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Use of the rapid molecular test in the diagnosis of pericardial tuberculosis: a case report

Uso do teste rápido molecular no diagnóstico da tuberculose pericárdica: relato de caso

Uso de la prueba rápida molecular en el diagnóstico de tuberculosis pericárdica: presentación de un caso

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This study aims at reporting the case of a patience who presented with drowsiness and mental confusion, received in the emergency room of a university hospital in São Paulo. Symptoms included fever, weight-loss and pneumonia. Computerized tomography and ecocardiography found: attenuation of the mediastinum, pleural effusions, discrete centrilobular opaqueness in both lung lobes and mediastinum lymph nodes, left ventricle diffuse hypokinesia with a discrete systolic dysfunction, left atrium dilation and moderate pericardial effusion. The patient presented positive serology for the human immunodeficiency virus (HIV). Baciloscopies of pleural liquid, pericardial liquid and catarrh were negative; the rapid molecular test (RMT-TB) of the pericardial liquid, however, was positive for *Mycobacterium tuberculosis*, with no rifampicin resistance. The culture evidenced the growth of *M. tuberculosis*. An anti-retroviral treatment for TB was started. The access to the RMT-TB in cases of extrapulmonary tuberculosis is paramount for an early diagnosis, with direct impact in the prognosis of serious cases of patients who are co-infected by HIV/TB.
Descriptors: Tuberculous pericarditis; Real-time polymerase chain reaction; *Mycobacterium tuberculosis*.

Este estudo tem como objetivo relatar o caso de um paciente com sintomas de sonolência e confusão mental recebido no pronto atendimento de um hospital universitário de São Paulo, apresentando febre, perda de peso e diagnóstico de pneumonia. Na tomografia computadorizada e no ecodopplercardiograma foram revelados atenuação de mediastino, derrame pleural e discreta opacidade centrolobular em ambos os campos pulmonares e linfonodos mediastinais, hipocinesia difusa de ventrículo esquerdo com discreta disfunção sistólica, dilatação de átrio esquerdo e derrame pericárdico moderado. Apresentou sorologia positiva para o vírus da imunodeficiência humana (HIV). A baciloscopia do líquido pleural, pericárdico e escarro foi negativa; no entanto, o teste rápido molecular (TRM-TB) do líquido pericárdico foi positivo para *Mycobacterium tuberculosis* sem resistência à rifampicina. A cultura evidenciou crescimento do *M. tuberculosis*. Iniciou-se tratamento antirretroviral e para a TB. O acesso ao TRM-TB em casos de tuberculose extrapulmonar é fundamental para o diagnóstico precoce, com impacto direto no prognóstico de casos graves de pacientes co-infectados pelo HIV/TB.
Descritores: Pericardite tuberculosa; Reação em cadeia da polimerase em tempo real; *Mycobacterium tuberculosis*.

Este estudio tiene como objetivo relatar el caso de un paciente con síntomas de somnolencia y confusión mental recibido en la guardia de un hospital universitario de São Paulo, presentando fiebre, pérdida de peso y diagnóstico de neumonía. En la tomografía computadorizada y en el eco doppler cardiograma fueron revelados atenuación de mediastino, derrame pleural y discreta opacidad centro lobular en ambos campos pulmonares y linfonodos mediastinos, hipocinesia difusa de ventrículo izquierdo con discreta disfunción sistólica, dilatación de atrio izquierdo y derrame pericárdico moderado. Presentó serología positiva para el virus de la inmunodeficiencia humana (VIH). La baciloscopia del líquido pleural, pericárdico y esputo fue negativa: sin embargo, el test rápido molecular (TRM-TB) del líquido pericárdico fue positivo para *Mycobacterium tuberculosis* sin resistencia a la rifampicina. El cultivo mostró crecimiento del M. tuberculosis. Se inició tratamiento antirretroviral y para la TB. El acceso al TRM-TB en casos de tuberculosis extra pulmonar es fundamental para el diagnóstico precoz, con impacto directo en el pronóstico de casos graves de pacientes co-infectados por el VIH/TB.
Descriptores: Pericarditis tuberculosa; Reacción en cadena de la polimerasis en tiempo real; *Mycobacterium tuberculosis*.

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INTRODUCTION

Pericardial tuberculosis is associated to chronic pericardial effusion, but can have variable clinical manifestations, thus making a diagnosis more difficult and slowing the beginning of a specific therapy[1]. Frequent symptoms, although nonspecific, are cough, dyspnea, precordial pain, orthopnea, lower limb edema, and possibly fever and weight loss. The most frequent signs are cardiomegaly, pericardial attrition and tachycardia. Paradoxic pulse, hepatomegaly, engorging of jugular veins, and pleural effusions could also be mentioned. No entanto, em alguns casos, a pericardite e/ou o comprometimento pleural podem ser a única manifestação da tuberculose[2].

