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Pulmonary tuberculosis as a risk factor for deep vein thrombosis

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ABSTRACT: Deep vein thrombosis prevalence's during TB disease is estimated of 1.5 to 3.4%. The association of thus two diseases could be worsen prognosis of the patient hence the necessity of good diagnosis and early management. In the present report which concern two cases of pulmonary tuberculosis and deep vein thrombosis association, the goal is to determine the mechanism of this association. The first case is a 40-year-old woman clinically presenting chronic cough, fever and general impairment. Sputum examination for tuberculosis was negative when using bacilloscopic examination and was positive when using PCR GeneXpert® test. In addition she had edema of the right lower limb suggestive of deep vein thrombosis confirmed by venous doppler ultrasonography. A treatment combining antituberculosis and fluindione has been introduced. We note a favourable evolution after 3 months of anticoagulant treatment. The second case is a 55-year-old man with chronic fever, hemoptysis and general impairment. The diagnosis of pulmonary tuberculosis was made using the GeneXpert® test on the bronchoalveolar lavage fluid. Painful left malleolar edema occurred on the 6th day of TB treatment in favor of venous thrombosis of the lower limb. This will be confirmed by venous Doppler ultrasound. The evolution was favorable under 6 months of antituberculous treatment and Fluindione for 3 months. **Conclusion:** Deep vein thrombosis and tuberculosis is an association not to neglect.

Keyword: vitamin K antagonist, thromboenbolic desease, tuberculosis

Introduction

The deep vein thrombosis and tuberculosis association remains rare. According to Ambrosetti et al, its prevalence is 0.6% during the first month of tuberculosis treatment and the one third of this complication occurs during the first week [1]. This type of association may worsen the prognosis, especially in case of severe pulmonary lesions or disseminated tuberculosis, hence the need for diagnosis and early management at the same time as tuberculosis. In the present report which concern two cases of pulmonary tuberculosis and deep vein thrombosis association, the goals is to determine the mechanism of this association

Observations I

This is a 40-year-old female, farmer with a chronic productive cough -with a whitish expectoration- that has evolving for 6 months in a context of general impairement and an unencrypted evening fever.

No personal or family history of thromboembolic disease, no history of abortion, no risk factor for thromboembolism were reported. The physical examination found a crackling rale at the upper level of the right lung, an inflammatory unilateral edema of the right lower limb with Homans sign.

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The chest X-ray showed infiltrative lesions of the right lung upper lobe. Abdominal ultrasound was normal. Sputum Acid-Fast Bacilli smear examination was negative and positive when using the geneXpert molecular test without resistance to rifampicin. The venous doppler ultrasonographie of the lower limbs showed partial thrombosis of the left external iliac vein, of the left common femoral vein (Figure I), and complete thrombosis of the superficial and right popliteal femoral vein. HIV serology was negative. The patient received an antituberculous treatment with 2-months regimen of ethambutol, rifampicin, isoniazid, pyrazynamide as a combination drug and 4 months of rifampicin and isoniazid, combined with a vitamin K antagonist (fluindione) with a dose ranging from 15 to 25 mg / day. The objective of the internationnal normalized ratio (INR) was between 2 and 3. The evolution of this patient was favourable after 3 months despite the difficulty of stabilizing the INR. The vitamin K antagonist was stopped after 3 months of treatment.

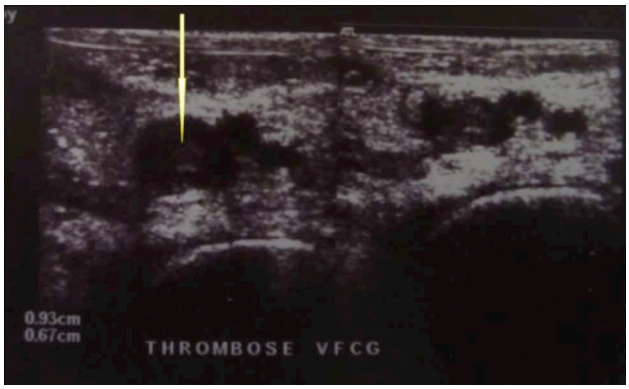
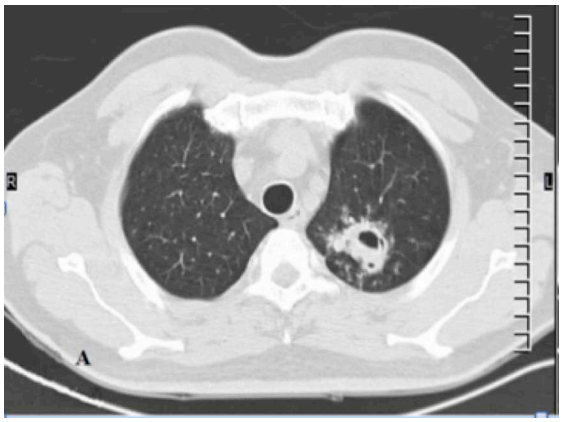


Figure I: Venous doppler ultrasonography of the lower limbs show thrombosis of the left common femoral vein

Observation II

A 55-year-old nurse, man active smoker, prensented a night fever since one month, an haemoptysis and general impairment. Clinically, there was fever at 38.9°C, with stable hemodynamic status.

