INTRODUCTION

Chronic pulmonary embolism is a condition of low incidence and with diagnostic challenges during its initial phase. This entity results from acute pulmonary embolism with organization of thrombotic material within pulmonary arteries, chronic evolution and recanalization.\(^1\)\(^-\)\(^5\) Anticoagulation is the main tool for both its prophylaxis and clinical treatment. Persistent obstructions can cause pulmonary artery hypertension, phenomenon that is associated with high mortality rate. In 95% of the cases of pulmonary embolism, the thrombi have origin in deep-vein thrombosis of lower limbs. Clinical manifestations of chronic pulmonary embolism are often variable and unspecific; factors that contribute to delay in diagnosis.\(^1\)\(^-\)\(^6\) Patients may be asymptomatic, or present gradually progressive breathlessness, thoracic pain following physical efforts, palpitations,
syncope or \textit{cor pulmonale}. Suspicion of chronic pulmonary embolism should be confirmed by thorax imaging (echocardiography, ventilation/perfusion scanning, computed tomography, angiotomography, and angioresonance).\textsuperscript{1,3,5,7}

\textbf{CASE REPORT}

After an international air-travel in 2004, a 72-year-old man presented with deep-vein thrombosis in the right lower limb. In another service, he was treated with nonsteroidal anti-inflammatory drug; although anticoagulation was not employed, his curse seemed uneventful. Clinical evaluation in November, 2005 revealed BMI: 26.47 Kg/m\textsuperscript{2}; he was asymptomatic and there was no remarkable change in physical examination or in laboratory determinations. Images from chest radiography and computed angiotomography (Figure 1A) did not disclose parenchyma or vascular changes.

He remained symptomless for three years before being submitted to evaluation in our hospital, and a pulmonary scintigraphy study was performed aiming to discard the hypothesis of eventual subclinical embolism. The images revealed bilateral deficit of peripheral perfusion. His six minute walk test showed \textit{SpO}\textsubscript{2} basal 96\% and final 88\%. Investigation about thrombophilia conditions was negative, including antithrombin III, anti-cardiolipin antibodies, C and S proteins, lupus anticoagulant, factor V Leiden, and \textit{β}-2 microglobulin. Other laboratory findings were: cholesterol 191 mg/dL, HDL 50 mg/dL, LDL 118 mg/dL, VLDL 23 mg/dL, triglycerides 116 mg/dL, Castelli indexes (1 and 2) 3.8 and 2.4; erythrocytes 4.78x10\textsuperscript{10}/mm\textsuperscript{3}, hemoglobin 15.3 g/dL, hematocrit 43.7\%, MCV 91 fl, MCHC 35\%, leukocytes 6.3x10\textsuperscript{9}/mm\textsuperscript{3}, neutrophils 70\%, platelets 183x10\textsuperscript{10}/mm\textsuperscript{3}; prothrombin time 15.9”\textsuperscript{1}, prothrombin activity 69\%, ISI 1.02, RNI 1.35; urea 37.8 mg/dL, creatinine 1.1 mg/dL.

Angiotomography done in June, 2008 showed intraluminal defects at right pulmonary artery extending to the arterial trunk, with diminished distal contrast enhancement (Figure 1B). As a whole, clinical features and imaging data contributed to confirm the diagnosis of chronic pulmonary embolism. He utilized enoxaparin and warfarin, with almost total improvement of the vascular changes, as observed in the image of the follow-up angiotomography obtained in March, 2009 (Figure 2). The patient remains asymptomatic, under specialized ambulatory surveillance.

\textbf{DISCUSSION}

The patient’s age above 60 years and his prolonged immobility due to air-travel contributed to the occurrence of deep-vein thrombosis, which is a main factor in the occurrence of acute pulmonary embolism.\textsuperscript{4,7-10} The real incidence of pulmonary embolism seems to be underestimated.\textsuperscript{5} Although acute pulmonary embolism may be idiopathic, its association with venous thromboembolisms is well-known. Additionally to ageing and immobility, the venous thromboembolism risk factors include: acquired or congenial thrombophilia; active malignancy; acute infectious disease; central vein catheterization; chronic obstructive pulmonary disease; dehydration; drugs (aromatase inhibitor, erythroid stimulators, estrogen receptor modulators, megestrol acetate, and hormonal replacement therapy); familial or personal history of venous thromboembolism; heart failure; hypercoagulable state; inflammatory intestinal disease; obesity; pregnancy/puerperium; prolonged air-travel; rheumatoid arthritis; surgery and major trauma.\textsuperscript{4,5,11,12} Worth of note, 0.1 to 5.1\% of the acute pulmonary embolism may evolve to chronic...
occlusion of pulmonary arteries and can lead to chronic pulmonary embolism, and near 40% of the cases of pulmonary hypertension due to this entity are not preceded by venous thromboembolism.