Traditionally, the confirmation of the diagnosis is done by the identification of the *Mycobacterium tuberculosis* (MTB) in a culture of pericardial liquid, or through the finding of caseation granuloma through a pericardial biopsy.[3] The treatment of pericarditis consists in the use of the quadruple anti-tuberculosis scheme[4].

Recently, the Ministry of Health, together with several institutions, is conducting studies in Brazil to evaluate the impact of the incorporation of the RMT-TB in the Universal Health System (SUS), especially for more vulnerable people, as those affected by HIV[5]. It is a fast method to diagnose tuberculosis, based on the real time nested PCR technique in a closed system, automated and with minimal sample processing[6].

In Brazil, very few data is available to inform the recommendations for the use of this test in extra-pulmonary samples, especially for the pericardial liquid, when possible tuberculosis cases are investigated[7;8]. The objective of this study was to present a case of pericarditis caused by the MTB, in a patient who had the HIV virus, and confirmed by the RMT-TB.

METHOD

This is a case study that shows the way in which care was provided to a patient with tuberculosis and HIV, developed in the context of a hospital during some months in 2016, in a university public hospital. The use of a specific test was also described.

In addition to the description of the use of the MRT-TB, other aspects of the case were also presented, such as: imaging tests, lab tests, clinical tests, therapies, and the evolution of the patient.

Respecting ethics precepts, the study does not present the name or the initials of the subject, and the description below was authorized by the institution that cared for the patient, which did so in order to make a scientific contribution.

RESULTS

A 32 years old male patient was admitted in the Emergency Room (ER) of the University Hospital (UH) of the University of São Paulo (USP) in 01/06/2016, presenting mental confusion and agitation.

Family members reported a history of fever and weight loss approximately one month before. Fifteen days before the hospitalization, the patient received the diagnosis of pneumonia, and the treatment than provided was not identified.

When arriving at the ER, the patient was confused, drowsy, Glasgow 11 (E 4, V 1, M 6), Blood Pressure 100x60 mmHg, CR 109 heartbeats per minute, , temperature 38.5ºC. No neck stiffness, nor apparent focal deficits. During cardiac and pulmonary auscultation, no abnormalities were detected. In the abdominal exam, the patient reported to feel discomfort during the palpation.

In the lab evaluation, hemoglobinemia (8.6g/dL), leukopenia (2,580/mm^3) and positive serology for HIV were identified. Skull computerized tomography (CT) did not show any brain abnormalities; a chest CT showed a discrete cardiomegaly, mediastinum attenuation, pleural effusions, discrete centrilobular opaqueness with ground glass opacity in both pulmonary lobes (Figure 1) and mediastinum lymph nodes.

Figure 1. Chest computerized tomography with no contrast. A: First image (scout) revealing the discrete cardiomegaly. B: Mediastinum attenuation and pericardial effusion. C: Discrete ground-glass opacity in both lung fields. São Paulo, 2016.

Cytochemical cerebrospinal fluid tests, blood culture, baciloscopy of tracheal secretion and urine culture did not present any abnormalities. The echocardiography (ECHO) showed diffuse left ventricle hypokinesia with a discrete systolic dysfunction (ejection fraction of 51%), left atrium dilatation and moderate pericardial effusion with granular aspect (no images).

The test treatment for pneumonia and pericarditis was started with ceftriaxone and oxacillin, followed by a transferring of the patient to the Intensive Care Unit (ICU). The patient was intubated due to respiratory failure, possibly secondary to a cardiac tamponade.

He evolved through a progressive hemodynamic improvement, although the pericardial liquid had not been drained. A bronchoscopy and a bronco-alveolar lavage were conducted. Many catarrh samples were collected for the research for acid-fast bacilli, with negative results. In 06/09/2016, the draining of the pericardial liquid (PL) was performed, and it was submitted to a baciloscopy, also yielding a negative result.

