J Clin Tuberc Other Mycobact Dis 20 (2020) 100165

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

The exudative-constrictive tuberculosis pericarditis diagnosed by toracoscopic biopsy

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ARTICLE INFO

Keywords:
Exudative-constrictive pericarditis
Tuberculosis
Ponse's disease
Thoracoscopic biopsy
Tuberculostatic therapy
Corticosteroids
Pericardiectomy

ABSTRACT

Purpose: To present the problems and possibilities of diagnostic and treatment in a patient with resistant exudative-constrictive pericarditis.

Methods: The male patient 31 y. was admitted to the clinic due to exudative pericarditis and arthritis of the left knee joint. His medical history periodic febrile fever with a cough, episodes of syncope and atrial fibrillation, treatment with antibiotics and corticosteroids with a temporary effect.

Results: No data were received for systemic disease, hypothyroidism, tumors. With CT in both lungs, small areas of fibrosis and lymphadenopathy were identified. Pericardial sheets diffusely thickened. EchoCG shows one liter of pericardial fluid with fibrin. All tests for viruses and tuberculosis are negative. Thoracoscopy was performed. Morphological examination showed tuberculosis granulomas with caseous necrosis. The growth of mycobacteria of tuberculosis from sputum was obtained. Therapy included pyrazinamide, ethambutol, levofloxacin, prednisolone 20 mg / day. Ponce's disease regressed. Due to the increase of constriction, subtotal pericardectomy was performed.

Conclusion: Tuberculosis is one of the real causes of pericarditis with massive effusion and an outcome in constriction. The negative results of all laboratory tests for tuberculosis do not exclude the diagnosis. It is necessary to use invasive morphological diagnosis, including thoracoscopic biopsy.

1. Introduction

Pericarditis remains one of the biggest diagnostic problems in cardiology. According to the authors of the European guidelines for the diagnosis and management of pericardial diseases (2015), up to half of all cases are considered as idiopathic [1]. The use of invasive diagnostic methods (including pericardioscopy and pericardial biopsy) gives an incomparably larger percentage of established nosological diagnoses. B. Maisch and A. Ristić diagnosed a specific cause / form of pericarditis in almost all 259 patients and insist on that the diagnosis of "idiopathic" pericarditis should not exist [2]. However, the achievement of this goal is possible only with the use of morphological diagnosis.

In the Marburg register of pericarditis, auto reactive (lymphocytes), viral pericarditis and pericarditis in malignant tumors are most common. The incidence of all bacterial forms, including tuberculosis, was only 2% [2]. Tuberculous etiology is also rare in European patients with constructive forms of pericarditis (about 3–6%, [1]). However, the frequency of tuberculous pericarditis is very different depending on the overall prevalence of tuberculosis in the region, as well as in special categories of patients (for example, HIV-infected). For example, among patients with constructive pericarditis, the South African Hospital, tuberculosis was diagnosed in 29.8% of patients [3].

We will present a case of extremely difficult diagnosis and treatment of tuberculous pericarditis in the absence of evident manifestations of pulmonary tuberculosis.

2. Purpose

To present the problems and possibilities of diagnostic and treatment in a patient with resistant exudative-constrictive pericarditis.

3. Case report

Patient, 31 years old, was admitted to the clinic with general

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https://doi.org/10.1016/j.jctube.2020.100165

weakness, increased fatigue, decreased tolerance to exertion, episodes of palpitations, piercing pain in the heart, pain and limited movement in the left knee joint, cough with a small amount of light sputum in the morning.

Medical history: he lived and worked in Moscow. Since May 2016, the appearance of subfebrile temperature, dry cough, weakness, and muscle aches have been observed. The patient received an amoxiclav with some effect. Radiography revealed the expansion of the heart, EchoCG - effusion in the pericardial cavity (700–800 ml). He was hospitalized in city hospital with a diagnosis of acute exudative pericarditis. ESR was 42 mm / hour; anti-nuclear antibodies, antibodies to DNA were normal. Radiography revealed a bilateral hydrothorax. By Echo-CG EF was 55%, the heart chambers were not dilated. The pericardial effusion behind the back of the left ventricle wall was 5 cm, behind the front wall − 2 cm. Blood was obtained by attempting a pericardial puncture. Two paroxysms of atrial fibrillation (AF) have developed in the hospital.

