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Case Presentation

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Acute Cholecystitis as an Epiphenomenon of Pericarditis with Systemic Involvement in Polyserositis: Case Report and Review of the Literature

Bizzi E[1*], Mauro A[2], Gidaro A[3], Pedroli A[1], Pancrazi M[1], Mascolo R[1], Trotta L[1] and Brucato A[1,4]

[1]Division of Internal Medicine, ASST Fatebenefratelli Sacco, Fatebenefratelli Hospital, University of Milan, Italy

[2]Department of Pediatrics and Neonatology, ASST Fatebenefratelli - Sacco, Fatebenefratelli Hospital, Italy

[3]Division of Internal Medicine, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, University of Milan, Italy

[4]Department of Biomedical and Clinical Sciences, University of Milan, Fatebenefratelli Hospital, Italy

[*]**Corresponding author**: Emanuele Bizzi, Division of Internal Medicine, Fatebenefratelli Hospital, University of Milan, Piazzale Principessa Clotilde 3, 20121, Milan, Italy

Learning Points

The recognition of idiopathic pericarditis associated to polylyserositis corroborate the concept that pericarditis may be the expression of an autoinflammatory pathology not only organ-specific and that is an important knowledge for the management and treatment of the disease.

Abstract

Background and Aim: Acute pericarditis is an inflammatory disease of the pericardium that has several underlying etiologies. This pathology can exclusively affect the pericardium or extend and affect other serosae, including pleura and peritoneum. The involvement and dysregulation of the inflammasome, a protein complex responsible for the innate immune response, seems to be the master in many forms of idiopathic pericarditis, this multi-district interest leads to consider recurrent pericarditis also as a possible systemic disease.

Methods: We report the case of a 56-year-old male, with a silent remote pathological history, who presented with subjective dyspnea, chest pain, mild and diffuse abdominal pain and low-grade fever. Routine investigations and echocardiography were compatible with acute pericarditis, chest X-ray showed pleural effusion and US-abomend highlighted firstly a modest peritoneal effusion, then a condition of cholecystitis.

Results: The symptoms completely regressed within 24 hours by the start of therapy with NSAIDs and colchicine; pericardical, pleural and peritoneal effusions with cholecystitis regressed in few days.

Conclusions: This is the first report in whom pericarditis with polyserositis also involved the gallbladder in the inflammatory process. It appears that the therapy coded for pericarditis was able to induce remission of the extracardiac inflammatory processes, going to corroborate the idea of an autoinflammatory etiology of the cholecystic inflammatory process as well. Early identification of pericarditis with systemic involvement would mean shorter hospitalization times and a better therapeutic classification of the patient, with shorter recovery times, avoiding generating conditions of corticosteroid-dependent pericarditis and guaranteeing a significant reduction in the number of relapses.

Keywords: Idiopathic pericarditis; Polylyserositis; Autoinflammatory pathology; Cholecystitis

Introduction

Acute pericarditis is an inflammatory disease of the pericardium that has several underlying etiologies [1-4]. Tremendous progress has recently been made in understanding this pathology through the recognition of the underlying pathogenetic mechanisms in idiopathic forms. The involvement and dysregulation of the inflammasome, a protein complex responsible for the innate immune response, seems to be the master in many forms of idiopathic pericarditis, an idea corroborated by the effectiveness of anti- Interleukin 1 (IL-1) drugs in this pathology [5-9]. The inflammasome, when dysregulated, would tend to produce high quantities of IL-1. In addition to great progress in understanding the pathogenetic mechanisms underlying pericarditis, recent studies have shown that this pathology can be isolated and exclusively affect the pericardium, but can also extend and affect other serosae of the body, including the pleura and the peritoneum [10]. This multi-district interest raises numerous questions and has led to considering recurrent pericarditis not only as an autoinflammatory pathology of the heart but also as a possible systemic disease [11,12]. It has recently been reported that the inflammatory, clinical and laboratory characteristics of pericarditis with systemic involvement are more marked than those with exclusive involvement of the pericardium, and therefore very similar to systemic autoinflammatory pathologies [10]. The systemic involvement of the serosa during pericarditis poses countless diagnostic doubts and is often the cause of diagnostic delay due to its

peculiar presentation. More rarely there are cases in which, in addition to pleural and pericardial involvement, peritoneal involvement is observable, with conditions of diffuse abdominal pain that are difficult to interpret. Frequently in these patients it is possible to find layers of peritoneal effusion, while the abdominal symptoms remain vague, diffuse and can be mild or very significant, almost resembling an acute abdomen **[13,14]**.

