

## CLINICAL PROBLEM SOLVING

# A woman with abdominal symptoms, hyperdynamic shock and ARDS

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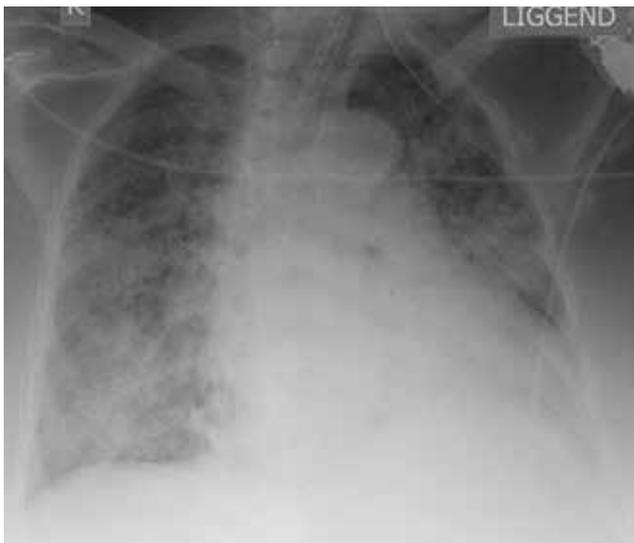
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A 73-year-old woman presented with a general feeling of discomfort. She called an ambulance herself, which brought her to the emergency department. This Afro-Surinam woman was previously seen in this hospital with morbid overweight (BMI 51), hypertension and both right- and left-sided heart failure. She had previously been diagnosed with gastric ulcer disease and Bell's palsy. Eight years before she had undergone a laparoscopic cholecystectomy. Her Pickwick syndrome was the cause of limited chronic hypercapnia. In the last two weeks, she became progressively tired with nausea, vomiting and diarrhoea. She complained of headache and pain in her chest, back and abdomen during the last week, with progressive intensity. On physical examination the vital signs were: respiratory rate 20-24/min, arterial blood pressure 100/60 mmHg, heart rate 130/min, O<sub>2</sub> saturation 91% and core temperature 38.2°C. Physical examination did not reveal any disturbances except her overweight. Skin and acra did not show any abnormalities.

Her most recent medication at home was: furosemide 20 mg once daily, amlodipine 5 mg once daily, metoprolol 100 mg once daily, pantoprazole 40 mg once daily, aliskiren 150 mg once daily.

The laboratory results showed a haemoglobin level of 8.2 mmol/l, the leucocyte count was  $16.7 \times 10^9/l$  (74% neutrophils, 18% lymphocytes, 0.5% eosinophils), the thrombocytes count was  $388 \times 10^9/l$ , the PTT 12 seconds and the APTT 27 seconds. The serum sodium was 126 mmol/l, potassium 3.7 mmol/l, creatinine 94 µmol/l, eGFR 60 ml/min, creatine kinase 49 U/l, albumin 23 g/dl, ALAT 41 U/l, blood glucose 16 mmol/l, troponin T 0.035 µg/l and the CRP 133 mg/l. The ECG showed a sinus tachycardia (140/min), an intermediate axis and negative T in aVL and I. The chest X-ray showed an enlarged heart and signs of congestion. A pulmonary infiltrate could not be excluded (*figure 1*).

She was admitted to the ICU with a preliminary diagnosis of sepsis of unknown origin. She became progressively dyspnoeic. On admission the blood gases were repeated and showed pH 7.37, PaCO<sub>2</sub> 47 mmHg, PaO<sub>2</sub> 49 mmHg, bicarbonate 26.6 mmol/l, base excess 1.4, and O<sub>2</sub> saturation 79%. The sodium was now 127 mmol/l. Her blood pressure progressively dropped to 65/26 mmHg. A deep venous line was inserted and noradrenalin was started together with fluids. She was intubated and mechanically ventilated.



