Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Correspondence

Human rhinovirus infection and cirrhosis: A potential fatal complication

Dear Editor,

A 39-year-old male patient was admitted to our hospital for fever, chest pain, altered mental status, and vomiting. Medical history included active alcoholic liver cirrhosis (Child Pugh B9, MELD 15). On initial examination Glasgow Coma Scale score was 11, body temperature was 38.2 °C, poor nutritional status was poor (body mass index 15.8) and ascites was present. Laboratory results showed: C-reactive protein (CRP) 106 mg/L, white blood cell count (WBC) 9.8 Giga/L (84% neutrophils), international normalised ratio (INR) 1.83, and total bilirubin 64 μmol/L. Blood gas analysis showed respiratory alkalosis (pH 7.55, $paCO_2$ 17 mmHg, HCO_3^- 15 mmol/L), without hypoxaemia (paO_2 109 mmHg). Brain computed tomography (CT) was normal, and chest X-rays showed diffuse alveolar pneumonia, mainly affecting the right lung.

Aspiration pneumonia with acute-on-chronic liver failure was suspected due to the vomiting and altered mental status, and antibiotic therapy with ceftriaxone and metronidazole was started in the Emergency Room, along with disaccharides. After an initial improvement, his respiratory status worsened 5 days later. Blood gas analysis showed compensated metabolic acidosis (pH 7.39, $paCO_2$ 19 mmHg, HCO_3^- 11 mmol/L) with hypoxaemia (paO_2 81 mmHg on 6 L/min oxygen). The WBC increased to 16.7 Giga/L (83% neutrophils). CRP value had initially improved and remained unchanged (31 mg/L). Chest CT (Fig. 1) showed an alveolar and interstitial infiltrate different from the initial images and led to a suspicion of opportunistic *Pneumocystis jirovecii* pulmonary infection. Human immunodeficiency virus testing was negative. Bronchoscopy with bronchoalveolar lavage (BAL) was performed: immunofluorescence assay and polymerase chain reaction (PCR) for *P. jirovecii* was negative, and other classical opportunistic microorganisms. Other unusual microorganisms were considered and human rhinovirus (HRV) was identified by culture and PCR, with rhinovirus A/B/C detection. No other viruses (Influenza, Parainfluenza, Syncytial, Coronavirus, Metapneumovirus, Cytomegalovirus, Human bocavirus) were detected.

Despite the worsening of respiratory status, after consulting a pulmonologist and an infectious disease specialist, corticosteroids were not administered in this immunocompromised patient with a viral lung infection. The patient developed acute respiratory syndrome distress and died following multi-organ failure.

To our knowledge, this is the first reported case of fatal HRV infection in a cirrhotic patient. Cirrhotic patients are immunocompromised [1], and can develop more obvious and more severe infections compared to non-cirrhotics; bacterial infections result in higher mortality in cirrhotic patients and spontaneous opportunistic infections have been described [2]. In this patient, alcohol abuse and malnutrition might have contributed to a dysfunction of cellular immunity with a reduction in T-lymphocyte-mediated response [3] that worsened the immunosuppression due to cirrhosis. Furthermore, malnutrition and alcohol abuse increased the risk of pneumonia with a poor prognosis once established.

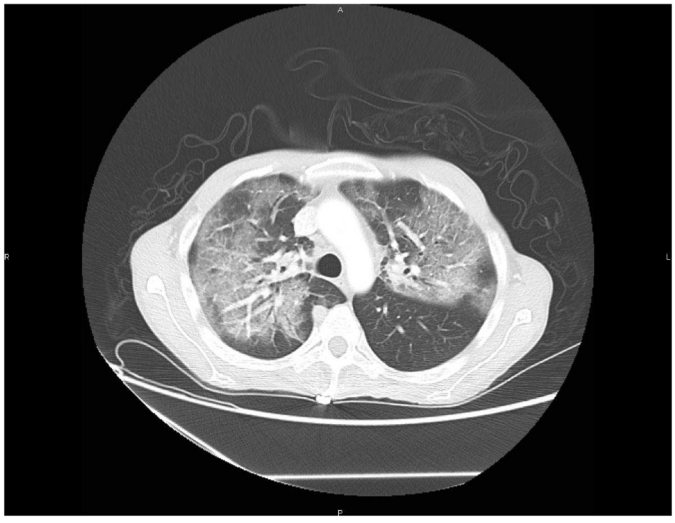

Fig. 1. Lung computed tomography scan at Day 5, showing alveolar and interstitial pneumonia.