Serositis was considered autoimmune. Prednisone 15 mg / day, aspirin 2 g / day were prescribed. The state of health improved somewhat. However, on the second day after discharge, the patient developed a fever of up to 39 °C. He was hospitalized again with AF paroxism. Sinus rhythm was restored with medication. Transient Frederick's syndrome was recorded. Subfebrile fever, leukocytosis, increase of CRP up to 36 mg/dL (normal up to 0.8), increase of antibodies to herpes viruses of 1.2.6 type, ALT up to 244 IU/L, AST up to 59 IU/L, creatine kinase up to 518 IU/L were registered in the hospital. Troponin I was negative. The CT revealed mediastinal lymphadenopathy. The patient was consulted by a tuberculosis specialist (diaskin test negative, no data on tuberculosis), rheumatologist (no data on immune disease).

From August 2016, the patient reduced the dose of prednisone to 5 mg per 2 weeks, complete withdrawal from September. According to EchoCG, pericardial effusion was maintained at the level of up to 2.4 cm. The patient noted the appearance of shortness of breath during moderate exercise (walking at a distance of 100–200 m). A cardiologist prescribed ibuprofen 200 mg / day. From November 2016, the patient noted an increase in the volume of the left knee joint, restriction of movement. He was hospitalized in the cardiology department of the University Therapeutic Clinic.

There was no swelling during the medical examination. Peripheral lymph nodes were not enlarged. Active and passive movements in joints and spine were painless. Swelling and hyperthermia of the left knee joint were identified. Hard breathing in the lungs was detected. Cervical veins were not swollen. No paradoxical pulse. Pulse 88 per minute, no arrhythmia, BP 120/80 Hg mm. Liver enlarged by 1 cm, spleen did not palpate.

In blood tests, leukocytes were 5.7 × 109, neutrophils 65.9%, lymphocytes 15.0%, eosinophils 4.6%, platelets 257 × 109, ESR 26 mm / h, fibrinogen 5.50 g / l, CRP 2, 8 mg / dL. Electrophoresis shows the normal level of proteins fractions. There were the moderate signs of cholestasis. Thyrotropic hormone was normal (1.50 μIU / ml). No elevated levels of anti-heart antibodies, ANCA, ENA-profile antibodies, DNA and cardiolipin antibodies, rheumatoid factor, genome of cardiotropic viruses, HIV antibodies were found in the blood. The analysis of urine showed minimal protein content.

On ECG (Fig. 1b) found sinus rhythm, heart rate 80 / min., negative T waves in leads I, II, aVL, V_4-V_6. Holter monitoring showed the heart rate during the day 76–117 beats / min (90 beats / min), at night 66–105 beats / min (85 beats / min), 23 supraventricular and 5 ventricular extrasystoles. During radiography, there were no focal and infiltrative changes in the lungs. The borders of the heart were enlarged (Fig. 1a). CT (Fig. 1d) in both lungs revealed small areas of fibrosis, few dense foci up to 5 mm in size, as well as "tree-in-bud sign" structures, more pronounced in the right lung. There was no fluid in the pleural cavity. Multiple enlarged lymph nodes were defined: the upper mediastinum up to 9 mm, paratracheal, bronchopulmonary in size up to 12 mm, prepericardial in size up to 9 mm, some were calcified. Pericardial sheets were thickened diffusely. The effusion up to 20 mm were found in the pericardium cavity.