**Figure 1.** Chest X-ray on admission to the ICU

The symptoms and signs of this patient are unspecific and can be present in many diseases. However, the nausea and vomiting may point to an abdominal cause. This is combined with hypoxic respiratory failure and hypotension. Respiratory failure and hypotension are suggestive of severe sepsis or septic shock. The two major causes that I would consider are sepsis with an abdominal source (intra-abdominal sepsis) and pneumococcal sepsis. Intra-abdominal sepsis can be caused by a primary or secondary peritonitis. As this patient did not have liver cirrhosis with ascites, it is highly unlikely that primary peritonitis is present. Secondary peritonitis due to perforation of the digestive tract cannot be ruled out, although the absence of peritoneal pain on physical examination makes this unlikely. Pneumococcal bacteraemia with sepsis is known for its abdominal symptoms and can even present with peritonitis. Several laparotomies are performed every year which later appear to be unnecessary because the abdominal pain was

a symptom of pneumococcal sepsis. Many other diagnoses presenting with abdominal signs must be in our differential, including gastroenteritis and bowel ischaemia. The presentation of bowel ischaemia lacks specific symptoms. Most patients with an ischaemic bowel suffer from abdominal pain that may be low grade but peritonitis may be present when perforation has occurred or is nearby. The other abdominal symptoms that this patient also presents can be found in case of bowel ischaemia.

At this moment intra-abdominal sepsis with or without bowel ischaemia was the diagnosis made by the attending physicians. It was treated with the antibiotics ciprofloxacin, cefotaxime and metronidazole. A CT scan of the abdomen was performed (figure 2). The CT scan showed an increased thickness of the small bowel in the right lower quadrant (figure 2a). Air is seen in branches of the superior mesenteric vein (figure 2b). Pneumatosis and free abdominal air is absent. The superior mesenteric artery shows an origin stenosis but all arteries appear to be filled with contrast. The proximal small bowel and stomach show stasis. An abdominal herniation is seen without incarceration. In addition, a status after cholecystectomy with air in the common bile duct and diverticulosis coli are seen. Based on these findings a laparoscopy was performed. Neither ischaemia nor perforation were found. Surgical inspection of the small bowel showed no abnormalities on the serosa side. Intensified haemodynamic monitoring was started. A pulse contour continuous cardiac output measurement (using PiCCO) showed a cardiac index of 5.1 l/min, the Extra Vascular Lung Water Index was 5.8 ml/kg and the Intra Thoracic Blood Volume Index 788 ml/m<sup>2</sup>. Transthoracic echocardiography showed a hyperdynamic left ventricle but no other abnormalities.



**Figure 2a.** CT scan of the abdomen on the day of admission to the ICU. Arrow points out to thickened small bowel loops



**Figure 2b.** CT scan of the abdomen on the day of admission to the ICU. Arrow points out to air in branches of the superior mesenteric vein

At this stage, peritonitis was excluded by laparoscopy. The diagnosis of full thickness bowel ischaemia was unlikely but mucosal ischaemia may still be present. However, mucosal ischaemia does not lead to multiple organ failure. The multiple organ failure of this patient consisted of respiratory and circulatory failure. The circulatory parameters and cardiac ultrasonography show a hyperdynamic circulation congruent with sepsis. The associated multiple organ failure and persistent hypotension are usually signs of septic shock. The nature of the septic shock is, however, still unknown. The presumed pneumococcal sepsis is still a possibility as well as gastroenteritis. Several other uncommon systemic diseases cannot be ruled out at this time point, such as haematological disease, autoimmune disease and infections such as tuberculosis. Her afro-Surinam background may predispose for diseases such as sarcoidosis and less common infectious diseases such as histoplasmosis and mycobacteria. A HIV test would be informative at this point as the accompanying immunodeficiency may predispose for these and other opportunistic infections. In particular, Cytomegalovirus (CMV) and Herpes infections can induce an interstitial pulmonary infection with chest X-ray findings as seen in this patient.

