

## Triple Whammy of Acute Pancreatitis Chronic Liver Disease and Infective Endocarditis in a Young Male

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### **Abstract:**

**Objective:** We wish to present an interesting case of a young male who is a chronic alcoholic who presented with abdominal pain to our outpatient department. In this case patient had liver cirrhosis with acute pancreatitis complicated by infective endocarditis.

**Design:** He had clinical, laboratory and radiological features of acute pancreatitis and chronic liver disease at time of admission.

**Results:** He was treated and discharged. He came back with high grade fever and hypotension. A repeat CT scan of abdomen showed sequelae of acute pancreatitis including developing pseudocyst. As he continued to have high grade fever despite antibiotics an echocardiogram was done which was suggestive of severe mitral regurgitation with vegetation on the mitral valve. Patient received treatment for same.

**Conclusion:** This association of three diseases in a single patient was unusual and highlights the importance of suspecting other causes of fever.

**Keywords:** acute pancreatitis, chronic liver disease, infective endocarditis, pseudocyst of pancreas.

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### **I. Introduction**

While acute pancreatitis is a common and serious medical emergency mainly caused by alcohol, it is unusual to see patients with chronic liver disease caused by same aetiology, and also to have infective endocarditis of the native valve in the same setting.

### **II. Methods**

A young male patient aged 37 years presented to outpatient department with history of abdominal pain and jaundice of 3 days duration in January 2015. Patient consumed alcohol every day. Pain was epigastric in location with radiation to back suggestive of the pain of acute pancreatitis. He was admitted to ICU for further management. All routine blood investigations were ordered.

### **III. Results**

At admission haemoglobin was 13.2mg/dl, total blood count was 19,100 cells/cu mm with neutrophil response. Liver Function Test showed elevated liver enzymes with serum bilirubin being 2.5 mg/dl. Alkaline phosphatase was also high being 352 U/L. Platelet was 3,63,000/cu mm. Amylase was 129 U/L and Lipase was 1159 U/L which was above normal values of our lab.

Ultrasound of abdomen was suggestive of bulky pancreas with cholelithiasis. The liver was enlarged and fatty with splenomegaly. With the above information, a diagnosis of acute pancreatitis with a possibility of chronic liver disease was made. A CT scan of abdomen was done after three days of admission which was suggestive of acute pancreatitis with fluid collections, hepatomegaly with fatty infiltration, splenomegaly, cholelithiasis, minimal ascites and left pleural effusion. The common bile duct was normal.

Patient gradually improved and began to take food orally. He was shifted out of ICU. After a week patient was discharged in stable condition. Patient was advised to undergo MRI and MRCP to evaluate the pancreatic duct and common bile duct in detail. He was lost to follow up. Four weeks later patient got admitted with high grade fever and hypotension in the department of medicine. Investigations revealed very high blood counts 30,600/cu mm. Platelet count was 110000/cu.mm. Prothrombin time was mildly prolonged. Peripheral blood picture was suggestive of mild normochromic anemia, with neutrophilic leucocytosis and mild thrombocytopenia. Amylase was 115U/L. Lipase was still elevated at 836 U/L. In view of high grade fever blood and urine culture was done. Blood cultures were negative even after 7 days. Patient was transferred back to gastroenterology department. He was looking ill and hence transferred to ICU. Treatment with broad spectrum antibiotics was started. CT abdomen done was suggestive of acute pancreatitis (CTSI 5) with pseudocyst formation, cholelithiasis, ascites, and features of chronic liver disease, splenomegaly, and minimal bilateral effusion.

Patient continued to have high grade fever despite the antibiotics. Blood and urine cultures were persistently negative. There was a clinical suspicion of infected pseudocyst which was however very small in size (measuring 2.2x2.3 cm).

Since there was no other focus of infection an echocardiogram was done to rule out infective endocarditis. This was suggestive of severe mitral regurgitation with eccentric jet vegetation on the posterior mitral leaflet with left atrium and right atrium dilated with severe tricuspid regurgitation and moderate pulmonary artery hypertension. (Fig 1) In view of this finding both cardiology and cardiothoracic surgery consult was taken and a combination of antibiotics was started and patient was in the hospital for nearly 2 months till his antibiotic course was completed. Patient improved and is still on follow up. He is being considered for mitral valve replacement at our centre after full work up.

#### **IV. Discussion and Literature Review**

This patient had a triad of chronic liver disease related to alcohol, acute pancreatitis and infective endocarditis at the time of treatment in our department. There was no history of drug abuse by the patient. There was no history of valvular heart disease. Central venous catheter was not used during the course of treatment.

