PROTOTHECOSIS: A REPORT OF TWO CASES IN JAPAN AND
A REVIEW OF THE LITERATURE

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Key words: Prototheca - Protothecosis - Human cases

Protothecosis is an emerging opportunistic infection caused by species belonging to the genus Prototheca. Two Japanese cases of protothecosis are documented with a critical review of the literature. A current perspective concerning the microbiology and disease entity of protothecosis is described in detail.

INTRODUCTION

Protothecosis is a relatively rare infection caused by the species of the achlorophyllic genus Prototheca Krüger, microorganisms morphologically similar to those of the genus Chlorella. The cases of protothecosis in human have been classified into the three clinical forms: 1) cutaneous and/or subcutaneous infection, 2) synovitis of olecranon bursa or other fibrous tissue, and 3) systemic infection. Recently, the disease has become very important both to physicians and microbiologists because of the increasing number of the reported cases, characteristic clinical features, and a distinct morphology of the etiologic agents in vitro as well as in vivo.

The purposes of this presentation are to describe two Japanese cases of protothecosis, and to review and discuss of the literature of human protothecosis.

Report of the cases

Case 1.

An 80-year-old Japanese male patient noticed a spontaneous, asymptomatic red papule on his right antecuboidal fossa in March 1987. He did not have any apparent antecedent traumatic history at the site of the lesion. He visited his neighbor physician, who diagnosed the lesion as chronic eczema. In spite of topical corticosteroid application for a couple of months, the lesion gradually spread, and he developed another extending plaque on his left arm. He consulted to the Dermatology Clinic, Kyushu University Hospital in August 1987.

On physical examination, irregularly shaped, well demarcated, erythematous, infiltrated plaques are distributed symmetrically on the flexor surface of his arms. The surface of the lesions were slightly elevated and accompanied with vesicles, pustules, crusts, and fine scale (Fig. 1). No regional lymph nodes were palpable.

He is a retired rice farmer in Kyushu island, the south-western area of Japan, and occasionally enters the rice paddy. Laboratory investigation revealed that he had an untreated diabetes and hyperglycemia. No immunological abnormality was detected.

A skin biopsy specimen taken from a plaque on his right upper arm, stained with hematoxylin and eosin was histologically examined. In the dermis, there revealed a dense, granulomatous infiltration consisted mainly of lymphocytes, histiocytes, and scattered foreign body giant cells. Small, hyaline,
round and yeast-like cells and large spherical cells were abundantly recognized within the multinuclear giant cells or in the interstitial tissue of the middle to reticular dermis. Further detailed observation of the microorganisms was performed with periodic acid-Schiff staining. Small and single cells contained a large and single nucleus. Large cells were divided by nuclear and cytoplasmic cleavages, and appeared like wheels. Very large cells, containing 4-20 endospores, showed morula-like appearance (Fig. 2).

Several pieces from a biopsy specimen were inoculated on Sabouraud dextrose agar plates and incubated at 25°C. From each of these, identical colonies were obtained in pure culture. The isolated organism yielded rapidly growing, smooth, moist, and creamy colonies. Microscopically, single cells were hyaline, globose to ovoid, and variable in size, measuring 3 to 12 μm in diameter. Some of the larger components were divided by cleavages, and endospores were contained within the others (Fig. 3). The mother cells were ruptured to release the spores, then each spore increased in size and eventually became mother cell. The isolate grew well at 37°C, and failed to hydrolyze urea. Assimilation test by the API 20 system showed positive results with galactose, glucose, glycerol, and trehalose. On the basis of morphologic and physiologic characteristics, the isolate was identified as *Prototheca wickerhamii* Tubaki et Soneda. Immunohistopathologic study by anti-*P. wickerhamii* globulin, which was performed at the Centers for Diseases Control’s Division of Mycotic Diseases, also confirmed this identification.

The patient was treated with oral administration of ketoconazole, a daily dose of 200 mg. Clinical effect appeared rapidly as the plaques discolored and the induration decreased. After 19 weeks of chemotherapy, each lesions healed leaving superficial scars. A biopsy specimen taken after 17 week ketoconazole therapy revealed no distinct microorganisms. The patient showed no recurrence during 3 year follow-up period, as of May 1991.

**Case 2.**

A 13-year-old Japanese boy complained of general fatigue and palpitation in December 1987. He admitted to Hamanomachi Hospital in Fukuoka and was diagnosed as a patient with iron deficiency anemia due to gastrointestinal bleedings from unknown lesions. In October 1988, he developed a high fever...