The chronic pulmonary embolism can cause persistent pulmonary artery hypertension, with high mortality rate; but patients with this condition may evolve asymptomatic for a long period before developing hemodynamic changes with severe sequelae, potential causes of death. Although, pulmonary hypertension constitutes a well-known burden associated with chronic pulmonary embolism, clinical recognition of this condition is difficult in elderly patients, but diagnosis can be confirmed by images.

Alonso-Martínez et al. very recently reported data about diagnostic delays and misdiagnosis among 375 Spanish patients (51% male; median age: 75 years) with diagnosis of acute pulmonary embolism. Misdiagnosis occurred in 50% of the cases and the mortality rate was high (36%). Studies about the incidence and clinical features of acute pulmonary embolism have been scarcely done in developing regions. Interestingly, venous thromboembolisms have been considered less common in Asian than among European individuals; however, recent clinical and necropsy findings from Thai patients with acute pulmonary embolism and chronic pulmonary embolism have showed comparable data. As more than 42% of Thai patients had idiopathic acute pulmonary embolism, several of those cases could be clinically unsuspected and thus, underestimated and underreported. Immobilization was also a main risk factor, and routine thromboprophylaxis was indicated as has been done for Eastern inpatients.

Lehmann et al. reviewed data from 257 patients with diagnosis of pulmonary embolism and 62 (24%) had travel-associated events, which were confirmed by computed tomography scans in 50 (81%) of the cases. The distribution of thrombus was predominantly bilateral (67%), and right sided (23%). The mean age of this group was 54 ± 13 years, 48% were male, body mass index average was 28 ± 8 kg/m², and deep-venous thrombosis occurred in 30 (48%) individuals. Patients with travel-associated pulmonary embolism often have other risk factors, and the events are due to immobilization and lower limb vein stasis. Chandra et al. performed meta-analysis of 14 studies about travel and venous thromboembolism, and found near 3-fold risk for this entity, with enhanced risk for each 2-hour increase in travel duration. Those authors also emphasized the likelihood of underestimating the true association between travels and venous thromboembolism due to study selection bias.

It is important to the general physician to be aware of both asymptomatic venous thromboembolism and acute pulmonary embolism, keeping in mind the possibility of underdiagnosing cases of chronic pulmonary embolism after prolonged air-travels.

DISCLOSURE

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

REFERENCES


A randomized trial of rosuvastatin in the prevention of venous thromboembolism

Controversy persists regarding the extent of shared pathways between arterial and venous thrombosis and whether treatments of known efficacy for one disease process have consistent benefits for the other. Observational studies have yielded variable estimates of the effect of statin therapy on the risk of venous thromboembolism, and evidence from randomized trials is lacking. We randomly assigned 17,802 apparently healthy men and women with both low-density lipoprotein (LDL) cholesterol levels of less than 130 mg per deciliter (3.4 mmol per liter) and high-sensitivity C-reactive protein levels of 2.0 mg per liter or higher to receive rosuvastatin, 20 mg per day, or placebo. We followed participants for the first occurrence of pulmonary embolism or deep-vein thrombosis and performed analyses of the data on an intention-to-treat basis. During a median follow-up period of 1.9 years (maximum, 5.0), symptomatic venous thromboembolism occurred in 94 participants: 34 in the rosuvastatin group and 60 in the placebo group. The rates of venous thromboembolism were 0.18 and 0.32 event per 100 person-years of follow-up in the rosuvastatin and placebo groups, respectively (hazard ratio with rosuvastatin, 0.57; 95% confidence interval [CI], 0.37 to 0.86; P=0.007); the corresponding rates for unprovoked venous thromboembolism (i.e., occurring in the absence of a known malignant condition, trauma, hospitalization, or surgery) were 0.10 and 0.17 (hazard ratio, 0.61; 95% CI, 0.35 to 1.09; P=0.09) and for provoked venous thromboembolism (i.e., occurring in patients with cancer or during or shortly after trauma, hospitalization, or surgery), 0.08 and 0.16 (hazard ratio, 0.52; 95% CI, 0.28 to 0.96; P=0.03). The rates of pulmonary embolism were 0.09 in the rosuvastatin group and 0.12 in the placebo group (hazard ratio, 0.77; 95% CI, 0.41 to 1.45; P=0.42), whereas the rates of deep-vein thrombosis only were 0.09 and 0.20, respectively (hazard ratio, 0.45; 95% CI, 0.25 to 0.79; P=0.004). Consistent effects were observed in all the subgroups examined. No significant differences were seen between treatment groups in the rates of bleeding episodes. In this trial of apparently healthy persons, rosuvastatin significantly reduced the occurrence of symptomatic venous thromboembolism.