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CASE REPORT

Elevated liver enzymes and renal failure, with a surprising outcome. Two similar cases

A.E. Boendermaker[1], D. Boumans[2], R.A.A. van Zanten[2], H. Idzerda[3], H. van de Hout[4], Th.F. Veneman[1,2]

[1] Department of Intensive Care Medicine, Ziekenhuisgroep Twente, Almelo, The Netherlands

[2] Department of Internal Medicine, Ziekenhuisgroep Twente, Almelo, The Netherlands

[3] Department of Cardiology, Ziekenhuisgroep Twente, Almelo, The Netherlands

[4] Department of Radiology, Ziekenhuisgroep Twente, Almelo, The Netherlands

Correspondence

A.E. Boendermaker – e-mail: a.boendermaker@zgt.nl

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Introduction

The prevalence of elevated liver enzymes and acute renal failure is high and the differential diagnosis of both conditions, separately and combined, is extensive.[1-3] We present two cases of rapidly increasing liver enzymes in combination with (oliguric) renal failure with surprising outcomes. In both cases the medical condition was caused by cardiac tamponade with almost complete restoration of both renal and liver function after pericardiocentesis. Pericardial effusion can be a complication of numerous medical conditions, such as malignancies, trauma, metabolic disorders and infections.[4-6] In some cases, the accumulation of pericardial fluid results in cardiac tamponade with subsequent cardiogenic shock. This life-threatening condition can then lead to multiple organ dysfunction and, unless treated promptly, even to death.[7,8] Both described cases of cardiac tamponade underline the necessity of a thorough search for the underlying cause of elevated liver enzymes and acute renal failure.

Case A

A previously healthy 49-year-old man (patient A) was admitted to our intensive care unit (ICU) with signs of haemodynamic impairment, elevated liver enzymes and renal failure.

Several hours before admission to our ICU, the patient presented at the emergency department (ED) after an episode of transient loss of consciousness lasting a few seconds. His medical history was unremarkable. He complained of a slowly progressive cough with shortness of breath during exercise that he had had for a few months. During the few days prior to admission, he had experienced a sharp chest pain during coughing; this was accompanied by vomiting and a fever up to 38.5 ° Celsius. His general practitioner had prescribed amoxicillin under the clinical suspicion of pneumonia. Furthermore, his body weight had been stable and his appetite was unchanged. In addition, he admitted nicotine abuse estimated at approximately 25 pack years.

Physical examination performed by the ED resident showed a pale, slightly overweight man with a normal body temperature (37.2 ° C), a blood pressure of 90/67 mmHg with a heart rate 116 bpm, a respiratory rate of 30 breaths per minute and a peripheral oxygen saturation of 99% without additional oxygen. Heart sounds were normal and no murmurs or pericardial rub were heard. An expiratory wheeze and inspiratory crackles were noticed in the lower lung fields bilaterally. Examination of the abdomen was unremarkable. There were no signs of neurological pathology. Determination of jugular vein distention (JVD), Kussmaul's sign and pulsus paradoxus could at this point have directed towards obstructive cardiogenic shock. Unfortunately, none of these diagnostic tests were performed on admission.

Laboratory investigation revealed normocytic anaemia, acute renal failure, elevated liver enzymes and markers of inflammation (*table 1*). The chest X-ray (*figure 1*) showed a small consolidation of the left posterobasal segment of the lung, cardiac enlargement (cor thorax ratio (CTR) of 0.59) and loss of the aortopulmonary window. The electrocardiogram (ECG) showed a sinus rhythm

Table 1. Laboratory data from case A

Case A	Units	At admission ED 06-11-2011	At admission ICU 07-11-2011	22 days after admission 29-11-2011
Haemoglobin	mmol/L	7.4	6.8	7.8
C-reactive protein	mg/L	186	190	22
Leucocyte count	*10^9/L	15.9	17.5	9.5
Bilirubin total	µmol/l	22	19	5
Alkaline phosphatase	U/L	108	112	116
Gamma GT	U/L	91	88	40
ASAT	U/L	1.568	2.871	10
ALAT	U/L	2.496	3.968	27
Lactate dehydrogenase	U/L	3.607	4.749	184
Creatinine	µmol/l	184	248	95
Urea	mmol/L	20	26	8.3
Estimated GFR	mL/min	34	24	73

Figure 1. Case A, Posteroanterior and lateral chest X-ray showing a small consolidation of the left posterobasal segment of the lung, cardiac enlargement and loss of the aortopulmonary window