Case Description

We report here the case of a patient who presented to the emergency room complaining of subjective dyspnea, chest pain, mild and diffuse abdominal pain and low-grade fever. The patient reported the gradual onset of symptoms and their worsening in the last three days. The patient was a 56-year-old male, with a silent remote pathological history, not under treatment for any pathological condition, with no family history of autoimmune or autoinflammatory pathologies. In the emergency room the vital parameters were normal, with blood pressure of 100/60 mmHg, SpO2 94% in room air, heart rate of 90 beats per minute, body temperature was 37.3°C. The patient's objective examination highlighted a disappearance of vesicular murmur at the right base only. The patient was first subjected to an ECG, which resulted normal, and to routine investigations, including complete blood count, troponin, C-Reactive Protein (CRP), creatinine, urea nitrogen, transaminase, amylase, lipase, fibrinogen and D-Dimer dosage. A chest x-ray was also performed. While the renal, hepatic and pancreatic profiles and the troponin dosage were normal, the blood count showed a marked neutrophilia (White body cells 15.150, Neutrophils 11.500), together with elevated CRP values (321.5 mg/L), fibrinogen and D-Dimer (> 7 g/L and 1320 mcg/L respectively). Procalcitonin levels were within normal range. The chest x-ray **(Figure 1)** showed a pattern of right unilateral pleural effusion together with a consensual area of right basal pulmonary atelectasis. As aortic dissection or pulmonary thromboembolism were suspected, the patient underwent a chest Computerized Tomography (CT) scan with contrast mean, which confirmed the presence of pleural effusion but did not reveal pulmonary thromboembolism or aortic dissection. The ultrasound of the abdomen highlighted only a modest peritoneal effusion, while it reported a normal picture regarding the hepatic, gallbladder, renal, pancreatic and bladder profiles.

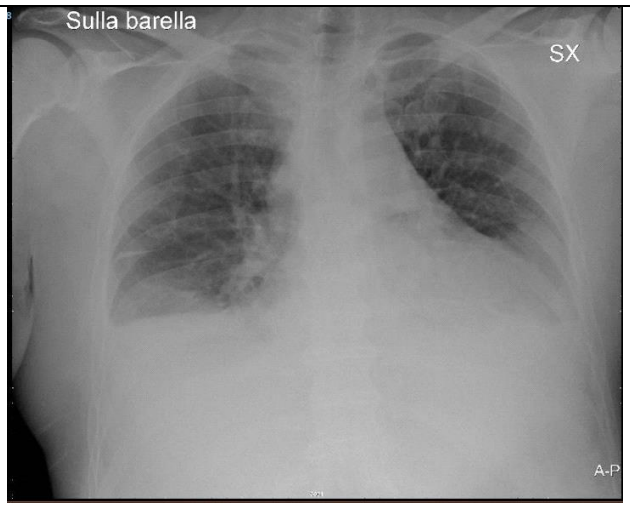

Figure 1: Chest x-ray shows a pattern of right unilateral pleural effusion together with a consensual area of right basal pulmonary atelectasis.

On suspicion of pleurisy, the patient was started on empirical therapy based on ceftriaxone 2 grams intravenously every 24 hours. The patient presented poor regression of chest and abdominal pain. Subjective dyspnea also remained unchanged. For further investigation, the patient was admitted to the internal medicine department. Blood tests confirmed elevated CRP, D-Dimer and fibrinogen, unaltered by the administration of ceftriaxone. Again, procalcitonin levels were within normal range. On the second day of hospitalization, due to the persistence of high CRP levels, the patient underwent a new chest x-ray **(Figure 2)**, which highlighted a slight enlargement of the cardiac area compared to the previous check-up and the unchanged presence of the pleural effusion. The ultrasound of the abdomen, performed during hospitalization on the second day, highlighted a condition of cholecystitis with walls of increased thickness and infiltration of intraparietal fluid on gallbladder with a diameter of 11 mm **(Figure 3)**; no stones were highlighted, intrahepatic biliary ducts were normal, common bile duct was of normal caliber and regular course, portal vein was of normal caliber. The liver appeared of normal size, regular margins, homogeneous parenchyma and regular echogenicity. A moderate abdominal effusion persisted. The patient underwent to an echocardiographic examination that highlighted a slight circumferential pericardial effusion layer, not haemodynamically significant, with a maximum size of 13 mm.