Cirrhosis, which can be the final stage of any chronic liver disease, is a diffuse process characterized by fibrosis and conversion of normal architecture to structurally abnormal nodules. These “regenerative” nodules lack normal lobular organization and are surrounded by fibrous tissue. The process involves the whole liver and is essentially irreversible. (1)

Acute pancreatitis is best defined clinically by a patient presenting with two of the following criteria: (a) symptoms, such as epigastric pain, consistent with the disease; (b) a serum amylase or lipase greater than three times the upper limit of normal; or (c) radiologic imaging consistent with the diagnosis, usually using computed tomography (CT) or magnetic resonance imaging. (2)

Infective endocarditis (IE) is defined as an infection, usually bacterial, of the endocardial surface of the heart. Infective endocarditis affects primarily the cardiac valves, although in some cases, the septa between the chambers, the mural endocardium, or cardiovascular implantable electronic devices may be involved. (3)

Bacterial infections complicating liver disease is common and a leading cause of death. (4, 5, 6). Infective endocarditis is a serious disease with high mortality. In cirrhotics the mortality varies from 36 to 92%. IE complicating liver cirrhosis is infrequently reported. Only small case series are available. (4, 5, 6, 7, 8, 9, 10, 11, 12).

R J Wyke in an article published in Gut in 1987, looked at the etiology of infections complicating liver cirrhosis. The frequency of endocarditis among patients admitted to hospital with cirrhosis was about 0.34% compared with 0-1% of patients without cirrhosis. Non-rheumatic calcific aortic stenosis appears to be more common in patients with cirrhosis and may account for this valve being the most common site for infection. The types of organism responsible were different from those isolated from patients without cirrhosis, with more frequent isolation of enteric Gram-negative bacteria and pneumococci. Pneumococcal endocarditis occurred almost exclusively in patients who are alcoholic or cirrhotic and may be accompanied by pneumococcal pneumonia or meningitis. The mortality from infective endocarditis was found to be high and the diagnosis could easily be overlooked in a patient with decompensated liver disease. (13)

About 7000 cases per year of IE may be occurring in India. Most of the cases are seen in young people with rheumatic or congenital heart disease. Blood culture is usually negative. Immune suppression should lead us to suspect IE with unusual organisms especially with a negative culture. While the common organisms are Streptococcus and Staphylococcus rarer organisms include Coxiella, Legionella and Fungal Organisms. Poly microbial infections are seen in IV drug abusers.

Subramanian et al published a study in Indian J Med Science in 2010. 121 patients were studied. 116 had IE. Most had native valve endocarditis. Rheumatic Heart Disease was the common predisposing factor. Viridans Streptococci was the commonest bacteria isolated.

The clinician should suspect infective endocarditis when there is a triad of cardiac murmur, fever and splenomegaly. New changing cardiac murmur, Osler's nodes, splinter haemorrhages, petechiae and Janeway lesions may be seen in these patients. Embolism causing CNS manifestation like stroke, abscess, mycotic aneurysms, pulmonary embolism and lung infarction can also occur. Cardiac problems like purulent pericarditis, conduction defects, functional valvular stenosis, severe valve regurgitation and chordal rupture are described. Duke's Criteria is the time honoured criteria for diagnosis of IE. Positive blood cultures and vegetation on echo are needed. Before starting antibiotics under strict aseptic precautions blood for culture from 3 separate sites (10 ml from each site in a one hour period) should be taken.

**Culture may be negative due to :-**

- 1) Use of Antibiotics before taking culture.
- 2) Fastidious organisms.
- 3) Fungus (rare)

Echo cardiography is a valuable tool for diagnosing this condition. Oscillating intra-cardiac mass on valve, or device, or supporting device, or in the path of stream may be noted. Abscess and dehiscence of the valve may be seen. There may be new valvular regurgitation. Trans Esophageal Echocardiography (TEE) is a valuable test. (7)

In the study published in 2004 by Ron-Bin Hsu et al over a period of 7 years from 1995 to 2002 only 26 patients with liver cirrhosis and IE were identified. The inclusion criteria was a diagnosis of infective endocarditis and liver cirrhosis. The diagnosis of infective endocarditis was based on the Duke's criteria. Patient characteristics were reviewed. Infective endocarditis was categorised as community acquired or nosocomial. Bacteremia was considered nosocomial when clinical signs developed after 3 days or more of hospitalization.