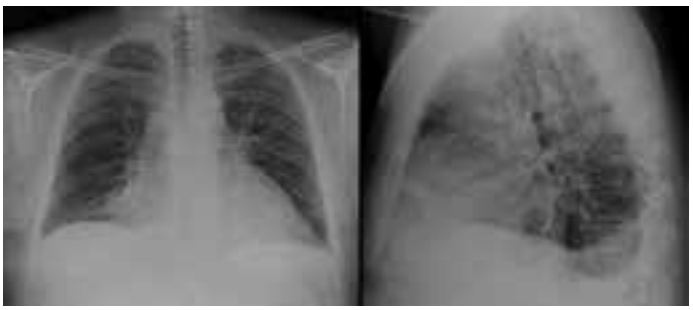
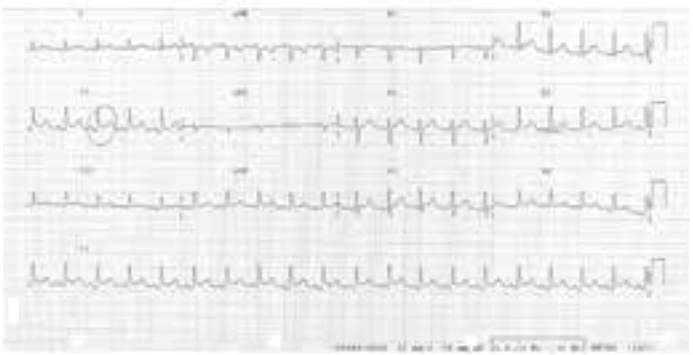


Figure 2. ECG Case A



without microvoltages or electrical alternans, and abnormal concavely elevated ST-segments in V3-V6, II, III and a VF with slight depression of the PRa-interval (*figure 2*).

Patient A was admitted to the internal medicine ward with the preliminary diagnosis of a severe sepsis with signs of organ failure due to a community acquired pneumonia of the left lung. He was treated accordingly with fluid resuscitation and broad-spectrum antibiotics. Despite all efforts the patient's condition deteriorated. Twelve hours after admission he was transferred to the ICU because of refractory hypotension (95/60 mmHg), signs of tissue hypoxia and progressive multiple organ dysfunction expressed by a marked increase of liver enzymes and progressive oliguric renal failure (*table 1*).

The JVD was elevated and heart sounds were muffled. Intra-arterial blood pressure measurement showed a pulsus paradoxus. Abdominal ultrasound showed venous congestion within the portal vein, inferior vena cava and liver veins, with normal directions of blood flow, and a thickened gall bladder wall. The transthoracic echocardiogram revealed a normal left ventricular ejection fraction and a tricuspid aortic valve with normal morphology and function. It showed circular pericardial effusion of apical 3.5 cm and of 4.4 cm at the right ventricle with a swinging heart. There were paradoxal septal movements and compression of the right atrium consistent with pericardial tamponade. An emergency pericardial drainage was performed. Within 15 minutes after pericardial drainage, the patient's haemodynamic parameters improved and stabilized. In the following 12 hours, approximately 900 cc of sanguinolent pericardial fluid was drained. During the next few days, the liver enzymes, renal function and diuresis gradually improved (*table 1*).

Pathologic investigation of the pericardial fluid revealed the presence of atypical cells, suspicious for metastases of adenocarinoma. The subsequent diagnostic work-up included a CT-scan of the abdomen and chest, and a bronchoscopy with lavage and biopsies. These studies confirmed the diagnosis of a cT1aN3M1a, stage IV adenocarcinoma of the lung without hepatic metastases. Treatment with palliative chemotherapy was initiated.

Case B

A 61-year-old man (patient B) presented at the ED with rapidly developing shortness of breath, a non-productive cough and peripheral oedema. His medical history revealed a viral pericarditis 12 years previously, a stent-graft reconstruction of the abdominal aorta 11 years previously, type 2 diabetes and chronic kidney disease stage III related to diabetic nephropathy. In addition, he admitted nicotine abuse estimated at approximately 15 pack years.

Physical examination showed a dyspnoeic patient with a respiratory rate of 24 breaths per minute and peripheral oxygen saturation of 96 % while breathing room air. The patient's blood pressure was 107/73 mmHg with a heart rate of 80 bpm and the body temperature was normal (36 °C). Chest auscultation revealed normal heart sounds without a heart murmur or pericardial rub, and mild to moderate bilateral inspiratory crackles. Furthermore, pitting oedema was seen in both legs. The presence of an increased JVD or a pulsus paradoxus was not tested.