The next day she still did not pass any stools, which more or less rules out gastroenteritis. The circulation parameters were: blood pressure 124/54 mmHg with noradrenalin dose 0.06 µg/kg/min; the heart rate was a sinus tachycardia of 127/min. In the laboratory results the leucocytes rose to 19 x 10<sup>9</sup>/l and CRP to 150 mg/l. The sodium normalised to 134 mmol/l. The cardiac enzymes were not raised and the ECG normalised. A



**Figure 3.** Chest X-ray on the third day of ICU treatment

gastroscopy was performed and showed a vulnerable gastric mucosa without ulcers. There were no signs of ischaemia but a remarkable nodular pattern of the stomach was seen. Biopsies were not taken. Three days after presentation, the chest X-ray showed progressive alveolar infiltration in the lungs (*figure 3*). The tracheal aspirate was progressively bloody. The blood gas analyses showed a PaO<sub>2</sub> of 76 mmHg with 50% FiO<sub>2</sub>. The PaO<sub>2</sub>/FiO<sub>2</sub> ratio dropped progressively to 125. Mechanical ventilation was set at CPAP 20 mbar above 10 mbar PEEP. The cumulative fluid balance was +14 litres at that moment. The creatinine was unchanged at around 95 µmol/l. HIV test was negative. The ANCA and ANA were negative. The blood cultures, although taken before the administration of antibiotics, were also still negative. Because of progressive pulmonary infiltrates and persistent shock she was additionally treated with prednisone (20 mg twice daily).

A diagnostic procedure was performed.

The clinical picture has shifted from an abdominal symptomatology towards pulmonary dysfunction with bloody aspirates, progressive infiltration and adult respiratory distress syndrome (ARDS). The septic profile persists with deterioration of hypoxic respiratory failure. No renal involvement was seen. The previously mentioned diagnosis of pneumococcal sepsis is less likely when renal involvement does not develop and with negative blood cultures. The results of the chest X-ray follow-up and PaO<sub>2</sub>/FiO<sub>2</sub> ratio are concordant with ARDS. The causes of ARDS are numerous (*table 1*). Primary ARDS because of pulmonary infection is common and the culture of tracheal aspirate or preferably bronchoalveolar lavage (BAL) may

**Table 1.** Causes of ARDS

Bacteraemia / sepsis
Trauma with or without pulmonary contusion
Fractures of long bones with fat emboli
Burns
Pancreatitis
Polytransfusion
Infection
Aspiration
Drug overdose
Near drowning
Postperfusion syndrome after cardiopulmonary bypass

provide a definite diagnosis. A secondary ARDS is often caused by infection at a distant location, such as the abdomen, but in this case is less likely based on previously given considerations. My thoughts are primary focused on a pulmonary infection with systemic inflammation and organ failure. Autoimmune disease is less likely with a negative ANCA and ANA test. The absence of eosinophilia in the blood rules out diseases such as eosinophilic pneumonia but cannot rule out disseminated parasitic infections such as *Strongyloidiasis*. The infection can be bacterial or opportunistic infection including *Pneumocystis jirovecii* pneumonia and parasites. *Pneumocystis* is unlikely as the HIV test is negative unless another lymphotropic virus such as human T-lymphotropic virus type I (HTLV-1) is present. Disseminated bacterial infection is usually accompanied with positive blood cultures and some degree of renal failure, which are both absent in this case. Viral causes for diffuse pulmonary infection, such as CMV and Herpes Simplex virus (HSV), may be present but cannot lead to multiple organ failure by themselves.

#### Clinical diagnosis

Disseminated infection with multiple organ failure, probably opportunistic.

A diagnostic BAL was performed. The BAL showed *Strongyloides* larvae in the Giemsa preparation (*figure 4*). In addition, the PCR for *Pneumocystis jirovecii* and CMV were also positive. No pathological studies of the gastric mucosa were performed.



**Figure 4.** *Strongyloides* larva in BAL fluid

Stool test using the Baermann technique found *Strongyloides stercoralis* larvae as well. No other parasites were found.

