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CASE REPORT

# A case report of positive Charcot´s triad from a rare infectious etiology

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**Abstract**

Chlamydia pneumoniae (C. pneumoniae) is an obligate intracellular bacterial pathogen, which has long been investigated as a potential developmental or exacerbating factor in various pathologies. C. pneumoniae infects mainly the respiratory tract, but also has been associated with extrarespiratory manifestations. We report on an uncommon case of young patient with acute acalculous cholecystitis (AAC) and acute pericarditis during the chlamydia pneumoniae infection with hematogenous / lymphogenous routes of systemic dissemination of Chlamydia pneumoniae infection.

## INTRODUCTION

Acute cholangitis is acute bacterial infection of intrahepatic bile ducts arising in the field of stagnant bile during obstruction of bile ducts. The most common cause of bile obstruction is choledocholithiasis, further then tumor or inflammatory stenosis of bile ducts. The cause of infection is mainly Escherichia coli, Klebsiella, Enterobacter or Haemophilus influenzae. The route of spread of infection is predominantly ascending spread from the duodenum, it is also possible hematogenous spread via vena portae. Typical symtoms include Charcot´s triad: fever, jaundice, right upper quadrant abdominal pain. Other symptoms may be nausea, vomiting, rigors, pruritus. In advanced cases develops hypotension, septic shock and multiorgan dysfuntion (Češka *et al.* 2010).

Acute cholecystitis may occur as primary inflammation, but it is more common acute exacerbation of chronic cholecystitis. In this case, the gallstones act as a reservoir of infection and as bile drainage barrier. The infection is spreading ascending from the small intestine (Escherichia coli, Salmonella) or by bloodstream (Streptococci). Acute cholecystitis as an inflammation of the gallbladder, most commonly occurs after cystic duct obstruction from cholelithiasis (calculous cholecystitis). Acalculous acute cholecystitis is less common and seen primarily in critically ill patients. Conditions that result in reduced perfusion and biliary stasis are e. g. multiorgan failure, severe trauma, burns, surgery, sepsis, total parenteral nutrition, prolonged fasting… Unlike clinical symptoms, which are typical for acute ascendant cholangitis (=Charcot´s triad), typical clinical signs for acute cholecystitis is positive Murphy´s sign and fever. During the physical examination, Murphy´s sign is useful

for differentiation pain in the right upper abdominal quadrant – it is positive in cholecystitis, but negative in choledocholithiasis, pyelonephritis and cholangitis (Češka *et al.* 2010). The diagnosis is made clinically and confirmed via ultrasound. Cholescintigraphy (radionuclide HIDA scan = hepatic iminodiacetic acid scan) is a useful adjunctive diagnostic tool if ultrasound is unconvincing. Treatment of acute cholecystitis depends on the severity of condition and the presence or absence of complications. Uncomplicated cases can often be treated on an outpatient basis, complicated cases may necessitate a surgical approach. The definitive treatment of complicated cholecystitis is laparoscopic cholecystectomy, either performed within 72 hours of onset or after a course of antibiotics when inflammation subsides (usually after at least 6 weeks). Complications of acute cholecystitis include gallbladder gangrene and rupture with biliary peritonitis, sepsis and septic shock, further empyema cholecystae, gallstone ileus, emphysematous cholecystitis, pericholecystic abscess formation, hepatic abscesses can also occur. Diagnostic imaging for complications of cholecystitis are CT/MR. Chronic cholecystitis, which also increases the risk of gallbladder carcinoma, is characterized by inflammatory cell infiltration on histopathologic examination. Thought to be caused by mechanical irritation and/or recurrent cholecystitis that leads to fibrosis of the gallbladder. Almost always is associated with gallstones (Shein *et al.* 2011).