Laboratory investigation at admission showed an acute on chronic renal failure, normocytic anaemia and elevated C-reactive protein (CRP) and NT-proBNP (*table 2*). The chest X-ray revealed a right sided retrocardial consolidation suggestive of pneumonia without significant cardiac enlargement (CTR of 0.50) (*figure 3*). The ECG showed a sinus rhythm with flattened ST-segments inferolateral and criteria for microvoltages were approximated but not met (*figure 4*).

Table 2. Laboratory data from case B

Case B	Units	At admission ED 05-12-2011	At admission CCU 07-12-2011	5 days after admission 12-12-2011
Haemoglobin	mmol/L	7.1	6.4	6.3
C-reactive protein	mg/L	56	67	51
Leucocyte count	*10^9/L	8	8.3	7.9
Bilirubin total	µmol/l	9	11	16
Alkaline phosphatase	U/L	146	-	125
Gamma GT	U/L	81	117	77
ASAT	U/L	32	3.802	61
ALAT	U/L	33	2.449	396
Lactate dehydrogenase	U/L	258	3.161	239
Creatinine	µmol/l	216	353	112
Urea	mmol/L	13.7	25.4	7.5
Estimated GFR	mL/min	27	15	58
NT-proBNP	pmol/L	85	110	110

Figure 3. Case B, Posteroanterior and lateral chest X-ray showing a right sided retrocardial consolidation suggestive of a pneumonia without significant cardiac enlargement

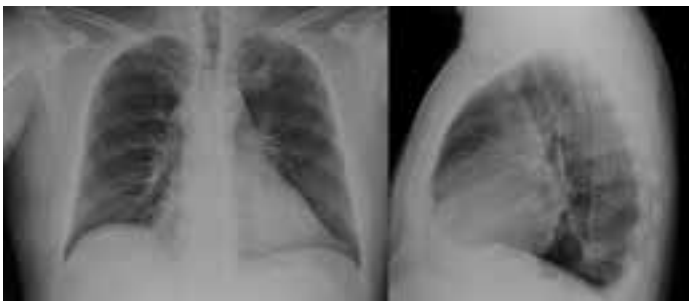
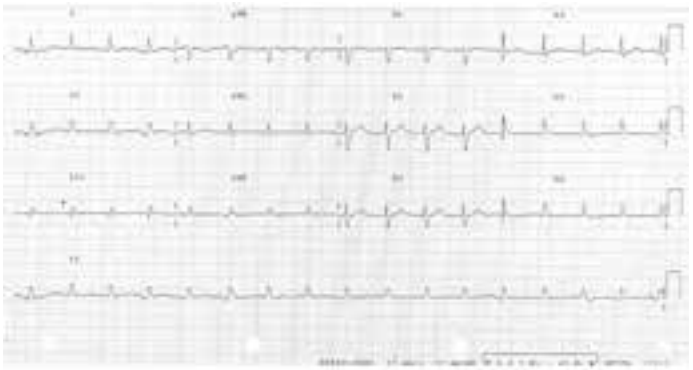


Figure 4. ECG Case B



The preliminary diagnosis was a community acquired pneumonia combined with right and left sided cardiac decompensation in presence of a previously unknown history of heart failure. Treatment was started accordingly with amoxicillin and intravenous administration of furosemide.

The next day patient B became hypotensive and oliguric. Furosemide infusion was ceased and intravenous volume resuscitation was initiated. As a result, the blood pressure gradually normalized but despite this the patient's condition deteriorated. Physical re-examination revealed increased bilateral lung crackles and peripheral oedema and elevated JVD, suggesting progressive heart failure for which furosemide infusion was restarted at a higher dose. During the next few hours, the patient became anuric, hypotensive and his respiratory distress progressed. Laboratory investigation showed a metabolic acidosis with respiratory compensation, dramatically increased parenchymal liver enzymes, further decrease in renal function and stable CRP (*table 2*). The chest X-ray (bed-side anterior posterior projection) now showed enlargement of the cardiac silhouette and the ECG remained unchanged. The patient was transferred to the Cardiac Care Unit (CCU).

Emergency transthoracic echocardiography had limited visualization, but showed a normal left ventricular ejection fraction and circular pericardial effusion, apical of 3.2 cm and of 3.1 cm over the right ventricle. Paradoxal septal movement was seen in combination with compression of the right atrium consistent with pericardial tamponade. An emergency pericardial drainage was performed. After drainage of a total 800 ml serosangulent pericardial fluid, the patient stabilized haemodynamically. During the next few days, his liver enzymes and renal function and diuresis improved gradually. Pathologic investigation of the pericardial fluid revealed the presence of adenocarcinoma-cells suspicious for metastases originating in the lung. CT-scan of the thorax and abdomen revealed a small mass in the apex of the left lung and bilateral pleural effusion. Thoracocentesis was performed showing malignant cells as well. This confirmed the diagnosis of adenocarcinoma of the lung with carcinomatous pericarditis and pleuritis (stage IV disease). Due to several complications in the course of the disease, palliative chemotherapy could not be initiated and the patient died four months later.