By EchoCG end-diastolic size of the left ventricle was 4.0 cm, EF 45–47% with diffuse hypokinesis, ventricular septum 0.9–1.0 cm, E / A = 1.22, right ventricle 2.6 cm, left atrium 52 ml, right atrium 45 ml. The inferior vena cava fell by more than 50% during inspiration. Systolic pulmonary artery pressure was 25 mm Hg mm. There was a large amount of fluid with fibrin in the pericardial cavity (to 4.2 cm along the lateral wall). Pericardial puncture according to Seldinger was performed. The serous fluid was obtained, passive aspiration was continued (about 500 ml were removed totally). The control EF was 53%.

The study of pericardial fluid showed density of 1010, light yellow color, protein 19.5‰, Rivalt's sample negative, pH 8.0, no glucose, white blood cells and red blood cells, mesothelium cells - a small amount, Koch bacteria, microflora were not found. PCR on DNA of cardiotropic viruses was negative. Studies on acid-resistant microorganisms and PCR on MBT were negative. An intradermal test with a tuberculin antigen gave a negative result. Patient noted episodes of low-grade fever, coughing with sputum. Sputum analysis showed 30–40 white blood cells. No atypical cells or Koch bacilli were found. A complex study of sputum was also conducted to detect mycobacteria, including PCR. The result was negative. Bacteriological analysis showed a growth of Haemophilus parainfluenzae 10^6. Ceftriaxone treatment was prescribed. Body temperature returned to normal, cough decreased.

The puncture of the left knee joint was also performed: protein 25.5‰, Rivalt's sample neg., glucose 50 mg%, erythrocytes 30–100, Koch's bacilli, atypical cells were not found. No microflora growth was obtained. X-ray of the knee joint (Fig. 1h) showed no changes in bone structures. According to the ultrasound examination the joint gap was not changed, the fluid was found to be up to 15 mm, and non-uniform thickening of the synovial shell to 2.6 mm; vascularization was not found. The contours of the femoral and tibial condyles are uneven due to erosive defects of the cortical and subcortical layers. The conclusion of the rheumatologist was: a synovitis of the knee joint of an unknown etiology. Fibrin deposits, degree of thickening and vascularization of the synovial membrane does not correspond to inflammatory arthropathy. During therapy with meloxicam 15 mg per day, joint pain was slightly reduced, but the inflammation persists.

Medical therapy was carried out with spironolactone 25 mg / day, metoprolol 75 mg / day, perindopril 2.5 mg / day. The nature of polyserositis remained unclear. There is no convincing evidence for tuberculosis. The effectiveness of low doses of prednisone was difficult to assess (temperature candles appeared, but some subjective improvement was noted). Along with tuberculosis, lymphoproliferative diseases (lymphogranulomatosis, lymphoma), as well as sarcoidosis (with liver damage) were considered as the most likely diagnoses.

A video-assisted thoracoscopy was performed on the right. When examining the pleura and lung, white bumps were revealed. An atypical resection of the upper lobe of the right lung, a biopsy of the mediastinal lymph nodes and a lung were performed. An urgent morphological study of the pleural nodules and lymph nodes showed chronic granulomatous inflammation with the large areas of hyalinosis and necrosis. By histological examination (Fig. 1e–g), caseous bronchitis and tuberculous granulomas are found in the lung tissue, containing foci of caseous necrosis in the center. The lymphoid tissue was replaced by epithelioid cell and giant cell granulomas of sarcoid type with foci of caseous necrosis in individual granulomas. The conclusion was: tuberculous inflammation in the lung tissue and lymph node tissue with multiple disseminata on lung tissue, a moderate degree of activity.

