Successful Interferon Treatment for Lichen Planus Associated with Chronic Active Hepatitis due to Hepatitis C Virus Infection

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In the last 20 years attention has been drawn to the possible association of lichen planus (LP) with chronic liver diseases, especially primary biliary cirrhosis and chronic active hepatitis (1). The overall prevalence of liver disease in patients with LP varies widely in the literature, ranging between 0.1 and 11.3% (1). Recently, the simultaneous occurrence of LP and hepatitis C has been repeatedly reported, and LP should be added to the list of dermatologic diseases associated with hepatitis C virus (HCV)-induced chronic active hepatitis (2). A search for HCV infection should therefore be systematically performed in patients with chronic LP.

Since interferon is now accepted as routine therapy for chronic HCV (3), and since severe worsening of LP during interferon treatment for chronic HCV had been reported (4), we here report on the disappearance of LP during interferon treatment for HCV-induced chronic active hepatitis.

CASE REPORT
A 62-year-old woman presented with diffuse, flat-topped, violaceous, polygonal papules on the forearms and thighs. Her past history was unremarkable. Histologically, the papule showed thickening of the granular layer, liquefaction degeneration of the basement membrane and basal cells, and a band-like lymphocytic infiltrate in the upper dermis. Routine laboratory investigations, including liver function tests, were within normal limits. Nine months later, elective cholecystectomy was performed because of cholelithiasis and hydrops of the gall bladder, and the following parameters were noted: alanine aminotransferase 105 IU/l and aspartate aminotransferase 84 IU/l (normal values for both <40 IU/l) and lactate dehydrogenase 347 IU/l (normal value <225 IU/l); alkaline phosphatase, gammaglutamyl transpeptidase and bilirubin were within normal limits. Serologic tests for hepatitis B virus and hepatitis C virus were negative, while anti-HCV antibodies were detected (ELISA method). During the cholecystectomy a macronodular, irregular liver was noted and a liver biopsy revealed micronodular hepatic cirrhosis. There were no changes in laboratory findings or in LP appearance following cholecystectomy. Eight months later the patient was treated with interferon alpha-2a 3 x 10^6 units intramuscularly, three times a week for 6 months. After 3 months of treatment, all the cutaneous lesions cleared, and marked improvement on the liver function tests was observed. The lesions remained clear for the 3 years of follow-up, as did the improvement in liver function.

DISCUSSION
There are histologic and immunologic similarities between LP and chronic active hepatitis which resemble graft versus host reactions - lymphocytic infiltrate, colloid bodies and a fibrosclerotic healing process. So far there is conflicting evidence concerning the primary process that initiates the events leading to the histopathologic changes in LP. LP may begin with the processing of some unidentified antigens by the Langerhans’ cells, followed by migration and activation of lymphocytes against the epidermal basal cells. The damage to basal cells is thought to be mediated by cytokines, lymphotoxins, and cytotoxic T-cells. An alteration in epidermal antigenicity, induced by a virus, might provoke this reaction.

Interferon-alpha is now accepted as routine therapy for chronic HCV. In two recent prospective studies (5, 6), more than 100 patients with hepatitis C received interferon-alpha, and no case of LP was noted during follow-up. Rodrigues et al. (7) presented a case of LP induced by interferon-alpha in a patient with IgG myeloma. There are four more reports on the induction or aggravation of LP by interferon-alpha given for chronic HCV (4, 8). A possible explanation for this observation is the stimulation of keratinocytes to express hidden surface antigens or to release chemotactants, thereby enhancing the migration of T-cells into the dermis (8).

In the present case, as in 2 previous cases reported by Doutré et al. (9), LP lesions disappeared concomitantly with interferon treatment. It is possible that the antiviral and immunologic actions of interferon play a role in the treatment of LP associated with HCV. The efficacy of therapy is always difficult to appreciate in cases of LP, because its evolution is totally unpredictable, with occasional cures even in the absence of any treatment. Thus, the contradictory observations regarding the role of interferon in the treatment of LP are not surprising. To date, insufficient data are available to define the exact role of interferon in the treatment of LP.

