Padrão de crazy-paving na leptospirose pulmonar:
Correlação entre a tomografia computadorizada de alta resolução e os achados anatomopatológicos

Resumo
Os autores apresentam os aspectos na tomografia computadorizada de alta resolução de um doente com hemorragia pulmonar difusa por leptospirose. O achado predominante consistiu de opacidades em vidro despolido difusas, com espessamento de septos interlobulares sobrepostos, resultando no padrão de crazy-paving. O doente morreu, e na necrópsia foi observada extensa hemorragia alveolar, com sangue infiltrando os septos interlobulares. É realçada a correlação entre os

Abstract
The authors present the high-resolution CT findings of a patient with diffuse pulmonary hemorrhage due to leptospirosis. The main finding consisted of extensive ground-glass opacities superimposed on mild interlobular septal thickening, resulting in the appearance termed “crazy-paving”. The patient died and the necropsy showed extensive haemorrhage filling the airspace and blood infiltrating the interlobular sep-
Introduction

Leptospirosis is a zoonosis caused by *Leptospira interrogans*. Humans become infected when mucous membranes or abraded skin come into direct contact with the urine of infected animals, especially rats. The exposure to soil, water, or other matter contaminated with the infected urine is also commonly related as a cause of human infection by the *L. interrogans*. Leptospirosis produces several clinical findings, but two presentations are usually seen. In the less severe and generally non-fatal form, often called anicteric leptospirosis, the illness commonly begins abruptly and presents with headache, myalgias, conjunctival suffusion, fever, nausea, vomiting, and meningismus. In addition to these features, the more severe form of leptospirosis, called icteric leptospirosis or Weill’s disease, is commonly associated with jaundice, renal impairment, and major haemorrhagic complications. Pulmonary involvement is frequent, but often mild and of uncomplicated clinical significance. However, over the last two decades, an increasing number of cases with pulmonary haemorrhage as a prominent feature have been reported.

Case report

A 31-year-old female patient presented with a five-days history of fever, rigors and severe calf and thigh pain. Two days before admission she began to expectorate small amounts of blood and became progressively breathless. The patient had a history of immersion in dirty water during a recent urban flood,
and reported the presence of rodents in the surroundings of her home. On admission, she was febrile, dyspneic, and had cyanotic extremities.

Chest radiographs revealed extensive bilateral alveolar infiltrates in the lower thirds of lungs. High-resolution CT scan demonstrated diffuse ground-glass attenuation in both lungs, with superimposed mild interlobular septal thickening in the antero-superior regions (“crazy paving” pattern) (Fig. 1). Blood cultures demonstrated growing *L. interrogans* serovar *Copenhageni*, and treatment was initiated with intravenous benzylpenicillin and hydrocortisone, associated with O₂ by a nasal catheter. The patient also required blood transfusion. Despite treatment, she developed worsening dyspnea and massive haemoptysis, requiring intubation and positive pressure ventilation. Two days after admission, she had a cardiac arrest and died despite reanimation attempts.

The necropsy showed congestion and haemorrhage in the kidneys, liver, spleen and lungs. *Leptospirosis* were found in the kidney’s sections. In the lungs, petechiae were observed on the pleural surfaces, and the cut sections of the parenchyma were grossly

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**Fig. 1** – 31 year-old female patient with leptospirosis. High-resolution CT at the level of the aortic arch (A) and lower pulmonary veins (B) demonstrates bilateral areas of ground-glass attenuation with superimposed interlobular septal thickening (“crazy-paving” pattern).

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**Fig. 2** – (A) Histological section of the lung shows diffuse filling of the air-spaces by blood and an interlobular septum thickened due to blood infiltration (arrows). In the right side there is a secondary pulmonary lobule normally aired (hematoxylin/eosin × 40). (B) Histological section demonstrates the air-spaces partially filled by haemorrhage (hematoxylin/eosin × 40).
haemorrhagic. Histologically, there was haemorrhage filling the air-spaces and infiltration of the interlobular septa by blood (Fig. 2).

Discussion
The patients with leptospirosis usually manifest two main clinical presentations. The milder anicteric form accounts for 90-95% of cases, and those patients commonly refer fever, myalgia, conjunctival suffusion and mild gastrointestinal upset. The other 5-10% of the patients presents the icteric form, also known as Weil’s syndrome, which is characterised by jaundice, renal dysfunction, haemorrhagic manifestations, pulmonary involvement, and a high mortality rate. Our case presented with the latter form on the infection, with involvement of the lungs, kidneys, spleen and liver.

Im et al. described the chest radiographic findings in 58 patients with leptospirosis. The predominant abnormality consisted of poorly defined and diffuse ground-glass opacities, which were seen in 27% of cases. They postulated that this pattern was a result of pulmonary haemorrhage. Marchiori and Müller presented the high-resolution CT findings in a series of five patients with leptospirosis involving the lungs. All patients showed ground-glass opacities and four presented areas of air-space consolidation. The authors suggested that those findings were secondary to pulmonary haemorrhage, which was seen in bronchoalveolar lavage and autopsy studies. Although ground-glass opacities and air-space consolidations may be seen in patients with diffuse pulmonary haemorrhage, these findings are usually non-specific. The differential diagnosis should include cardiogenic and non-cardiogenic pulmonary edema, as well as infectious pneumonia.

The “crazy-paving” pattern is described in the high-resolution CT scan as areas of ground-glass attenuation with superimposed interlobular septal thickening. This pattern was initially described by Murch and Carr as pathognomonic of pulmonary alveolar proteinosis. Since then, several diseases, such as bronchioloalveolar carcinoma, sarcoidosis, nonspecific interstitial pneumonia, cryptogenic organising pneumonia and infectious diseases have demonstrated this finding, making the differential diagnosis by high-resolution CT sometimes difficult. To our knowledge, the “crazy-paving” pattern was not previously described in patients with leptospirosis.

The macroscopical study of the lungs of patients with leptospirosis generally demonstrates extensive pulmonary haemorrhage, with numerous foci of bleeding with different sizes. Some patients may show pleural-based lung lesions with pyramidal form, suggesting haemorrhagic infarcts. The histological sections usually demonstrate pulmonary congestion, several foci of interstitial and intra-alveolar bleeding, and pulmonary oedema, with different degrees of severity. In the present case, the histological examination demonstrated haemorrhage filling the air-spaces, which were seen as areas of ground-glass attenuation on the high-resolution CT, and infiltration of the interlobular septa by blood, justifying the interlobular septal thickening seen on the CT scan.

In conclusion, leptospirosis should be included in the differential diagnosis of lung lesions presenting with “crazy-paving” pattern on the high-resolution CT, particularly in patients with suggestive epidemiological
history. In addition, the study of the histological sections of our case demonstrated that the areas of ground-glass attenuation are related to the filling of the air-spaces by haemorrhage and the interlobular septal thickening is secondary to infiltration of those septa by blood.

Bibliography