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Case report

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Tuberculosis and thromboembolic disease in a pediatric case: causal link or fortuitous association

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Abstract

The development of deep vein thrombosis (DVT) in children is a rare event. It is usually due to hereditary thrombophilias, central venous catheterization, and surgical interventions, as it can occur as a complication of neoplasia, autoimmune disease, or cardiac malformation. The occurrence of DVT during tuberculosis remains exceptional in children. We report the case of DVT in a 13-year-old boy with bacteriologically confirmed tuberculosis and TB treatment for 10 days. The patient was placed on low molecular weight heparin with relay by the anti vitamin K. Its evolution was marked by clinical improvement and complete resolution of thrombosis. Pulmonary tuberculosis complicated by DVT in children is rare but can be potentially serious, hence the interest of looking for it and treat it early in any evocative context.

Introduction

Venous thromboembolic events are much rarer in children than in adults, but they remain an important cause of morbidity and mortality in the pediatric population [1]. They are mainly due to hereditary thrombophilias, central venous catheterization, and surgical interventions, as they can occur as a complication of neoplasia, autoimmune disease or cardiac malformation [1,2]. Their occurrence in children during infections including *Mycobacterium* tuberculosis is exceptional [3]. We report the case of a combination of DVT and bacteriologically confirmed pulmonary tuberculosis in a 13-year-old child.

Patient and observation

A 13-year-old boy, with no significant pathological antecedents, who has presented for ten days before admission a cough bringing purulent sputum in a context of unencrypted fever and deterioration of the general condition. Clinical examination at admission objectified a conscious child, feverish at 39◦C, hemodynamically stable with left basithoracic condensation syndrome. Standard chest X-ray showed an image of left pleuropneumopathy with right mediothoracic reticulomicronodular and nodular opacity (Figure 1). The three sputum BK searches were negative on direct examination, the blood count revealed normochromic normocytic anemia with a hemoglobin level of 8.7, thrombocytosis at 552000, white cell and lymphocyte levels were normal. The CRP was elevated to 237, the blood ionogram revealed a hyponatremia at 122 mEq/L. Tuberculin intradermal reaction was negative, serology of hepatitis B, C and HIV were negative, ECBU and blood cultures were also negative. The investigations were supplemented by the search for BK by gastric tubing which came back positive for direct examination and by the Genexpert in the sputum which also came back positive. The patient started anti-tuberculosis treatment and correction scheme for hyponatremia with onset of clinical improvement. However, after 10 days of treatment, the child presented pain with swelling of the entire lower left limb, clinical examination objectified an oedematous and sensitive limb. D-dimers returned positive at 9.595 µg/ml and the Doppler echo of the lower extremities revealed ileum-femoro popliteal DVT (Figure 2). The patient started the low molecular weight heparin with early relays by vitamin K antagonists (the INR target was between 2 and 3). Eventually the patient´s clinical status improved. The balance sheet showed normal levels of factor V, protein C, protein S, prothrombin and homocysteine. The thoraco-abdomino-pelvic computerised topography (CT) showed parenchymal condensation of the left lower lobe with multiple nodules and micronodules distributed in both lung fields. Doppler ultrasound radiographic examinations of the lower limbs were performed after two months and at the end of the treatment objectivizing the deep and superficial venous and continental venous axes without postphlebitic sequential lesions.

