Negative	Negative

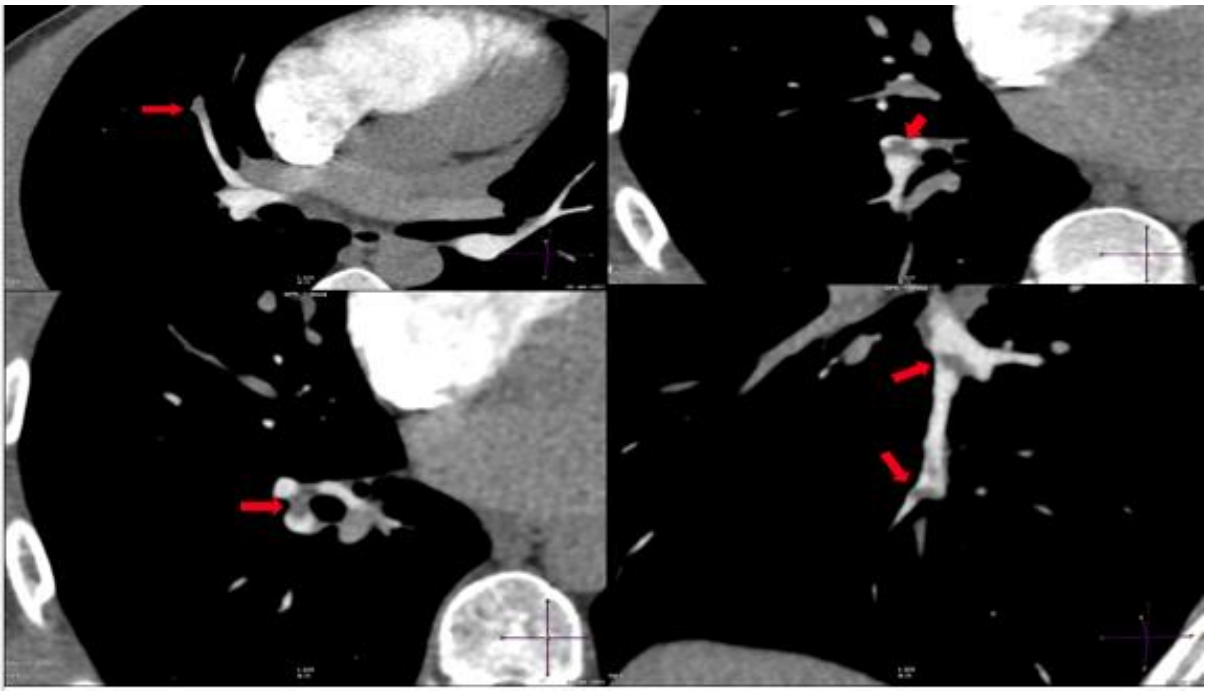

Fig. 1 Pulmonary vessel angiotomography shows several foci of contrast filling defects in segmental and subsegmental arteries in the right lung (red arrows). The presence of a rim of contrast surrounding the filling defects and the increased diameter are compatible with the diagnosis of acute pulmonary embolism.

about returning to professional soccer, given the quantifiable risk.

3. Discussion

Venous thromboembolism is often clinically silent; in many cases, the first sign is a sudden fatal pulmonary embolism [10]. Cases of pulmonary thromboembolism involving athletes have already been described in the literature [11]. Overall, athletes are exposed to some acquired risk factors that can predispose them to clots, including frequent travel, repetitive microtrauma, and hemoconcentration from dehydration [12], on the other hand, the sequelae and outcomes in athletes with previous COVID-19 infection remain unknown. The main finding is that although the athlete in this study was asymptomatic during the acute illness, the athlete developed a new symptom of late-onset pulmonary thromboembolism that was not present during the acute infection. This highlights the need for ongoing clinical assessment, as symptoms may only become evident under the physiological stress of returning to exercise.

Exercise influences clotting, fibrinolysis, and platelet aggregation [12]. However, this condition is normally kept in balance. It hardly manifests itself, but in some individuals, the immediate postexercise period is characterized by a hypercoagulable state with increased factor VIII (intrinsic pathway activation) and platelet activation. COVID-19 infection is characterized by an immune response and has the potential for thrombotic events due to increased endothelial activation and a prothrombotic state [10, 11].

At baseline, our athlete was fit, had no symptoms, and did not require hospital admission due to COVID-19, but he had a family history of deep vein thrombosis. According to the World Health Organization, the average clinical recovery time after COVID-19 is two weeks for mild cases, but after the 14-day quarantine period [9] of our athletes who returned to structured training and after the 10th day, he started to develop symptoms of dyspnea during the exercise training session. However, the relationship between severity, intensity, and sequelae

of COVID-19 is still not fully understood, but more severely affected individuals may show more signs of lung involvement [1, 3, 5], which could have led to exercise-induced thromboembolism [10, 12]. Even so, these can go unnoticed in milder cases, but later they can have serious consequences, especially in athletes under intense exercise as in this case [11, 12].

Simultaneously, in our athlete, dexamethasone therapy may have reduced the viral load of SARS-CoV-2, and may have temporarily prevented the coagulopathy of COVID-19, but the risk of procoagulant events may have increased after its withdrawal, due to the reduction in steroid levels, increasing intravascular micro-thrombosis [13].

In addition, Antithrombin III deficiency increases the risk of thrombosis by 30% due to genetic predisposition, mainly associated with acquired risk factors [14, 15]. In the present case, he had a family history of thrombosis (maternal grandfather, mother, and brother) and post-COVID-19. Moreover, he showed an Antithrombin III deficit, with negative results for lupus anticoagulant and there was no mutation of factor V Leiden and prothrombin [15].

Unfortunately, the safety and optimal timing of resuming exercise after COVID-19 are unknown, and there are no evidence-based guidelines for returning to competitive play to help clinicians decide. It is important to emphasize that the safe residual level for competitive contact sports in athletes on anticoagulant therapy is unknown because of the considerable risk of body contact, bleeding, and intracranial hemorrhage. As the athlete in this case has hereditary thrombophilia, and by medical indication is taking rivaroxaban for the long term, the therapeutic possibility of intermittent anticoagulant treatment is not indicated and it was decided not to release the athlete to play soccer at the professional level again.

4. Final Considerations

This case illustrates the potential risk of COVID-19-induced pulmonary thromboembolism, which can be affected by genetic predisposition, exercise-related, and dexamethasone therapy or the consequences of COVID-19. Although dexamethasone increases anticoagulant factors and modulates cytokines, which can suppress thrombus formation during treatment, there is a risk of a rebound effect after the end of treatment, triggering cascades of cytokines and coagulation that can lead to thromboembolic diseases [14, 15]. In this clinical period, the athlete's condition may be overlooked due to the masking effects of other clinical conditions and physical abnormalities. For athletes preparing to return to play, even those with mild to moderate severity of COVID-19, the residual effects of the disease can appear late, requiring caution and follow-up by the medical team before releasing the athlete into a training program [16].

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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