REFERENCES


**Scedosporium apiospermum Skin Infection in a Patient with Nephrotic Syndrome**

**Sir,**

With the advance in the treatment of malignancies and the widespread use of corticosteroids, there has been a prominent increase in the occurrence of opportunistic pathogens. Recently, *Scedosporium apiospermum* infection of various sites has been reported (1). The organism has low inherent virulence but is a fungal opportunist able to elicit infections. Apart from mycetoma, cutaneous and subcutaneous infection with *Scedosporium apiospermum* is rarely encountered in clinical practice. We here describe a case of *Scedosporium apiospermum* skin infection in a patient with nephrotic syndrome.

**CASE REPORT**

The patient was a 59-year-old male retired office worker, with a history of nephrotic syndrome diagnosed 9 years previously. He had received 10–30 mg/day of oral prednisolone for treatment. In 1990, he developed chronic renal failure, which deteriorated in 1995, and he was referred to the Division of Dermatology for multiple painful abscesses of his left forearm (Fig. 1). When the nodules were punctured, a yellowish white sticky exudate was discharged. No grains were visible in the discharge. Intravenous administration of penicillin was not effective. Routine bacteriological culture of swabs taken from the skin lesions was unhelpful. Direct microscopic examination of scrapings and pus from the area showed no hyphae. A biopsy specimen was taken from the nodule. A haematoxylin and eosin-stained section showed a granulomatous infiltrate containing histiocytes, neutrophils and multinucleate giant cells within the deep dermis to the subcutaneous tissue. The biopsy specimen stained by periodic acid-Schiff revealed fungal elements within the subcutaneous tissue. Culture of the specimen was performed on Sabouraud dextrose agar at 32°C. It revealed woolly colonies, at first white, then becoming dark brown 4 weeks later. Microscopically, the hyphae were hyaline and septate. Ovoid to round-shaped, smooth conidia were borne singly or in small groups on short simple conidiophores (Fig. 2). Cleistothecia were not observed. The fungus was finally identified as *Scedosporium apiospermum*. The patient was commenced on itraconazole 50 mg once daily for a week. Due to lack of effect, the dose of itraconazole was increased to 100 mg/day (1.8 mg/kg). Two weeks later, most abscesses disappeared. However, the patient refused further intake of the drug. The fungal disease relapsed, and the patient died of deteriorated nephrotic syndrome and disseminated intravascular coagulation. An autopsy could not be performed, thus the fungal involvement of the internal organs could not be investigated.

**DISCUSSION**

*Scedosporium apiospermum*, an anamorph of *Pseudallescheria boydii*, appears to have a worldwide distribution and is a soil- and water-inhabiting fungus. The organism has low inherent virulence. But in the past few years an increasing number of cases of the fatal disseminated disease have been encountered in severely compromised hosts (1). The fungus grows rapidly on most laboratory media.

The clinical manifestations of infection by *Scedosporium apiospermum* are quite varied. The most frequent form is mycetomas, a localized type of infection occurring in a normal immune status host following trauma (1, 2). The present case was not a mycetoma, as the infection was multifocal; there was no drain sinus and grains were not seen. Apart from mycetomas, reports of cutaneous and subcutaneous infection with this fungus are still rare. Additionally, there are a few cases of a lymphocutaneous infection in a sporotrichoid fashion (1, 3).

In our present case, oral treatment with itraconazole was effective. Itraconazole seems to be one of the most useful drugs in the treatment of *Scedosporium apiospermum* infection (3, 4).

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Fig. 1. Multiple cutaneous to subcutaneous nodules, 0.5–1.5 cm in diameter, are seen on the left forearm. (The linear scar of the lesion is due to injury suffered 5 years earlier.)

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Fig. 2. Slide culture method stained with lactophenol cotton blue demonstrated the presence of *Scedosporium apiospermum*. 