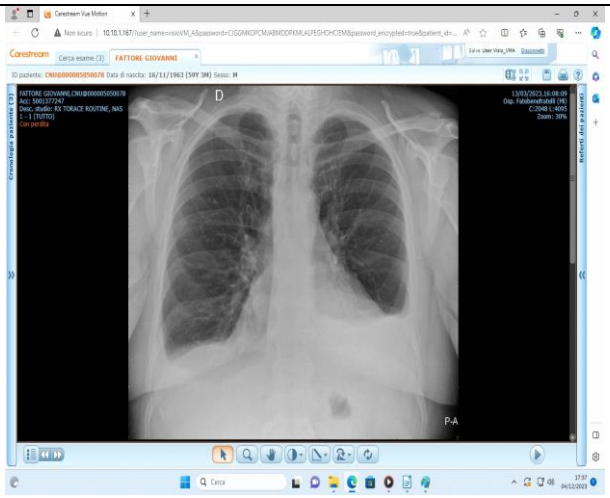

Figure 2: Second chest x-ray which highlights a slight enlargement of the cardiac area compared to the previous check-up and the unchanged presence of the pleural effusion.

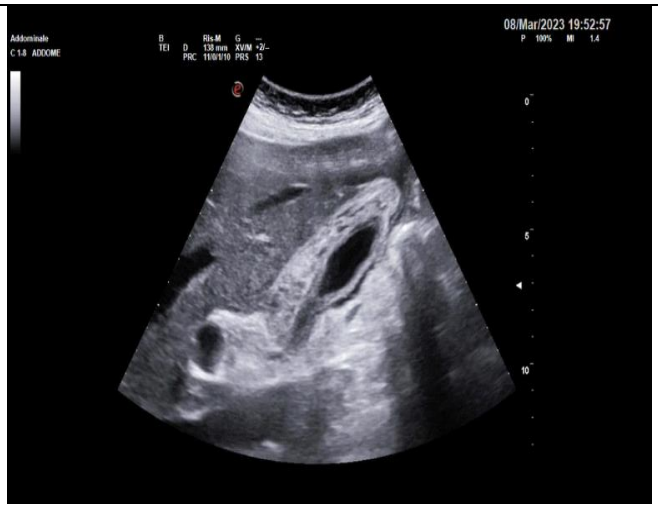

Figure 3: Abdomen ultrasound highlights a condition of cholecystitis with walls of increased thickness and infiltration of intraparietal fluid on gallbladder with a diameter of 11 mm, no stones, normal intrahepatic biliary ducts, common bile duct of normal caliber and regular course, portal vein of normal caliber.

The presence of pericardial effusion, typical chest pain together with the elevation of the CRP values allowed the diagnosis of pericarditis, complicated by pleural and peritoneal effusion, configuring a condition of a pericarditis with systemic involvement. The patient underwent laboratory tests to search for autoimmunity which were negative, and a serological test for tuberculosis which was negative. The patient was promptly started on therapy based on indomethacin 50 mg intravenously with prolonged release over 24 hours and colchicine 1 mg orally every 24 hours. The symptoms completely regressed within 24 hours. Although the pleural effusion remained evident al physical

examination, both the dyspnea and abdominal pain disappeared. CRP values normalized approximately 96 hours later, with a gradual decrease. The patient was discharged four days later, with a therapy based on indomethacin 50mg every 8 hours and colchicine 1mg every 24 hours. At visit carried out 7 days after discharge, the patient reported complete disappearance of the symptoms. During this visit the patient underwent an echocardiographic examination which showed the permanence of the pericardial effusion (11 mm maximum), unchanged pleural effusion, while the abdomen ultrasound examination showed that peritoneal effusion had disappeared **(Figure 4)**. The parietal thickness of the gallbladder also appeared to decrease. Slow decalages of indomethacin dosages were scheduled only in case of normality at monthly CRP checks. The patient, currently in the eighth month of follow-up, has not presented any relapses of pericarditis and the pericardial, pleural and abdominal effusions have disappeared, as has the wall thickening of the gallbladder, despite the progressive reduction of the indomethacin-based therapy. The CRP values, according to the clinic, were always within the normal range.