Discussion

The incidence of venous thromboembolism is 100 times lower in children than in adults [2], it is in the order of 0.07 to 0.49 per 10,000 children per year [1] and it is a major cause of morbidity and mortality in pediatrics [4]. Risk factors for development of thromboembolic disease in the pediatric population are represented by central venous catheterization, congenital prothrombotics (protein C, protein S or prothrombin deficiency, Leiden factor V mutation, G20210A mutation prothrombin gene and hyperhomocysteinemia), surgical procedures, especially cardiac and orthopedic surgery, trauma, autoimmune diseases, neoplasia, chemotherapy (including L-asparginase) and oral contraceptive use by adolescents. In particular, tuberculous infection is an exceptional risk factor in the occurrence of DVT in children and few cases have been reported in the literature in this context [3]. Jayech S *et al*. reported the case of pulmonary tuberculosis with DVT in an 11-year-old child with a ten-day period between diagnosis of tuberculosis and DVT, which is identical to our observation. Similarly, the radiological lesions were extensive as in our patient [5]. Sepou Yanza M *et al.* also reported a case of DVT that occurred during tuberculosis in a 10-year-old child [6]. Geeta Gathwala *et al*. reported the case of a 13-year-old girl with abdominal tuberculosis complicated by DVT and thrombosis of the intracranial sinus [3]. Casanova *et al*. Reported a case of DVT associated with pulmonary tuberculosis in a child with transient protein S deficiency and elevation of anti-phospholipid antibodies. In this case, the criminalization of tuberculosis in the occurrence of DVT remains controversial [7].

The mechanism responsible for the development of DVT in tuberculosis includes increased plasma fibrinogen and factor VIII, decreased antithrombin III, and reactive thrombocytosis. In addition, the release of proinflammatory cytokines during tuberculosis can cause lesions of the endothelium [5,8]. In a study, hypoprothrombinemia was observed in one-third of tuberculosis patients with DVT [9]. Thrombosis may also result from venous compression of the lymph nodes in ganglionic forms of tuberculosis [10]. Isoniazid and rifampicin may also aggravate hypercoagulability due to tuberculosis by increasing the release of interleukin-6 by mononuclear cells. The possible association between DVT and rifampicin use has been demonstrated with a relative risk of 4.74 [11]. In our observation, the assessment made it possible to eliminate hereditary thrombophilia and thrombocytosis was objectified. In addition, our patient was on anti-tuberculosis treatment ten days before the onset of DVT. Low molecular weight heparin remains the treatment of choice in children with deep vein thrombosis because of its easier handling and efficacy [6]. Vitamin K antagonists are generally not recommended before the age of 12 months. For older children, the use of Vitamin K antagonists is possible and widespread in clinical partial [12]. The recommended duration of anticoagulant therapy is three to six months, with the possibility of further continuation if prothrombotic risk factors persist. Prophylaxis of thromboembolic disease during tuberculosis remains controversial [6].

Conclusion

The occurrence of DVT in childhood tuberculosis is a rare event but remains an important cause of morbidity and mortality in pediatrics. Hence the interest to evoke and treat early to avoid complications that can be fatal. In addition, the prophylactic treatment of thromboembolic disease during tuberculosis, especially in children, is an important subject that should be of interest for future studies.

Competing interests

The authors declare no competing interests.

Authors' contributions

All the authors have read and agreed to the final manuscript.

Figures

Figure 1: standard chest X-ray showing an image of left pleuropneumopathy with right mediothoracic reticulomicronodular and nodular opacity

Figure 2: Doppler echo of the lower extremities showing ileum-femoro popliteal DVT