The chest CT scan (Figure III) showed excavated opacity at the left upper lobe and hilo axillary alveolar opacities of the left upper lobe. Sputum direct Acid Fast Bacilli examination was negative while the GeneXpert test of bronchoalveolar lavage fluid was positive, without Rifampicin's resistance. The patient has been treated with an anti-tuberculosis treatment that included 2 months of ethambutol, rifampicin, isoniazid, pyrazynamide as a combination drug and 4 months of rifampicin and isoniazid. After 6 days of treatment, calf pain and left malleolar edema of inflammatory type appeared. The venous doppler ultrasonography of the lower limbs showed complete thrombosis of the posterior tibial vein. The patient was treated with fluindione at dose ranging from 15 to 20 mg / day to reach the target INR between 2 to 3. The evolution was favourable after 3 months of treatment and antivitamin K was stopped.



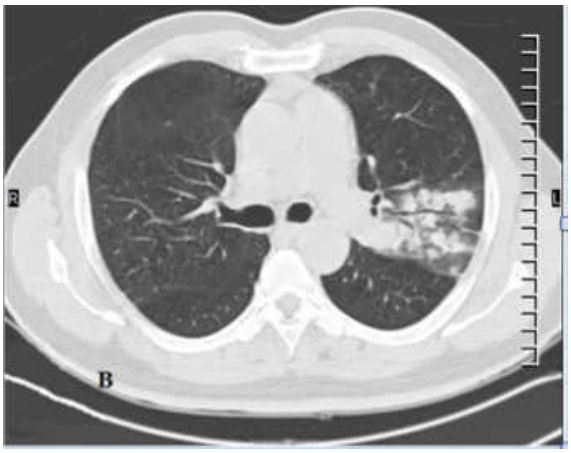


Figure II: Thoracic CT scan, lung window show on the image (A) a cavitation at the left upper lobe, (B) consolidation of the left upper lobe

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Discussion

The prevalence of thromboembolic complications during tuberculosis disease is estimated of 1.5 to 3.4% [2, 3] and the risk of developing deep vein thrombosis is proportional to the severity of tuberculosis (4). It may occur at the time of diagnosis or during treatment as the case of our two patients. Several mechanisms have been mentioned in the development of this association, namely hypercoagulability, blood stasis and vascular lesion responding to the Virchow triad. In fact, the hypercoagulable state is secondary to an increase in fibrinogenemia, an alteration of the fibrinolysis function, a platelet hyperactivation associated with a decrease in protein C, protein S and antithrombin III which are physiological anticoagulants [5, 6]. On the other hand, this complication may be related to venous compression by deep lymphadenopathy of tubercular origin, as in the case of retro-peritoneal lymphadenopathy, which leads to blood stasis upstream of the obstacle and leads to the appearance of deep venous thrombosis in the absence of any abnormality of coagulation. Finally, the systemic inflammation due to tuberculosis will cause damage on the vascular endothelium which in turn leads to the appearance of a local thrombus.
In addition, the immobility caused by hospitalization is added to these different mechanisms. This risk of thrombosis is important during the first 2 weeks but it will regress after one month of antituberculous treatment [7] hence the need to immediately introduce both anti-tuberculosis treatment and the anticoagulant one. As this is a transient and reversible over time risk factor for thromboembolic disease, the duration of anticoagulation treatment for our patients according to the recommendation of the American College of Chest Physicians (ACCP) was 3 months [8] .

There are may be some difficulties for stabilize the INR during treatment because the enzyme inducing effect of rifampicin, may require the use of high dose anticoagulant therapy, as the case with our patients.

Conclusion

Tuberculosis is a risk factor for deep vein thrombosis due to the frequent presence of Virchow's triad elements in this context, aggravated by bedridden patients, especially in advanced forms of the disease. Deep vein thrombosis can worsen the prognosis of the patient especially in cases of severe tuberculosis' lung injury . Treatments should be initiated early and concomitantly in order to avoid the spread of thromboses while knowing the pharmacological properties of rifampicin which is one of the potent enzyme inducers that can interfere with the action of vitamin K antagonists.

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There are no conflicts of interest.

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