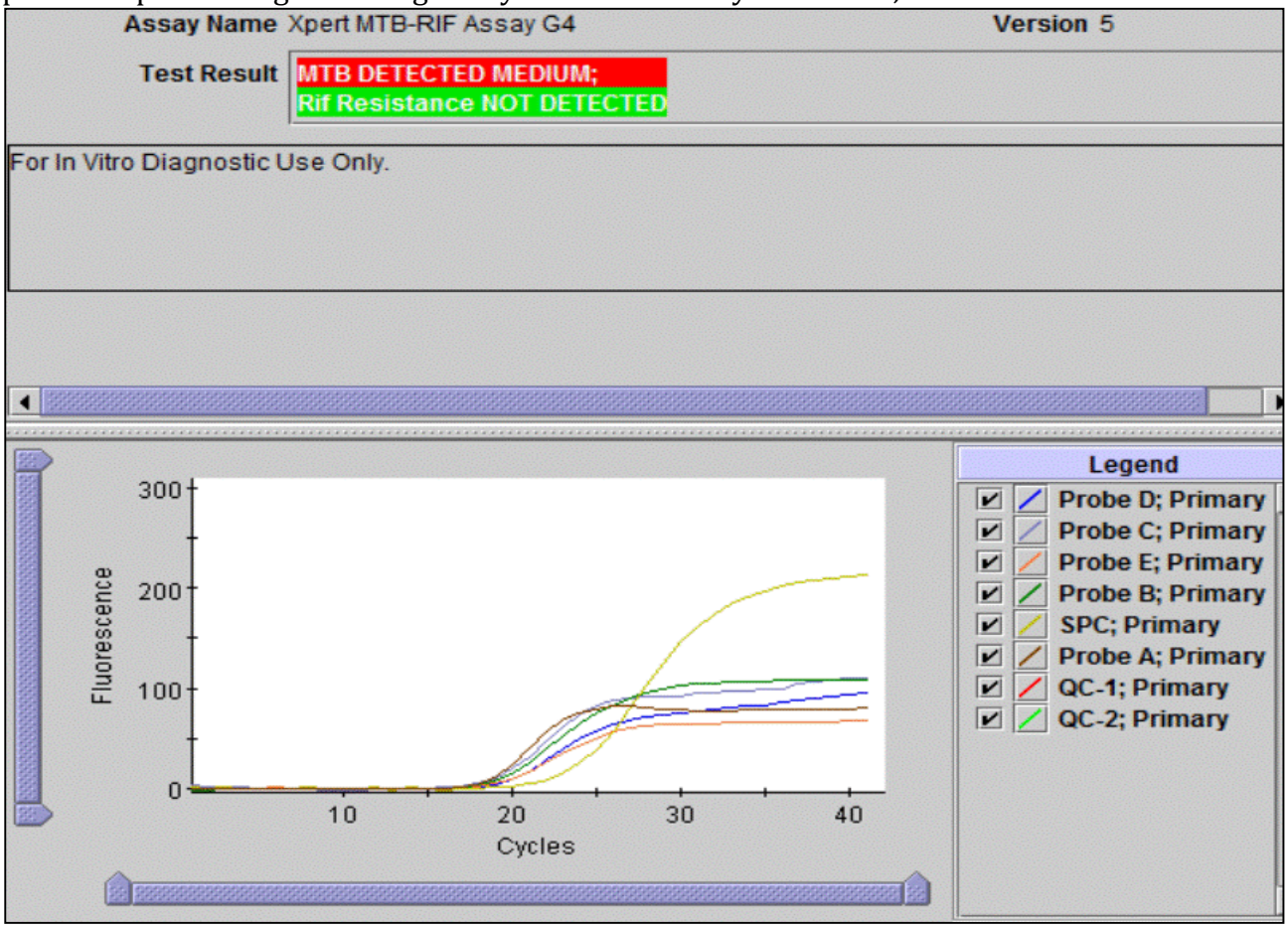
The suspicion of pericardial tuberculosis was finally confirmed in the following day through a RMT-TB, which detected rifampicin susceptible *M. tuberculosis* (Figure 2), and was conducted in the Center of the Regional Lab VII - Adolfo Lutz Institute (CLR VIII-IAL)-Santo André/SP/Brazil. At the same time, the culture in the equipment BACTEC/MGIT 960™ (Becton Dickinson Surgical Industries Inc.), presented a positive result for mycobacteria in 06/23/2016. The sediment for the culture was colored by the *Ziehl-Neelsen* method, and a positive cord factor was noted.

Additionally, the rapid identification lateral flow test was conducted for the complex *M. tuberculosis* (Alere ™ TBAg MPT-64) that presented a positive result for the MPT-64 antigen. This antigen is part of a group of proteins that is secreted in a culture for the mycobacteria, and it is only found in cultures of the *M. tuberculosis* complex. In the phenotypic test of anti-tuberculosis drug susceptibility, conducted through the BACTEC/MGIT 960™, no resistence was identified, corroborating the result of the TRM-B.