In their study of the 26 patients, 18 were males and 8 were females. Mean age was 56 years (range, 43 to 87 years). Twenty patients had virus related liver disease (Hepatitis B, C). Rest of the cases were either alcoholic cirrhosis, primary biliary cirrhosis or cardiac cirrhosis. 5 of these patients had concurrent or previous malignancies. The potential source could not be identified in 16(62%) of patients. Of the 10 cases in which a cause was identified were as follows:-

1. Gastrointestinal bleeding in 2 patients
2. Central venous catheters in 2 patients
3. Haemodialysis in 2 patients
4. Spontaneous bacterial endocarditis, osteomyelitis, septic arthritis, Trans arterial embolization and percutaneous alcohol ablation for hepatocellular carcinoma.

Staphylococci and streptococci were the commonest organisms cultured in blood. Aortic valve was most involved {14 out of 26 patients (53.84%)}. Mitral valve involvement was seen in 8 out of 26 patients (30.76%). Tricuspid valve was involved in 2 out of 26 patients (7.69%). Both aortic and mitral valve was involved in 2 patients (7.69%). Systemic embolization to spleen was seen in 2 patients (7.69%) and to brain in 1 patient (3.84%). 13 out of 26 patients were in Child class A (50%), 4 out of 26 (15.38%) in Child class B and 9 out of 26 (34.61%) were in Child class C. The hospital outcome was poor with 27% patients dying due to sepsis and 1 patient died of ruptured HCC. (14)

In a study by Synder et al the incidence of IE was 0.34% as compared to 0.1% in patients without cirrhosis (8). Denton et al on the contrary found that 0.58% of patients with cirrhosis had IE as against 0.59% in patients without cirrhosis (15). IE in cirrhosis is uncommon and the clinical features are differ from those in patients without cirrhosis. (8, 9, 10, 11, 12). Bookbinder NA et al in published in 1973 identified alcoholism as an important but under emphasized factor predisposing to infective endocarditis. (10). Pearce et al in a study published in 1961 identified 12 patients with liver cirrhosis and infective endocarditis all of whom were alcoholic. Aortic valve was the most involved and Streptococcus species accounted for 50% of the infections. (12)

Vilde JL et al in their study in 2000 observed that streptococcus bovis was the organism in 7 out of 10 patients suggesting that gastrointestinal tract was the portal of entry. The common cause for cirrhosis was alcohol and aortic valve was the most affected valve. IE in cirrhosis was often a complication of diagnostic and therapeutic procedures. In 1994 McCashland TM et al published a study of 10 patients with infective endocarditis and liver cirrhosis in which there was a higher frequency of females and a greater likelihood of mitral valve involvement. In the same study S.aureus was isolated in 80% of patients. In the study of Ron-Bin Hsu et al published in 2004, of the 9 cases with staphylococcal infections, 5 resulted from percutaneous procedures including 2 patients due to central catheters, 2 in hemodialysis patients and 1 due to percutaneous ethanol injection.

Three studies published between 2001 to 2002 highlighted the growing incidence of methicillin resistant staphylococcus species in cirrhotics as we continue to perform more invasive procedures in these patients. (16, 17, 18)

Acute pancreatitis complicating chronic liver disease is not well described. In the American J of Obstetrics and Gynaecology in 2004 Julie S. Moldenhauer, MD et al published a review on acute pancreatitis complicating acute fatty liver of pregnancy. In the case of alcohol related pancreatitis and cirrhosis, whereas etiology is common for both diseases, it is distinctly unusual to see patients with both diseases in the same setting. In a study published in World J Gastroenterology in 2008 authors Luis Aparisi et al studied the possible association between chronic pancreatitis and cirrhosis related to alcohol alone. They concluded that though the etiology was same the evolution of these diseases was different. (19)

What could be the relation between acute pancreatitis, chronic liver disease and infective endocarditis?

An excellent review on Non-bacterial thrombotic endocarditis (NBTE) was published in European J Of Cardio-thoracic surgery in 2007 by Sanjay Asopa et al. NBTE is a disease characterized by the presence of vegetations on cardiac valves, which consist of fibrin and platelet aggregates and devoid of inflammation or bacteria. NBTE has increasingly been recognized as a condition associated with numerous diseases. It is a potentially life-threatening source of thromboembolism and is not very common. The echocardiographic features of NBTE and true IE vary. NBTE vegetations are typically small, <1 cm in diameter, broad based, irregular in shape with valve abscess and rupture being uncommon. In case of IE echo would show mobile mass, of variable size, localized on the atrial surface of the atrio-ventricular valves or aortic surface of aortic valve with valve abscess and rupture being common. (20)

