The phialides were brown, thick-walled, and acicular. They were 15–50 \( \mu \text{m} \) long with both prominent and inconspicuous funnel-shaped collarettes. The phialides showed percurrent proliferation. The conidia were 3–6 \( \mu \text{m} \) in length, hyaline, thin-walled, cylindrical to sausage shaped, and aggregated in slimy heads at the apices of the phialides.

The organism was identified as *P. parasitica* and confirmed by David Ellis at the Mycology Reference Laboratory of the Women’s and Children’s Hospital in Adelaide, Australia. In vitro testing revealed that the organism was susceptible to all antifungals except 5-flucytosine. Therapy with iv amphotericin B (0.5 mg/[kg \( \cdot \) d]) was started immediately and continued until the lesion healed on day 87 (cumulative dose, 600 mg).

The patient’s second OLT was complicated by biliary obstruction, renal failure, intraabdominal infection, and bilateral pleural effusions. Blood samples collected on day 111 of hospitalization showed fungal elements in the aerobic bottle after 7 days of incubation, and the organisms cultured were subsequently identified as *P. parasitica*. Parenteral amphotericin B therapy was restarted and continued until day 150 (cumulative dose, 1,150 mg), after which it was replaced with oral fluconazole (400 mg postdialysis).

One week later, *P. parasitica* was isolated from blood samples collected 7 days previously. Fluconazole therapy was replaced with itraconazole therapy (400 mg/d). Six additional blood cultures were positive over the next week. Intravenous therapy with amphotericin B (1 mg/[kg \( \cdot \) d]) was then added to the itraconazole regimen. A transesophageal echocardiogram showed a large tricuspid valve vegetation and mitral and aortic valve vegetations. Therapy with amphotericin B (total dose, 1,800 mg) and itraconazole was continued until day 181, at which time active therapy was discontinued; the patient died 2 days later. Autopsy revealed a 3.5-cm vegetation on the tricuspid valve and smaller vegetations on the mitral and aortic valves, from which *P. parasitica* was isolated. Histological examination of autopsy specimens revealed fungal myocarditis, fungal pneumonitis, and fungal microabscesses in the kidneys.

The optimal therapy for *P. parasitica* infection is unknown, but complete surgical resection of small localized cutaneous lesions is probably the treatment of choice. Antifungal agents that have been used to treat *P. parasitica* infection, with variable success, include amphotericin B, 5-flucytosine, ketoconazole, and terbinafine [5].

In summary, we present a case of *P. parasitica* endocarditis, fungemia, and disseminated infection following liver transplantation. As there are increasing numbers of immunosuppressed patients, the incidence of invasive fungal diseases—including infections with phaeoid fungi—will likely increase.

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References


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**Invasive Cryptococcosis in a Family with Epidermodysplasia Verruciformis and Idiopathic CD4 Cell Depletion**

Epidermodysplasia verruciformis (EV) is a rare autosomal recessive disease that was first described in 1922 [1]. Patients with this condition present with extensive flat and pityriasis-like warts in sun-exposed areas such as the face and hands [1, 2]. The onset of EV usually occurs in young adulthood, and the disease is associated with depressed cell-mediated immunity and a propensity for transformation of the warty lesions to squamous cell carcinoma [3–5]. Several human papilloma viruses have been associated with EV [2–4]. Other opportunistic infections have not been reported in patients with EV. We describe a consanguineous family with seven children in which two of three siblings who had EV developed disseminated cryptococcosis.

A 25-year-old woman was admitted to the hospital because of a 6-week history of headaches and intermittent fever. Her medical history was unremarkable except for multiple warts of different sizes that had appeared on her face, hands, and forearms over the 3 years before admission. Physical examination revealed a fever (temperature of 38.8°C), skin lesions, and bilateral papilledema. Lumbar puncture yielded CSF with a WBC count of 87/mm³; the CSF cryptococcal antigen titer was 1:1,024. Cultures of blood and CSF yielded *Cryptococcus neoformans* variety *neoformans* serotype A. The patient was treated with iv amphotericin B. After 2 weeks, her treatment was changed to oral fluconazole (400 mg/d), but all her symptoms, including papilledema, recurred. The patient was cured only after receiving another 6-week course of amphotericin B and several more weeks of oral fluconazole therapy.