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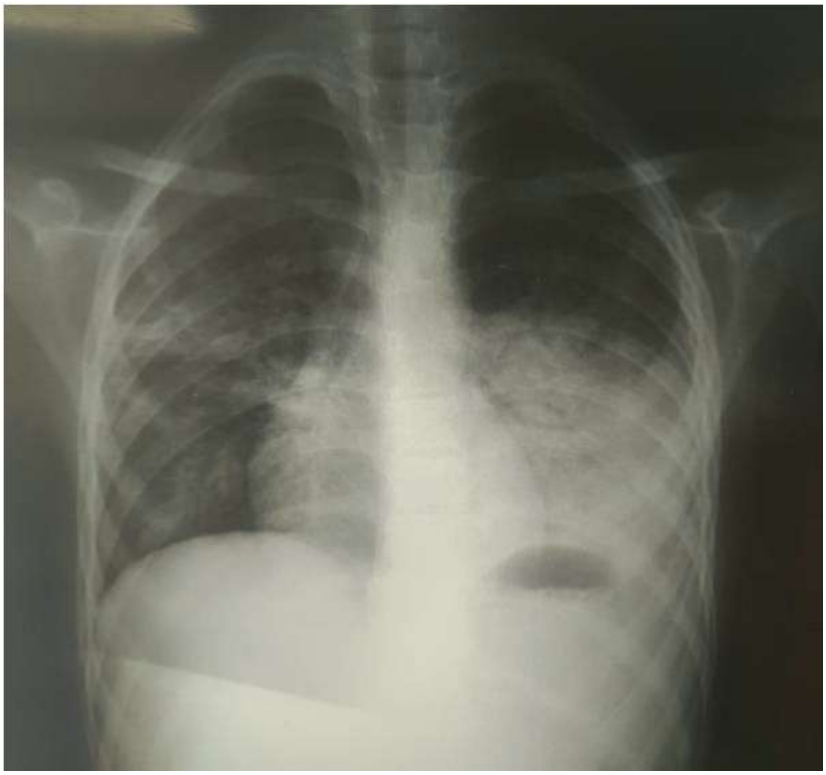

Figure 1: standard chest X-ray showing an image of left pleuropneumopathy with right mediothoracic reticulomicronodular and nodular opacity

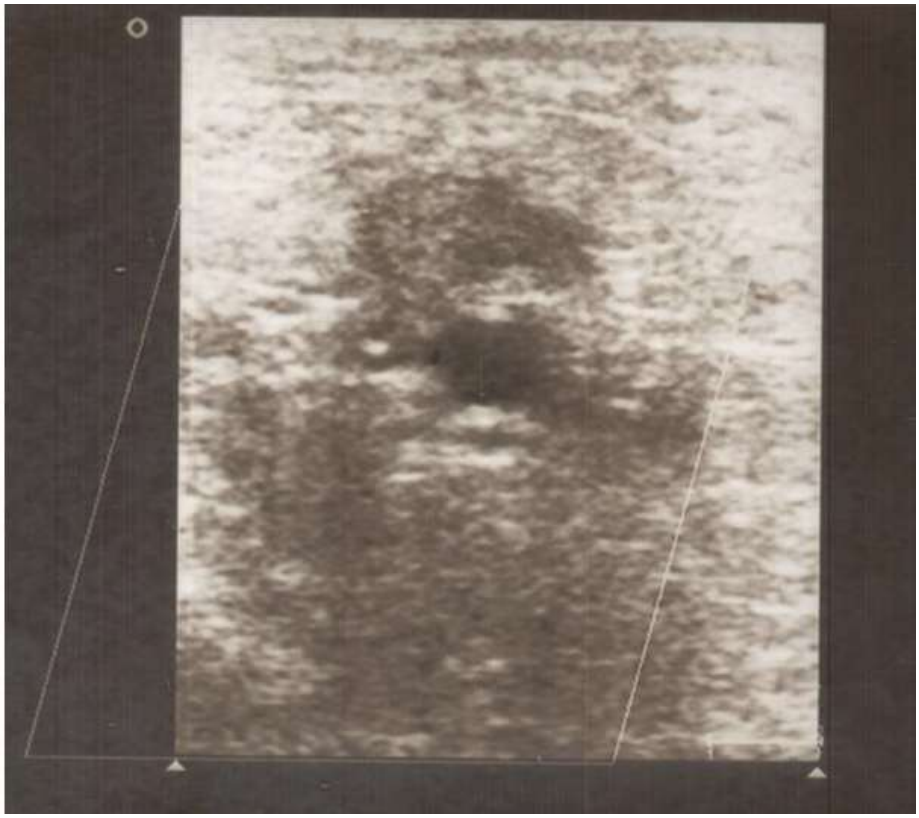

Figure 2: Doppler echo of the lower extremities showing ileum-femoro popliteal DVT