Discussion

The most common disease of the pericardium is acute pericarditis.[4-6] Major manifestations are a typical sharp retrosternal chest pain that is position dependent and intensifies on inspiration, a pericardial friction rub, typical ECG changes and pericardial effusion (PE). PE can also found by chance in asymptomatic patients during echocardiography. As a result of inflammation of the pericardium, PE can develop after an acute myocardial infarction, cardiac surgery, or as a consequence of autoimmune disease, trauma, metabolic disorders, infection and malignancies. Most cases are presumed to have a viral or autoimmune aetiology and follow a benign course.[4-6] PE can lead to impairment of cardiac function and tamponade as a rare complication.[7-8] Cardiac tamponade with subsequent obstructive cardiogenic shock, leading to hepatocellular damage and renal dysfunction, amongst other signs of end organ dysfunction, occurs in approximately 2 out of 10,000 people per year.[5]

Both pericarditis and cardiac tamponade are clinical diagnoses. They can, however, be supported by the results of additional diagnostics.[4,6,8,10] As the pericardial sac is filled with excessive fluid a compressive pericardial syndrome occurs, in which especially right ventricular filling pressures are increased, diastolic filling of the heart is reduced, and the interventricular septum deviates towards the left ventricle impairing cardiac output.[7-8,10] The septum deviation causes a pulsus paradoxus, in which the physiologic decrease in systolic blood pressure and pulse wave amplitude during inspiration become abnormally large.[7-8,11] Rapid accumulation of PE leads to Beck's triad of systolic hypotension, increased JVD and muffled heart sounds. The presence of Kussmaul's sign, which is the paradoxically increased distension of the jugular vein at inspiration, is difficult to determine and commonly only present in tamponade when a constrictive disease exists.[4-8]

PE can be suspected on a chest X-ray and by changes in the ECG. An enlarged cardiac silhouette, especially with loss of the aortopulmonary window supports any suspicion of PE with more than 200 mL of fluid. The ECG can show the following abnormalities divided into 4 stages based upon progression of pericarditis: diffuse concavely elevated or flattened ST-segment deviations or diffuse

T-wave inversions, PR-depression, and microvoltages with or without electrical alternans, due to PE.[7-8] Echocardiography is a simple, reliable, non-invasive and commonly used modality in the standard work-up of PE.[10]

In both patients described here, cardiac tamponade due to malignant pericarditis was the first presentation of disseminated lung cancer. An estimated four to seven percent of patients with pericarditis without known malignancy are ultimately diagnosed with malignant pericarditis (MP) as first presentation. In patients with a known malignancy, pericardial involvement occurs in one to twenty percent. The incidence of MP is the highest in lung carcinoma, followed by carcinoma of the breast, oesophagus, melanoma and lymphoma.[5-6,9]

Multi organ dysfunction expressed by acute kidney failure and elevated parenchymal liver enzymes preceded (refractory) haemodynamic instability in both cases. Circulatory shock in definition is haemodynamic failure to provide oxygen for end organ aerobic function. Three major phenomena of shock are hypotension, tachycardia and signs of end organ dysfunction. Due to compensatory mechanisms, hypotension can be a late sign of ongoing shock, as it was in our patients.[7,11]

The presence of acute renal failure in general is related to hypoperfusion, the so-called pre-renal kidney failure. This is generally due to hypotension or decreased cardiac output as a consequence of hypovolaemia, sepsis, cardiac failure or vasodilatation.[1,11] In both cases, the gradual improvement of kidney function after pericardiocentesis supports the hypothesis that the cause was directly related to renal hypoperfusion as a result of the cardiac tamponade.[1,7,11]

Pericardial effusion as the cause of acute renal failure is uncommon. The literature is limited to only several case reports.[12-14] Cardiac tamponade as a cause of the combination of acute renal failure and elevated liver enzymes, as in our patients, is also a rare finding.[14]

Increased liver enzymes can be caused by viral, toxic, or ischemic hepatitis. Hypoperfusion of the liver results in ischemia with hepatocellular damage which can be detected by a rapid rise in serum aminotransferase levels associated with an early massive rise in lactate dehydrogenase (LDH). Generally, the serum bilirubin level and phosphatase levels rise far less and hepatic synthetic function usually remains normal or is only mildly impaired.[2-3] Without ongoing haemodynamic instability, the biochemical markers usually return to normal. In addition to hypoperfusion of the liver, congestion of blood (congestive hepatopathy) due to heart failure or obstruction of heart function, can play a role in the aetiology of the elevated liver enzymes.[2-3,14]