## CASE REPORT

18-year-old Caucasian boy, active water polo player, was transferred from pediatric surgical emergency with clinical, laboratory a paraclinical signs suggesting to acute abdomen with localization to the right subchondral area. From the beginning of the hospitalization at the pediatric surgical ward the clinical symptoms involved positive Charcot´s triad: fever, jaundice and right upper quadrant abdominal pain with hepatomegaly + 1,5 cm in midclavicular line (MCL)by palpation and painful percussion across the width of the liver, mainly in the epigastrium. Laboratory findings include elevation of white blood cell count (WBC), ALP, ALT, conjugated and non-conjugated bilirubin, normocytic normochromic anemia, positive finding of urobilinogen in urine, C-reactive protein (CRP) was 212.0 mg/l, procalcitonin (PCT) was 0.16 ug/l, erythrocyte sedimentation rate (FW) was 78 mm/h. Diagnostic imaging concludes by ultrasonography thickened and edematous gall-bladder wall (double wall sign) with thickness of gall-bladder wall up to 6 mm without gallstones, without dilation of intrahepatic and extrahepatic biliary ducts, without pericholecystic fluid. In anamnesis patient talked about similar symptoms which occurred about a month ago. The symptoms contained fever up to 39.0 °C, right subchondral abdominal pain and chest pain at inspiration without others symptoms of abdominal discomfort or dysuric problems, without cough. CRP was 120 mg/l, the general practitioner prescribed Cefuroxim for 2 weeks. At the end of antibiotic therapy CRP was 6.8 mg/l and the patient felt well. But after 4 weeks the same symptoms appeared and the patient was admitted to the hospital. Under conservative treatment (parenteral application of Cefotaxim and Metronidazol, total parenteral nutrition, spasmoanalgetic infusions, proton pump inhibitor, hepatoprotectivum) showed abdominal ultrasound retreat of thickness of gall-bladder wall to 3.5 mm but developed calculus in gall-bladder with measurements 7.9 x 4 x 4 mm and hepatomegaly + 1.5 cm in MCL persisted. We continued in conservative treatment and increased intravenous hydration. The follow-up ultrasound did not show cholecystolithiasis. After withdrawal of antibiotic therapy developed again septic fever, elevation of laboratory markers of acute inflammation (WBC=12.38, CRP=205.6, FW=75/116, PCT=0.14) and a dry irritable cough worsening at night has been added. Clinical symptoms of Charcot´s triad, except of fever, were replaced by positive Murphy´s sign. On the X-ray image was not finding of bearing lung process and auscultation finding was without secondary breathing phenomena. Sonographic features for acute cholecystitis or cholecystolithiasis disappeared. In serological results we found positive antibodies against C. pneumoniae IgA (ELISA)=40.4 and C. pneumoniae IgG (ELISA)=90,1 with cut-off less than 11.0 by both values. Serological results of anti-CMV IgM and IgG, anti-EBV-VCA IgM and IgG, serum-Mycoplasma pneumoniae IgM and IgG were negative. With regard to the results of serology we chose to continue the antibiotic therapy with intravenous Ciprofloxacin. In differential diagnosis we effected following examinations: antistreptolysin O titer and rheumatoid factor were negative, X-ray of sinuses paranasal were without pathologic finding, culture of nose and tonsils had common microbial flora. Echocardiography (ECHOKG) did not verify structural cardiac anomaly, concludes good myocardial function, there was a recording on the electrocardiogram without rhythm disorders, inversion of T-wave above left precordium persists from 01/2019-v.s. as sequel of active sport activity. Currently was present pericardial effusion up to 10-15 mm in systole, which did not affect heart functions, patient was cardially compensated. The values of myocardial enzymes were as follows: CK=1.70 μkat/l – cut-off is less than 2.85 μkat/l, CKMB=0.13 μkat/l – cut-off is less than 0.4 μkat/l, troponin T=9.9 μg/l – cut-off is less than 0.05 μg/l, NT-proBNP=361.5 ng/l – cut-off is less than 125.0 ng/l. On repeated ECHOKG was confirmed pericardial effusion. Nonsteroidal anti-inflammatory drug (Ibuprofen 400 mg) and Potassium-sparing diuretics and Aldosterone antagonist (Spironolactone-VEROSPIRON) were added to the treatment. In differential diagnosis of focal infection we realized whole-body PET/CT with FDG (18-fluorodeoxyglucose) examination, which reported submandibular, supraclavicular and intrathoracal

lymphadenopathy, increased accumulation of radiofarmacum in pericardium with fluidopericard up to 25 mm and in basal bilateral subpleural areas with fluidothorax up to 15 mm, liver was without focal hypermetabolic activity, hepatomegaly=21 cm in the craniocaudal dimension, gall-blader bed minimally soaked, v.s. as a consequence of residual inflammatory (reactive) changes. Pancreas, kidneys, adrenal glands, bowel loops and peritoneal cavity were without pathologic accumulation of radiofarmacum, lymphadenitis mesenterialis and enlarged spleen to 15 cm in the axial dimension were presented, without finding of osteodestruction. Examinations for cardiotropic viruses (coxsackie, echovirus) were negative. The diagnosis was acute cholecystitis of secondary etiology with disposable sonographic capture of gallstone and acute pericarditis during Chlamydia pneumoniae infection. After two weeks of hospitalization at the surgical ward patient was transferred at the pediatric ward, where was recorded a decrease of liver enzymes to physiological levels and CRP to 28,3 mg/l. Serological tests for Chlamydia pneumonie infection were without significant changes. Patient was discharged in clinically stable condition.