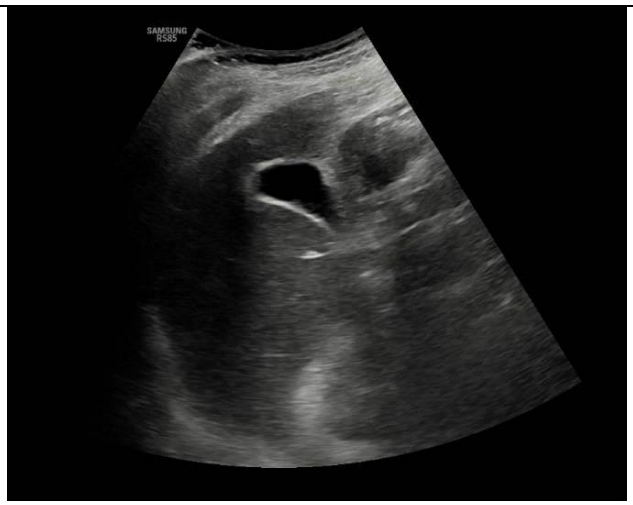

Figure 4: Second abdomen ultrasound examination showed that peritoneal effusion layer had disappeared.

Discussion

Pericarditis with extracardiac involvement of other serosae is frequently seen in patients with idiopathic pericarditis **[10]**. Polyserositides recognize several causes, although they often remain idiopathic **[15]**. In addition to pericarditis with systemic involvement, they can be found in a large number of diseases, not only neoplastic or infectious but also autoimmune and autoinflammatory **[16]**. The symptomatologic, radiologic, and laboratory parade of patients with polyserositis poses significant differential diagnosis problems, often creating diagnostic delays and poor initial therapeutic appropriateness **[15]**. A patient presenting with chest pain and pleural effusion, especially before the onset of pericardial effusion, is hardly diagnosed as suffering from an autoinflammatory process, even if CRP values are elevated, associated with neutrophilia and negative procalcitonin. When peritoneal involvement is also present, diagnostic doubts increase further, and it is only when pericardial effusion becomes manifest that a diagnosis is made according to Erupean Society of Cardiology (ESC) criteria. The recognition of idiopathic pericarditis as a disease often caused by autoinflammatory mechanisms leads to the consideration of the polyserositis found during

its course as an epiphenomenon of systemic autoinflammatory processes, going further to corroborate the concept that pericarditis may be the expression of an autoinflammatory pathology not only organ-specific and that at its basis there may be alterations capable of manifesting pathologically in the pericardium and in other serous layers **[10,17]**. In the reported case, not only was the pericardium involved by the likely autoinflammatory process, but the pleura and peritoneum were also involved, with a complex symptomatic parade characterized by both typical chest pain and dyspnea and abdominal pain. In addition to this, involvement of the gallbladder wall could be observed in the patient, which regressed with the same NSAIDs and colchicine therapy that proved effective in containing the pericarditic, pleuritic, and peritonitic process. This is the first report of a patient in whom pericarditis with polyserositis manifestation also involved the gallbladder wall in the inflammatory process, and from what has been observed, it appears that the therapy coded for pericarditis was able to induce remission of the extracardiac inflammatory processes as well, going to corroborate the idea of an autoinflammatory etiology of the cholecystic inflammatory process as well. Elevated CRP values accompanied by neutrophilia and normal procalcitonin values should lead to consider an autoinflammatory process underlying the pathology under investigation. Elevated D-dimer and fibrinogen levels, as recently demonstrated, may accompany the inflammatory process as markers of inflammation and are not necessarily related to thromboembolic events **[9,18]**.

Disclosure

Conflict of interest: The authors declare no conflict of interest.

Patient Consent: We obtained written informed consent from patient to secure permission for publishing their clinical history.

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