A long (two months) study on solid nutrient sputum obtained prior to biopsy revealed an increase in MBT (3 CFU). By repeated sputum examination (luminescent microscopy, seeding on dense media), the growth of MBT was confirmed. Some increase in the activity of the pulmonary process was regarded as a consequence of surgical intervention. By bronchoscopy, the pathology of the tracheobronchial tree

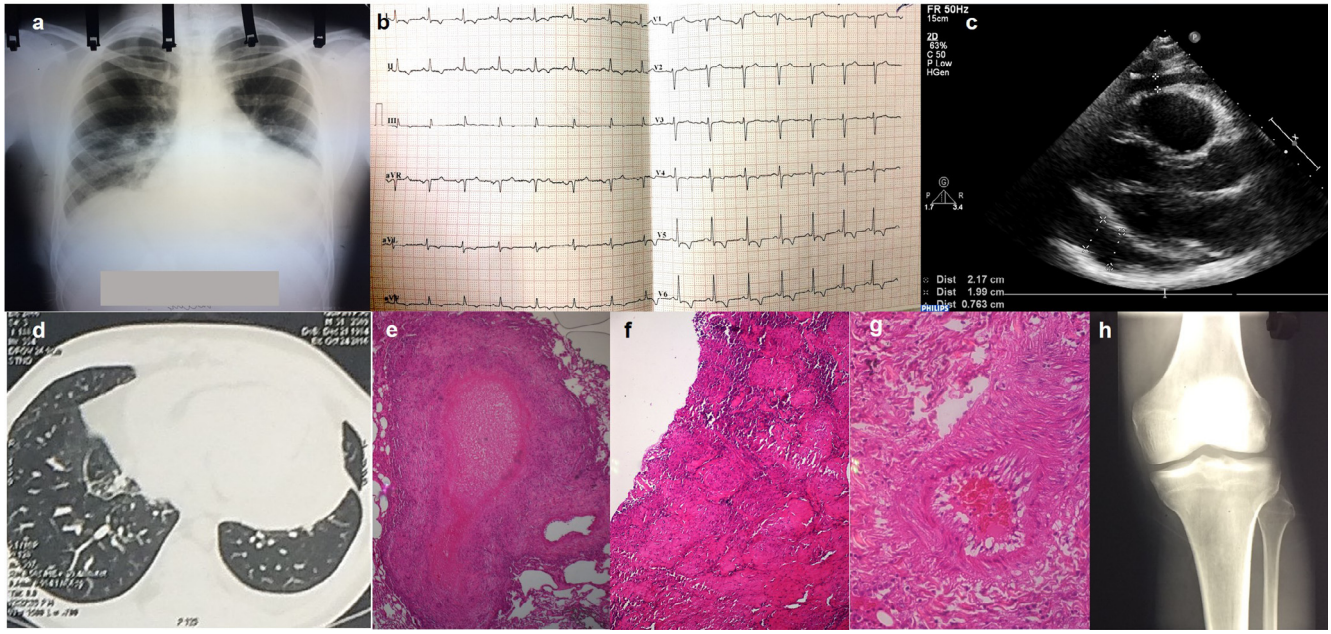

Fig. 1. The results of instrumental examination of the patient. a – radiograph of the chest (expansion of the shadow of the heart); b – ECG, 25 mm / s (negative T waves); c – EchoCG (pericardial effusion 2 cm); d – CT of the chest (few dense foci in the lungs up to 5 mm, fluid in the pericardial cavity); biopsy of intrathoracic lymph nodes (e, f) and lung (g), hematoxylin-eosin stain (lymphoid tissue is replaced by epithelioid and giant cell granulomas with foci of caseous necrosis, caseous bronchitis and tuberculous granulomas with foci of caseous necrosis in lung tissue); h – radiography of the left knee joint (changes in the bone structures were not detected).

was not revealed. Since January 2017, tuberculostatic therapy with isoniazid 1.2 mg, pyrazinamide 1.5 mg, rifampicin 0.6 mg was started. Due to the resistance of microorganisms it was necessary to replace initial drugs with pyrazinamide 1.5 mg, ethambutol 1.6 mg, levofloxacin 0.75 mg, capreomycin 1.0 w/m, cycloserine 0.5 mg. No MBTs have been detected in the sputum examination since February.

The fever did not recur. The amount of fluid in the cavities (including the pericardium) has been significantly reduced. But the clinical picture (oedema, dyspnea, diuretics need) indicated an increase in constriction. In this regard, 08.04.2017, the pericardectomy was successfully performed. After surgery, the patient's status improved markedly. After three years, the patient remains free from symptoms.

