Sarcoidosis complicated by cirrhosis and hepatopulmonary syndrome

Samir Gupta MD FRCPC1, Marie E Faughnan MD FRCPC1, Gerald J Prud’homme MD FRCPC2, David M Hwang BSc MD PhD FRCPC3, David G Munoz MD FRCPC2, Peter Kopplin MD FRCPC1

CASE REPORT

Sarcoidosis is a multisystem disorder commonly affecting the lungs, but also the liver, with cirrhosis and portal hypertension occurring in fewer than 1% of cases. Although hepatopulmonary syndrome (HPS) is seen in 15% to 20% of patients with cirrhosis of varying causes, it has rarely been associated with sarcoidosis. Also, although a brain abscess is not uncommon in patients with discrete pulmonary arteriovenous malformations, it is rarely seen in patients with the much smaller intrapulmonary vascular dilations that characterize HPS. A patient with an unusual series of uncommon sarcoidosis complications, including cirrhosis with HPS, brain abscess and finally Nocardia meningitis, is reported. The possibility of HPS should be considered in sarcoidosis patients with liver involvement, if gas-exchange abnormalities are out of proportion to the degree of lung involvement. These patients may also be susceptible to a cerebral abscess by paradoxical embolization, and to opportunistic infections due to cirrhosis.

Key Words: Cirrhosis; Liver failure; Pulmonary circulation; Sarcoidosis

Sarcoidosis is a multisystem granulomatous disorder that most commonly affects the lungs, but can also affect the liver. Cirrhosis and portal hypertension are rare manifestations of sarcoidosis, occurring in fewer than 1% of cases (1). In turn, hepatopulmonary syndrome (HPS) is defined by a triad of features: liver dysfunction or portal hypertension; intrapulmonary vascular dilations (IPVDs); and abnormal gas-exchange, defined by an alveolar-arterial gradient of 20 mmHg or greater. This syndrome is a well-recognized and common complication of liver disease, present in 15% to 20% of patients with cirrhosis of varying causes (2). Although HPS has been reported in cases of noncirrhotic portal hypertension with normal synthetic liver function, the most common cause is cirrhosis, although no specific etiology nor severity of cirrhosis has been found to be correlated with the incidence or severity of HPS (3). The majority of HPS patients (82%) initially present with features of liver disease; however, a minority (18%) present with pulmonary complaints. Thus, a diagnosis of HPS should be kept in mind in the clinical context of unexplained hypoxemia (4). We report a case involving an unusual series of uncommon complications of sarcoidosis, including cirrhosis with resulting HPS, brain abscess and finally, Nocardia meningitis.

CASE PRESENTATION

A lifetime nonsmoking Caucasian woman had initially presented in 1983, at 38 years of age, with iritis, hepatosplenomegaly and hypercalcemia, along with diffuse interstitial markings on chest x-ray. An open lung biopsy confirmed sarcoidosis, and she was treated with prednisone for two years, with disease remission. The patient remained well until 1990, when she developed an unexplained frontal lobe brain abscess after a dental procedure. She was successfully treated with intravenous antibiotics.

Between 1991 and 1995, the patient complained of gradually progressive exertional dyspnea. By 1995, she had cyanosis, digital clubbing and numerous spider nevi. Her chest x-ray was normal. Pulmonary function tests revealed normal spirometry and lung volumes, with a diffusion capacity of 43% predicted and partial pressure of O2 of 47 mmHg on room air. An ultrasound showed hepatosplenomegaly with varices at the porta hepatis. She had no history of alcohol consumption, and all
patient developed an unexplained brain abscess following a previous report in the literature (5). Furthermore, our patient had IPVDs long before the onset of symptomatic hypoxemia, and that her brain abscess might have resulted from right-to-left bacterial transit through lung IPVDs at the time of her dental procedure. This is supported by previous cross-sectional studies demonstrating the presence of IPVDs without hypoxemia among cirrhotic subjects (6). It is of note that although brain abscess is a recognized complication of pulmonary AVMs through this paradoxical embolization mechanism, it rarely occurs in HPS, presumably due to the relatively smaller calibre and decreased flow through IPVDs. However, two previously published case reports of a brain abscess in patients with HPS, have suggested that IPVDs may occasionally behave like ‘true’ pulmonary AVMs with respect to loss of the lung’s ‘filter’ function (7, 8).

In terms of the underlying cause of the IPVDs that characterize HPS, several pathophysiological models have been proposed (2). It has been suggested that IPVDs may result from increased production or impaired hepatic clearance of constitutively produced vasodilators, or alternatively, from decreased production of or lack of pulmonary vascular sensitivity to a vasoconstrictor normally emanating from a healthy liver. However, regardless of the upstream triggering pathway, it has become evident in rat models of this disease that locally released nitric oxide is an important end-mediator of vascular dilation at the level of the pulmonary microvasculature (9). Finally, in our patient, autopsy revealed the unexpected complication of Nocardia meningitis with resulting focal vasculitis and cerebral hemorrhage. The patient had none of the usual causes of an immunocompromised state, such as HIV or chronic steroid use, and we suspect that cirrhosis was the predisposing factor.

CONCLUSION
Cirrhosis from sarcoidosis may cause HPS, which must be kept in mind, especially if gas-exchange abnormalities are out of proportion to the degree of lung involvement by sarcoidosis. Also, patients with HPS may develop cerebral abscess as a result of right-to-left shunting of bacteria through IPVDs; this may occur even before the onset of symptomatic hypoxemia. Finally, HPS is an extremely rare complication of sarcoidosis, with only one previous report in the literature (5). Furthermore, our patient developed an unexplained brain abscess following a dental procedure, five years before the diagnosis of HPS. Given that IPVDs develop progressively, we hypothesized that the present patient had IPVDs long before the onset of symptomatic hypoxemia, and that her brain abscess might have resulted from right-to-left bacterial transit through lung IPVDs at the time of her dental procedure. This is supported by previous cross-sectional studies demonstrating the presence of IPVDs without hypoxemia among cirrhotic subjects (6). It is of note that although brain abscess is a recognized complication of pulmonary AVMs through this paradoxical embolization mechanism, it rarely occurs in HPS, presumably due to the relatively smaller calibre and decreased flow through IPVDs. However, two previously published case reports of a brain abscess in patients with HPS, have suggested that IPVDs may occasionally behave like ‘true’ pulmonary AVMs with respect to loss of the lung’s ‘filter’ function (7, 8).

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patients with cirrhosis may be functionally immunocompromised, and the possibility of opportunistic infections should be entertained.

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REFERENCES