## DISCUSSION

Chlamydia pneumoniae as a member of the Chlamydiaceae family, is a major causative agent for pulmonary infection. On top of the well – described respiratory diseases at the respective primary infection sites, Chlamydia are known to migrate and cause pathologies at remote sites of a host (Cheok *et al.* 2020; https://www.ncbi.nlm.nih.gov/books/NBK560874/).

Our submitted case report informs about an uncommon infectious reason of acute right upper quadrant abdominal pain, which was concluded as one of the symptoms of acute cholecystitis. We believe the cause of acute cholecystitis, as well as the cause of acute pericarditis, was hematogenous /lymphogenous routes of systemic dissemination of Chlamydia pneumoniae infection. Therefore, the clinical condition began to improve only after the start of treatment of Chlamydia pneumoniae infection and no surgical intervention was required for acute cholecystitis, which was secondary etiology. After the treatment by an antibiotic active against C. pneumoniae (Ciprofloxacin) the clinical, laboratory and sonographic signs of acute cholecystitis were disappeared, at the control echocardiography remained minimal pericardial effusion, the repeated serodynamics of Chlamydia pneumoniae infection was without significant changes. The disposable capture of gallstone in gallbladder was probably associated with elevated bile lithogenicity after prolonged fasting and receiving total parenteral nutrition. Similar cases (an organ expression of the acute Chlamydia pneumoniae infection) are very rarely described in the literature. This bacterium most frequently attacks the respiratory tract but in humans may also less frequent cause organic acute extra-respiratory complications such as reactive arthritis, neurological diseases (meningitis, encephalitis, Guillian –Barré syndrome), cardiovascular diseases (acute pericarditis, myocarditis or endocarditis)or can present as fever alone (Gaillat 1996; Rýzlová *et al.* 2008). Seroepidemiology studies have been shown an association with coronary artery disease and the atherosclerosis process. In addition, C. pneumoniae infection may contribute to a range of inflammatory diseases including asthma and lung cancer. Dissemination of C. pneumoniae from the lung throughout the body can possibly lead to atherosclerosis, arthritis and neurological diseases (Alzheimer´s disease, multiple sclerosis, schizophrenia). Some evidence suggests that C. pneumoniae may also be associated with primary biliary cirrhosis, type-2 diabetes and Behcet´s disease (Porritt *et al.* 2016). The medicine of choice is always long-term antibiotic therapy - macrolides, fluoroquinolones, tetracyclines (Gaillat 1996; Rýzlová *et al.* 2008). Centers for Disease Control and Prevention (CDC) recommends, if C. pneumoniae is diagnosed, Azithromycin (500 mg as a loading dose on day 1 and 250 mg maintenance dose for 4 days daily) is given. Tetracycline, Clarithomycin, Doxycycline or respiratory fluoroquinolones can be used as alternatives (https://www.ncbi.nlm.nih.gov/books/NBK560874/). Our case report points to association of C. pneumoniae seropositivity with acute cholecystitis and acute pericarditis, although there was a positive correlation with disease severity.

Additionally, we consider for necessary to include in differential diagnosis of recurrent attacks of fever accompanied by serositis (pleuritis-pleural effusion, pericarditis-pericardial effusion, peritonitis-ascites) that causes the clinical symptoms and by elevated of acute inflammatory markers without proven origo the diagnosis of familial Mediterranean fever (FMF). FMF is the most prevalent genetically determined autoinflammmatory disease, which significantly decreases the quality of life and limits life expectancy due to the development of amyloidosis in affected individuals and which diffuse or localized abdominal pain often mimicking acute abdomen. Hepatobiliary manifestation of FMF may include hepatomegaly, idiopathic liver cirrhosis, nonalcoholic steatohepatitis and cholecystolithiasis (Havlíčková *et al.* 2018; https://www.orpha.net/consor/www/cgi-bin/OC_Exp.php?lng=EN&Expert=342).

Acute acalculous cholecystitis is treated conservative with antibiotics, intravenous fluids and also bowel rest is recommended. Cholecystectomy is indicated if there is progressive clinical deterioration or persistent tender mass and/or increasing gallbladder distention on ultrasound (Shein *et al.* 2011). Our patient´s symptoms improved with an administration of antibiotic active against C. pneumoniae. No surgical intervention was needed. Repeated laboratory tests and ultrasound did not show any signs of cholecystitis at 6-week follow-up.

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