The treatment for tuberculosis was started with rifampicin, isoniazid, pyrazinamide and ethambutol, in addition to a corticosteroid prescription to diminish the chances of constrictive pericarditis. The patient showed a progressive improvement, and was extubated in 06/09/2016, and was discharged to the infirmary in 06/10/2016. In 06/11/2016, the patient presented a transient elevation of transaminases, and a gradual reduction during the treatment (AST 53 U/L and ALT 55 U/L). This is a common occurrence due to the liberation of antigens, triggered by the treatment of disseminated TB. The patient was discharged in 06/17/2016, and is still under a supervised

tuberculosis treatment. He was transferred to the Service of Specialized Assistance in HIV/Aids - Butantã Unit (SAE Butantã), where an antiretroviral treatment against HIV was also started.

Figure 2. The real time nested PCR assay using the Xpert®MTB/RIF System, showing a positive result for *Mycobacterium tuberculosis* (MTB) with no rifampin resistance in the sample of pericardial liquid. The MTB is identified when two from the five probes (A-E) present a positive signal during the cycles of the asssay. São Paulo, 2016.



DISCUSSION

Pericardial tuberculosis is a rare manifestation of tuberculosis described between 1% and 4% of cases, with a higher prevalence among individuals with HIV. In most cases, the lesion is contiguous, due to the dissemination of mediastinal lymph nodes, lung, vertebral column, sternum or during a miliary infection[1,9,10].

The ECHO helps in the presumptive diagnosis of pericarditis, though its typical findings are little specific, such as those described in the case described here. The CT, in almost all cases, evidences the thickening of the pericardial and mediastinal lymph nodes[1,9,10] that were present in this case. The great difficulty in the clinical management is to differentiate the most possible causes of the pericardial effusion (bacterial, mycobacterial, fungal, inflammatory and non-infections). That can result in a delay in the beginning of the specific therapy.

The definitive diagnostic criteria depends on the identification of the MTB culture and on pericardial liquid smears colored by *Ziehl-Neelsen*[2]**.** The MTB, however, has a slow growth, both in traditional culture means (Ogawa-Kudoh) as in automated systems (BACTEC/MGIT 960™). The sensibility and specificity of the results obtained through the TRM-TB, regarding the culture, vary from 98% to 100% and from 90.9% to 100%, respectively, for catarrh samples. The system allows for the acquiring,

in two hours, of a tuberculosis diagnostic, and to the simultaneous identification of changes in the *rpoB* gene that encodes the resistance of rifampicin. The system was endorsed by the World Health Organization (WHO) to be used in lower and medium income countries**,** especially in places with a high prevalence of tuberculosis associated to HIV and multiple drug resistances[5,6,11].

CONCLUSION

This was the first case of MTB in the pericardial liquid identified through the TRM-TB in the CLR IAL at Santo André VIII. The HIV research in confirmed TB cases is mandatory, and in extrapulmonary cases of the disease, is usually positive.

The conduction of an echocardiography was paramount for the elucidation of this case, once the results obtained reinforced the clinical suspicion of a pericardial tuberculosis, leading to the the pericardial liquid puncture, and to the complementary exams that confirm the diagnosis.

On the other hand, the TRM-TB, in cases where pericardial tuberculosis is suspected, can lead to an earlier diagnosis of this serious illness, that can evolve satisfactorily if managed precociously and appropriately.

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CONTRIBUTIONS

Andréia Moreira dos Santos Carmo contributed in the conception and design of the study, as well as in the analysis and interpretation of lab data, and in the critical writing and review of the article. **Maria Cecilia Cergole Novella** participated in the conduction of the phenotypic test of susceptibility to anti-tuberculosis drugs, as well as in the analysis of lab data and in the critical review of the article. **Paolo Jose Cesare Biselli** took part in the attention offered, in the clinical diagnosis and treatment, in the analysis and interpretation of clinical data and in the image and critical review of the article. **Wagner Issao Hoshino** conducted the clinical attention and diagnosis, and the monitoring of the patient during hospitalization in the ICU, and took part in the critical review of the article. **Akemi Oshiro Guirelli** took par in the test of pericardial liquid culture, in the identification of the *Mycobacterium tuberculosis* through the immunochromatographic method, as well as in the analysis and interpretation of lab data and in the critical review of the article. **Valéria dos Santos Candido** developed the rapid molecular test for the diagnosis of tuberculosis and the critical review of the article.

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