### Clinical diagnosis

Hyperinfection syndrome and disseminated Strongyloidiasis in combination with *Pneumocystis jirovecii* and CMV infection.

*Strongyloides stercoralis* is a roundworm that can have a life cycle within but also outside the human body. When *Strongyloides* larvae penetrate the skin and enter the human body, they transfer through the venous system to the pulmonary alveoli where they appear in the sputum. By coughing they reach the oral cavity. When the larvae are swallowed, they can grow and replicate in the small bowel. Larvae penetrate the bowel wall and will be excreted with the faeces. The diagnosis is usually made by a direct examination of a stool concentrate using the Baermann technique, which is based on the active movement of larvae from the stools into the water surrounding the stools. Immunoassay antibody detection has a sensitivity of around 90% but can cross-react with filaria or nematodes.

An acute infection results in a local skin reaction at the entry site. A chronic infection is usually asymptomatic, but can evolve into a hyperinfection syndrome and disseminated Strongyloidiasis. Patients at risk are those that are immune-compromised.<sup>[1]</sup> Usually this is the case with steroid treatment. However, HIV or HTLV infections can be a trigger as well. The symptoms and signs of this patient fully agree with the symptoms of hyperinfection syndrome and dissemination of the worm. The clinical presentation with sepsis can be caused by secondary bacterial or fungal infection. Due to massive infiltration of larvae in the gastrointestinal wall, bacteraemia or fungaemia can occur.<sup>[1]</sup> The gastrointestinal manifestations of hyperinfection are abdominal pain, nausea, vomiting, diarrhoea, ileus, bowel oedema and intestinal obstruction. In addition, mucosal ulceration of the digestive tract occurs. Massive haemorrhage and subsequent peritonitis or bacterial sepsis might complicate this situation. The pulmonary manifestations can be cough, wheezing, dyspnoea, hoarseness, haemoptysis and respiratory failure. The chest X-rays may show diffuse interstitial infiltrates or consolidation. Meningitis may occur. Enteropathy may lead to protein loss and hyponatraemia due to the syndrome of inappropriate anti-diuretic hormone secretion may be present. Interestingly, eosinophilia is usually absent in disseminated disease, maybe because these immune cells move from the systemic circulation to the local site of inflammation. Additional serological testing was positive for HTLV-1.

### HTLV-1 infection

Human T-lymphotropic virus type I (HTLV-1) is a lymphotropic virus that has a low prevalence in the Netherlands of around 1 per 40,000 inhabitants. HTLV-1 is pandemic with high prevalence rates in mid and South America and several African countries.

Most people are asymptomatic. However, HTLV-1 infection can cause uveitis, arthritis, myositis, alveolitis and dermatitis. It is associated with adult T-cell leukaemia/lymphoma, HTLV-I-associated myelopathy and Strongyloidiasis.

Immediately after the finding of *Strongyloides* in the BAL, treatment was started with ivermectin 18 mg daily.

The preferred treatment for disseminated Strongyloidiasis is ivermectin 200 µg/kg per day orally.<sup>[2,3]</sup> This treatment is usually well tolerated but rare cases of worsening after the start of treatment have been reported.<sup>[4]</sup> Therapy should be continued two weeks after the stools become negative for *Strongyloides* larvae. When oral treatment is impossible, for instance because of ileus, rectal treatment has been described or, experimentally, subcutaneous treatment can be tried. An alternative treatment is albendazole 400 mg twice daily, orally. In addition, immunosuppressive therapy should be discontinued as soon as possible.

After the start of ivermectin treatment and stopping prednisone, her clinical condition gradually improved. After 25 days she was extubated and discharged from the ICU after 28 days. The sputum became negative for *Strongyloides* after 18 days and the stools after 14 days. Further investigation of her haematological situation revealed a low-grade T-cell leukaemia or lymphoma, which are common which HTLV-1 infection.

### Disclosures

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