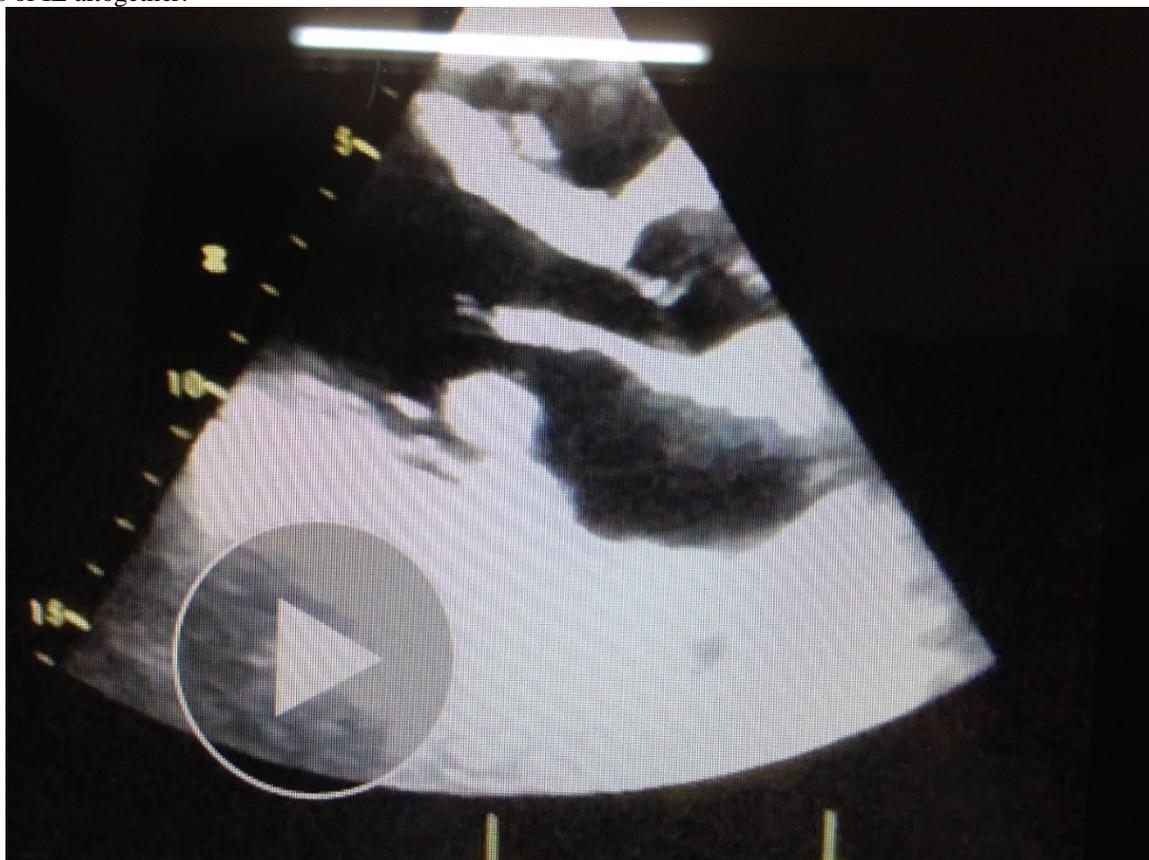
Few case reports were found on literature search using words Acute Pancreatitis and IE. In 1992 Andreas Stein et al published a report on *Eikenella corrodens* presenting as pancreatic abscess in Clinical Infectious Diseases. In 2007 Han L. et al reported a case with salmonella endocarditis and a large aortic root abscess, which presented as an acute pancreatitis in a 39-year-old male (21).

Ali Rıza Erbay et al in 2002 published a case report on *Brucella* endocarditis and pancreatitis in a 52-year-old male in the Turkish J of Infection. The diagnosis was made by clinical features, positive blood cultures, positive serology, and vegetation on the aortic valve, with high serum amylase and lipase level. Specific antimicrobial treatment for brucellosis was started and a surgical operation was planned; but the patient developed severe cardiac failure and died on the fifteenth day of his admission (22).

In our patient we feel that the underlying liver disease predisposed the patient to IE. The possibility of marantic endocarditis was considered since the blood cultures were repeatedly negative. However this could also be due to patient having received antibiotics before the diagnosis of IE was made. Future challenges include working the patient for valve replacement surgery and the possible complications of long term anticoagulation therapy in a patient with liver cirrhosis.

## V. Conclusion

Through this study we wish to highlight the importance of having a high index of suspicion in a patient with underlying chronic liver disease to diagnose IE which though not common, can have devastating effects on the patient. Once diagnosed it is challenging to treat these patients in view of cirrhosis. In this case study the fever could have been easily attributed to an infected fluid collection or pseudocyst infection while missing the diagnosis of IE altogether.



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