The patient’s older brother had been admitted to the hospital 9 years earlier (at age 23) because of a 2-week history of headaches. A CT scan of the brain revealed a posterior fossa mass. His medical history was also significant for multiple flat warts of various sizes that covered his forehead and arms. Cultures of brain tissue and CSF yielded *C. neoformans* variety *neoformans* serotype A. The patient received a 6-week course of amphotericin B therapy and completely recovered; he has been well ever since. Papillomavirus type 3 and 10 were detected by PCR of biopsy material from skin lesions.
Figure 1. Family tree for the family of two children with epidermodysplasia verruciformis who had invasive cryptococcosis. The results of HLA testing are shown. F = father; M = mother; a and b indicates the genotype of the HLA allele; shading indicates family member with epidermodysplasia verruciformis; arrow indicates family member with cryptococcal meningitis.

The family tree for the family of the two children whose cases are described herein is shown in figure 1. The tree includes the results of human lymphocyte antigen testing. The parents of these two patients are first cousins. Three of their seven children, including the two patients described herein, have EV. The leukocyte, lymphocyte, and CD4 cell counts were normal for all family members who did not have skin lesions. The total WBC count for the three siblings with multiple warts was 3,200–6,000/mm³ (6%–16% lymphocytes); the CD4 cell counts were 40–57/mm³, with a CD4:CD8 ratio of 0.2–0.6. Serological test results for HIV were negative for all family members. Additional immunological tests performed for all members did not reveal differences between the siblings with EV and the unaffected family members.

The three siblings with EV had low counts of CD4 helper cells compared with the other members of the family, a finding that confirms the association previously established between EV, hereditary CD4 cell depletion, and the development of multiple warts [1–4]. Human lymphocyte antigen class I and II analysis revealed that all seven children, including those with and without EV, were genotypically identical with regard to HLA-DRB1*07, which was contributed by the father. Therefore, although previous reports suggested an association between EV and HLA-DRB1*07 [5], our results show that no such relation exists, or that at least an additional gene and/or factor is required to trigger the disease; the gene involved remains to be elucidated. To our knowledge, this is the first report of an opportunistic infection other than papillomavirus infection to occur in a patient with EV.

IgG Response to Pneumococcal Polysaccharide–Protein Conjugate Appears Similar to IgG Response to Polysaccharide in Bone Marrow Transplant Recipients and Healthy Adults

Bone marrow transplant recipients mount inadequate antibody responses to polysaccharide antigens for at least 2 years after transplantation [1]. In the case of Haemophilus influenzae, vaccines composed of capsular polysaccharide conjugated to a protein have demonstrated greater immunogenicity than those composed of pure capsular polysaccharide [2]. We undertook this study to determine whether the same principle applies for Streptococcus pneumoniae.

H. influenzae polysaccharide–protein conjugate vaccine, Hib-TITER (Wyeth, Philadelphia) and either PNEUMOVAX 23 (Merck, West Point, PA) or heptavalent pneumococcal polysaccharide–protein conjugate vaccine (PPCV) (Merck), which contains serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F, each conjugated to the outer membrane protein of Neisseria meningitidis [3], were injected intramuscularly ~ 1 year after transplantation. Fifteen of the 27 patients randomized to the two vaccine groups were evaluable (nine received PPCV, and six received PNEUMOVAX 23). The two most common reasons that patients could not be evaluated were the administration of intravenous immunoglobulin and lack of a 1-month post-immunization blood sample.

The two vaccine groups were comparable with respect to age, gender, history of splenectomy, original disease, donor type, pre-transplantation cytomegalovirus (CMV) serostatus, conditioning