Different causes of the elevated liver enzymes, hepatic ischemia or congestive hepatopathy, could possibly explain the difference in elevation of serum aminotransferase levels and ASAT/ALAT ratio between patients A and B. Also, a combination of both conditions, with a different contribution of each cause, is possible in these patients. However, laboratory findings in both patients are highly suggestive of an ischemic cause since congestive hepatopathy is most commonly characterized by marked elevation of cholestatic liver enzymes and much lower levels of aminotransferase.[2-3]

When PE has been confirmed, a subsequent diagnostic and therapeutic pericardiocentesis can be performed either blinded or by means of ECG, echocardiographic, CT or fluoroscopic guidance.[4-7,10] In cases of cardiac tamponade, pericardiocentesis is instantly required to prevent further life-threatening complications and even death.[4-7] In patients with suspected malignancy, tuberculosis or purulent pericarditis, a pericardiocentesis should be performed as diagnostic measure, due to the necessity of specific therapy.[4-7]

In the cases described here, the initial evaluation and additional investigation either did not point directly to, or were not recognized as signs of the presence of pericardial effusion with cardiac tamponade. Both patients were initially considered to be suffering from hypoperfusion of the liver and kidneys due to severe pulmonary sepsis. However, in retrospect, misinterpretation of physical signs and additional diagnostics (ECG, chest X-ray and laboratory investigation) lead to the incorrect diagnosis on admission and eventually delayed the diagnosis of cardiac tamponade. This underlines the need for more awareness of PE as a cause of haemodynamic instability.

In conclusion, we have described two rare cases in which the presence of acute renal failure and elevated liver enzymes are the result of PE with cardiac tamponade as a consequence of underlying malignant disease. Simultaneous development of kidney and liver failure should increase the suspicion of the presence of shock.[1-3,11] Moreover, more rare forms of shock should be considered and sought for. Awareness amongst clinicians that signs of end organ dysfunction can precede haemodynamic shock, due to compensatory mechanisms, is necessary for prompt treatment of the underlying cause.

References

1. Lameire N, Van Biesen W, Vanholder R. Acute renal failure. Lancet. 2005;365(9457):417-30.
2. Birrer R, Takuda Y, Takara T. Hypoxic hepatopathy: pathophysiology and prognosis. Intern Med. 2007;46(14):1063.
3. Henrion J, Schapira M, Luwaert R, Colin L, Delannoy A, Heller FR, Hypoxic hepatitis: Clinical and hemodynamic study in 142 consecutive cases. Medicine 2003; 82(6):392-406
4. Sagristà-Sauleda J, Sarrias Mercé A, Soler-Soler J. Diagnosis and management of pericardial effusion. World J Cardiol 2011; 3(5): 35-143
5. Jacob R, Grimm RA. Pericardial disease. Carvey WD ed. Cleveland Clinic: Current clinical medicine. 1st ed. Philadelphia, Saunders Elsevier, 2008, chap 2
6. Imazio M, Trinchero R. Triage and management of acute pericarditis. Int J Cardiol 2007; 118 (3): 286-94.
7. Spodick DH, Acute cardiac tamponade, N Engl J Med 2003; 349:684-90
8. Roy CL, Minor MA, Brookhart MA, Choudhry NK, Does this patient with a pericardial effusion have cardiac tamponade? JAMA, 2007;297 (16): 1810-1818
9. Lestuzzi C. Neoplastic pericardial disease: Old and current strategies for diagnosis and management. World J Cardiol 2010; 2(9): 270-279
10. Merce J, Sagrista-Sauleda J, Permanyer-Miralda G, Evangelista A, Soler-Soler J. Correlation between clinical and doppler echocardiographic findings in patients with moderate and large pericardial effusion: implications for the diagnosis of cardiac tamponade. Am Heart J 1999;138: 759-764.
11. Abboud, FM. Pathophysiology of hypotension and shock. In: Hurst, JW (Ed), The heart, New York, McGraw-Hill, 1982. p. 452
12. Saklayen M, Anne VV, Lapuz M. Pericardial effusion leading to acute renal failure: two case reports and discussion of pathophysiology. Am J Kidney Dis 2002;40: 837-841
13. Gluck N, Fried M, Porat R, Acute renal failure as the presenting symptom of pericardial effusion, Intern Med 2011; 50:719-721
14. Khan R, Gessert C, Bockhold S, Pericardial effusion presenting with anuric acute renal failure and hepatocellular damage, J Hosp Med 2009;4:68-70