Tissue changes in cryptococcosis: histologic alteration from gelatinous to suppurative granulomatous tissue response with asteroid body

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Abstract

The histologic variety and transformation in cutaneous cryptococcosis with acute lymphocytic leukemia before antifungal treatment and after the start of treatment were studied by the light and electron microscopic examinations. The initial cutaneous lesions before treatment revealed gelatinous tissue reactions, and Cryptococcus neoformans (serotype A) were isolated from the skin biopsy specimen and blood. However, later recurrent cutaneous lesions receiving antifungal treatment revealed suppurative granulomatous tissue reactions, and fungal cultures of the skin biopsy specimen changed to negative even though numerous yeasts stained with PAS were observed in skin lesions. Moreover, in the later lesion a few giant cells contained asteroid bodies without central spores. Ultrastructure of the later cutaneous lesions is presented.

Introduction

In cryptococcosis, the types of tissue reactions chiefly consist of gelatinous and/or granulomatous lesions [1]. Although cultures should always be performed, the diagnosis of cryptococcosis can be made without positive culture [2]. On the other hand, there are pitfalls in diagnosing specific fungal infections on the basis of tissue reactions and morphologic findings of the organisms, and it emphasizes the necessity for culture proof in all fungal infections [3]. In the patient here described, we noted an unusual suppurative granulomatous tissue reaction with a few asteroid bodies, and studied the variety and transformation of the histologic tissue responses by the light and electron microscopic examinations.

Report of a case

A 63-year-old woman had been febrile since February, 1983. The result of laboratory studies was consistent with a diagnosis of acute lymphocytic leukemia(ALL)(FAB;L2) and a remission induction chemotherapy with THP-adriamycin, vincristin and prednisolone was began on March 3. Thereafter she went into CR(complete remission) on May 6. On May 8, her temperature increased to 38 °C with headache and nausea, and a few nodules developed the nose, knees and preauricles. In addition, an erythematous plaque occurred on her right thigh. On May 24, a skin biopsy specimen from the right thigh showed a gelatinous lesion in the dermis with many fungal organisms. The
histopathological findings were compatible with cryptococcosis.

On May 27, lumbar puncture showed an opening pressure of 170-mm water with clear, colorless fluid. The cell count was fifteen mononuclear cells. Cerebrospinal fluid glucose level was 36 mg/dl; protein was 57 mg/dl. India ink preparation of the smear showed yeast cells surrounded by large capsule. Cryptococcus neoformans (serotype A) were isolated from skin lesions and blood.

On May 29, therapy was begun with intravenous amphotericin B and oral 5-fluorocytosine. The dose of intravenous amphotericin B was increased from 1 to 20 mg daily, and the dose of intrathecal amphotericin B was increased from 0.025 to 0.3 mg twice weekly. The dose of 5-fluorocytosine was 4 g daily. On this treatment there was rapid resolution of meningitis. Her skin lesions resolved within 5 weeks. However, because of side effects such as severe phlebitis, fever and chilliness amphotericin B was replaced by ketoconazol or miconazol added to 5-fluorocytosine. Then, skin lesions, cutaneous and subcutaneous nodules, recurred, and mental disturbance, meningeal signs and small brain abscesses developed. But C. neoformans was never isolated from skin lesions. So both intravenous and intrathecal amphotericin B were reinstituted combination with 5-fluorocytosine. Her skin lesion completely resolved and small brain abscesses distinctly decreased.

The patient showed no recurrence of fungal infection during follow-up period, but because of exacerbation of ALL she died 12 July, 1986.

**Histopathology**

A biopsy was performed on erythematous plaque in the initial phase prior to treatment and recurrent cutaneous nodules in the later phase receiving antifungal treatment. Histologically, we compared the initial lesion with the later lesion.

**Light microscopic findings**

*Erythematous plaque-like lesion in the initial phase prior to treatment*

In H.E. sections, a large sized cystic space of mucoid change was located directly beneath the epidermis. Gelatinous lesions showed numerous

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**Fig. 1.** The initial lesion prior to antifungal treatment. Numerous yeast-like organisms are surrounded by clear halos representing gelatinous capsules (× 280).