4. Discussion

The tuberculosis etiology of polyserositis in this case is beyond doubt. This is confirmed by the results of morphological examination of the lungs and intradoracic lymph nodes, obtained by growth of mycobacteria in sputum re-sowing, expressed by the positive effect of tuberculosis statics on the lung process. However, biopsies were preceded by unsuccessful attempts to establish the etiology of the process by examining pericardial puncture, sputum and knee puncture, including immunological methods (PCR). In cases of high risk of thoracoscopic biopsy, we use bronchoscopy to obtain both bronchoalveolar fluid and transbronchial lung biopsy. However, the diagnostic result of these methods is significantly lower than that of thoracoscopic biopsy.

Apparently, the pericardium lesion was nonspecific (paratuberculosis), the pathogen was absent in the exudate. Even indirect signs of paratuberculosis inflammation were not detected. The item was cell poor, no typical prevalence of lymphocytes was detected. Differential diagnosis of the causes of pericarditis was also hampered by recent steroid therapy. In this situation, a negative diaskin test result cannot be considered unequivocal. Usually, we only use trial therapy (steroids or tuburostatics) as a diagnostic manoeuvre when the diagnostic possibilities are limited or exhausted.

However, the unusual nature of pericarditis was indicated by its progressive development with the accumulation of large amounts of fluid, signs of polyserosite. The fever could be seen as a manifestation of non-specific bronchitis. This opinion is confirmed by positive effect of cephalosporins. No laboratory signs of inflammation were found (CRP level normalized). The key to the diagnosis was invasive biopsy, which was initially directed to lymph nodes. Only the thoracoscopy process visually revealed changes in the pleura. They required additional material (lung tissue) to be taken.

The development of arthritis that fully meets the criteria of Poncet's disease was also unusual. The author (A. Poncet, 1897) called it “tuberculosis rheumatism”. Poncet's rheumatoid did not disappear from the clinic. Thus, 23 patients from India were described: 13 developed oligoarthritis, no erosions or joint deformities, Mantu's reaction was positive only in 81%. The symptoms were completely resolved on tuberculosis statists, [4]. The main criterion is non-erosive, non-deforming arthritis with no other cause of inflammatory arthropathy. An additional criterion is other manifestations of hypersensitivity to tuberculosis antigen (erythema nodosum, keratoconjunctivitis, etc.).

Another important issue in patients with tuberculosis pericarditis is the use of corticosteroids along with tuberostatics. European guidelines suggest that corticosteroids be considered in patients without HIV infection (class IIbC, [1]). However, it was HIV-infected patients who were predominantly included in the largest study (2/3 of 1400 adult patients). The study confirmed the ability of corticosteroids to reduce significantly the frequency of constrictive pericarditis (4.4% compared to 7.8% in the steroid-free group, HR 0.56, $p < 0.05$) and hospitalization [5]. Prednisolone was prescribed within 6 weeks according to the following scheme: 120 mg − 90 mg − 60 mg − 30 mg − 15 mg − 5 mg / week.

In another study, 383 patients with tuberculosis pericarditis (in 143 - constrictive) were treated with prednisone for 11 weeks and observed for 10 years. Prednisone reduced overall mortality after adjusting for sex and age ($p = 0.044$). It also significantly reduced the risk of death from pericarditis ($p = 0.004$) and the need for pericardiocentesis, [6]. Attempts to use colchicine to prevent the constriction effect have not been made so far [7]. These findings suggest that corticosteroids should

be used for at least tuberculostatics resistant effusions. In the presented patient, prednisone administered late suppressed the production of fluid, but did not prevent the constriction, which required surgical treatment.

5. Conclusion

Tuberculosis is one of the real causes of pericarditis with massive effusion and an outcome in constriction. The negative results of all laboratory tests for tuberculosis and the absence of an active pulmonary process do not exclude the diagnosis. It is necessary to use invasive morphological diagnosis, including thoracoscopic biopsy.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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