HRV is an RNA virus belonging to the Picornavirus family. Typically, it is found in the lungs and oropharynx and causes the "common cold" [4]. Generally, the course of infection is favourable and it mainly affects children. In adults, HRV can cause chronic bronchitis exacerbation and lobar lung infection. Patients with HRV are rarely admitted to the Intensive Care Unit unless they have comorbidities [4]. Severe HRV infections are described in severely immunocompromised patients, such as haematopoietic cells transplant recipients [5]. No specific treatment is available, although recent studies have examined potential therapies, such as pleconaril and BTA-798 [5].

In conclusion, Liver cirrhosis results in an immunosuppression condition that can expose the patient to various opportunistic infections. Here, we report the first case of fatal pneumonia due to HRV in a cirrhotic patient.

Opportunistic lung infections should be suspected in patients with alcoholic cirrhosis developing interstitial pneumonia. Extended research of opportunistic microorganisms included HRV

must be performed because of their potential life-threatening nature.

Conflict of interest
None declared.

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When should we consider transplantation in adult patients with sclerosing cholangitis due to multisystem Langerhans' cell histiocytosis?

Dear Editor,

A 49-year-old male presented with jaundice and rapid general health impairment. For a decade, he was managed for hypopituitarism due to a pituitary stalk lesion, diagnosed as optic glioma. Physical examination revealed clinical signs of cirrhosis and purpuric scalp lesions. Laboratory tests showed cholestasis and inflammation. Skin biopsy showed large cell infiltrate, staining with S-100 protein and CD1a, confirming Langerhans cell histiocytosis (LCH). Magnetic resonance imaging with cholangiogram found moderate segmental intrahepatic biliary ductal dilatation and distortion, consistent with sclerosing cholangitis (SC, Supplementary Fig. S1). Liver biopsy revealed micronodular cirrhosis with advanced fibrosis and positive immunostaining (S-100 protein and CD1a, Fig. 1). Ursodeoxycholic acid and corticosteroids were begun. After few months, LCH lesions partially resolved: cholestasis and inflammation improved and pituitary lesion decreased in size (Supplementary Fig. S2). Conversely, liver decompensation with bleeding esophageal varices, ascites, and encephalopathy ensued, and patient was referred for transplantation (MELD score 16); however patient's condition worsened, with hepatorenal syndrome which did not improve with terlipressin treatment. Two days later MELD score was 34, and orthotopic liver transplantation (OLT) was performed (Supplementary Fig. S3); however the patient died on post-operative day 17 from invasive aspergillosis, diagnosed through imaging and culture in bronchoalveolar lavage and serum, though treated with voriconazole.

LCH is a rare disease occurring mostly in children, characterized by Langerhans' cells tissue accumulation. Clinical presentation varies from benign bone lesions to severe multisystem disease (MS-LCH). SC occurs in 10–18% of MS-LCH, and may progress to biliary cirrhosis and liver failure. Thus, liver transplantation should be considered in LCH patients with cholestatic liver disease.

LCH liver involvement occurs in 10–35%, mainly in children. Main presentations are hepatomegaly and cholestasis with jaundice. According to Histiocyte Society recommendations, LCH diagnosis requires presence of Birbeck granules on electron-microscopy or CD207 (*i.e.* Langerin) and/or CD1a expression, as observed in our patient.

Management of multisystem disease with liver involvement in adults poses several issues. Current guidelines [1], based on paediatric studies, recommend dual therapy with prednisone and vinblastin. However, due to hepatobiliary elimination, vinblastin is contraindicated if cholestasis is present. No studies are available in adults with MS-LCH; several authors recommend chemotherapy and/or ursodeoxycholic acid, as first line treatment. LCH-SC progresses to biliary cirrhosis faster than primary SC [2]. In our case, ursodeoxycholic acid treatment improved LCH lesions but did not affect the outcome of cirrhosis and portal hypertension.

Several reports confirm fatal outcomes in LCH-induced cirrhosis, in the absence of OLT [2]. To our knowledge, only five cases of OLT in adults with LCH are published [3,4]. One patient died from pulmonary embolism 14 months post-transplantation. Another patient underwent two OLTs in a week, because of hepatic artery thrombosis, but was alive 14 months later [3]. One recurrence is described in an adult, 4 years post-OLT, successfully treated by chemotherapy. Two other patients were alive at 2 and 14 years post-OLT.

Reaching a MELD score of 15 is considered the right timing to refer patients for OLT, regardless of aetiology [5]. Despite this, our patient died soon after transplantation, from infectious complications [6].

We suggest that any eligible adult with MS-LCH involving liver, with biliary cirrhosis and symptomatic portal hypertension and/or jaundice, should be referred for transplantation, even if partial treatment response is observed.