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Probable Mother-to-Infant Transmission of *Pneumocystis carinii* f. sp. *hominis* Infection

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A mother and her 4.5-week-old infant had *Pneumocystis carinii* pneumonia contemporaneously. Genotyping of *P. carinii* f. sp. *hominis* DNA at three independent loci showed the same genotype in samples from mother and infant. These data suggest transmission of *P. carinii* organisms from the mother to her infant.

The acquisition and transmission of *Pneumocystis carinii* infection are still not clearly understood. The infection can be transmitted from one animal to another via the airborne route. In the rat model of the infection, transmission from infected rats to susceptible immunocompromised rats in close contact has been observed (5). Experiments using the mouse model have also shown airborne transmission of the infection (19). More recently, it has been shown that immunocompetent mice, transiently parasitized by *P. carinii* organisms after close contact with *P. carinii*-infected mice, were able to transmit the infection to *P. carinii*-free SCID mice (3).

In contrast, transmission of *P. carinii* infection in humans remains unclear. It is now widely accepted that *P. carinii* infection is host species specific and that the *P. carinii* organisms that infect humans, *P. carinii* f. sp. *hominis*, are different from those infecting other mammals and are not acquired from an animal reservoir (17). It is postulated that transmission of human-derived *P. carinii* infection is similar to that in rats and mice, based on data from a number of studies. Investigations of immunocompromised patients with recurrent episodes of *P. carinii* pneumonia suggest that exposure to *P. carinii* f. sp. *hominis* is frequent and that reinfection with different types of *P. carinii* f. sp. *hominis* is common (7, 14). Apparent clusters of *P. carinii* pneumonia, suggesting person-to-person transmission, have been described in immunosuppressed children with malignancy, transplant recipients, and adults with human immunodeficiency virus (HIV) infection (4). However, definitive demonstration of person-to-person transmission of the infection in humans is problematic. In this study, *P. carinii* organisms in respiratory tract samples from a mother and her 4.5-week-old infant, who had pneumonia contemporaneously, were genotyped and compared.

The mother was a 25-year-old, previously well, black African woman who gave birth to a full-term male infant weighing 3.7 kg (50th percentile) on 1 April 2000. She had been resident in the United Kingdom for the 4 years prior to delivery; during her antenatal care she had declined an HIV antibody test. There was no problem at birth; the infant was breast and bottle fed. At age 31 days the infant presented with a 2-day history of nonproductive cough, breathing difficulties, and poor feeding. Physical examination revealed a respiratory rate of 120/min, oxygen saturations in air of 87%, and a chest radiograph showing an interstitial pneumonitis with widespread ground-glass appearances. Mechanical ventilation was commenced for respiratory failure on 5 May 2000, and at the same time bronchoalveolar lavage (BAL) was carried out via the endotracheal tube. This revealed *P. carinii* (by methenamine silver staining), cytomegalovirus, *Candida albicans*, and *Staphylococcus aureus.* The infant was treated with parenteral, high-dose cotrimoxazole, ganciclovir, liposomal amphotericin, and adjuvant glucocorticoids and made a full recovery. HIV type 1 (HIV-1) antibodies were detected in blood, and subsequently HIV-1 RNA was detected; the plasma HIV-1 RNA level was 426,460 copies per ml, and the $CD4^+$-T-lymphocyte count was 32% of total, with an absolute $CD4^+$ count of 1997. The child remains well after 17 months of follow-up, the $CD4^+$-T-lymphocyte count = 32% of total, the absolute count = 2,929 cells/μl, the plasma HIV-1 RNA level is undetectable, and the baby is receiving antiretroviral therapy and cotrimoxazole as prophylaxis of *P. carinii* pneumonia.

The guidelines of the Joint University College London-University College London Committees on the Ethics of Human Research were followed in the conduct of this research. The mother gave informed written consent for her own and the infant's bronchoscopy.

On the same day that *P. carinii* pneumonia was diagnosed in the infant, the mother reported a 32-day history of increasing cough and exertional dyspnea with onset 3 days postpartum. Examination was normal apart from seborrhoeic dermatitis on the face. Investigations showed a radiographically diffuse pneumonia, hypoxemia, and a PaO_2 level of 6.6 kPa (breathing room air), and methenamine silver staining of BAL fluid (obtained on 16 May 2000, 43 days after the onset of symptoms) revealed *P. carinii.* HIV-1 antibodies were detected in blood, the $CD4^+$-T-lymphocyte count was 10 cells/μl, and the plasma HIV-1 RNA level was 87,600 copies/ml. With parenteral, high-dose cotrimoxazole and adjuvant methylprednisolone, the patient recovered. Secondary prophylaxis against *P. carinii* pneu-

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TABLE 1. Results of sequence analyses at three loci performed on samples from mother and infant

Identity of patient	Locus	PCR expt	Nucleotide position/identity	Amino acid position/identity	ITS genotype
Mother	mt LSU rRNA	1	85/C 248/C		
		2	85/C 248/C		
	DHPS	1	165/A 171/C	55/Thr 57/Pro	
		2	165/A 171/C	55/Thr 57/Pro	
		3	165/A 171/C	55/Thr 57/Pro	
	ITS	Clone 1			B_1a_3
		2			B_1a_3
		3			B_1a_3
		4			B_1a_3
		5			B_1b_1
		6			B_1a_3
		7			B_1a_3
		8			Ca_3
		9			B_1a_3
		10			B_1a_3
Infant	mt LSU rRNA	1	85/C 248/C		
		2	85/C 248/C		
	DHPS	1	165/A 171/C	55/Thr 57/Pro	
		2	165/A 171/C	55/Thr 57/Pro	
	ITS	Clone 1			B_1a_3
		2			B_1a_3
		3			B_1a_3
		4			B_1a_3
		5			B_1a_3
		6			B_1a_3
		7			B_1a_3

monia was started with cotrimoxazole, and antiretroviral therapy was commenced. The patient remains well after 17 months of follow-up. The infant's father was negative for HIV-1 antibody.

An aliquot of BAL fluid from the mother and infant was stored frozen at −20°C. DNA was extracted from the samples using the QIAamp DNA mini kit (Qiagen, Hilden, Germany), according to the manufacturer's protocol with minor modifications. DNA amplification was performed using a single round of PCR as previously described at three independent loci, the mitochondrial large subunit rRNA (mt LSU rRNA) (16, 18), dihydropteroate synthase (DHPS) using primers DHPS3 and DHPS4 (corresponding to primers A_{HUM} and BN [2]), and the internal transcribed spacer (ITS) regions of the nuclear rRNA using primers ITSF3 and ITS2R3 (13–15). The mt LSU rRNA and DHPS amplification products were sequenced directly. The ITS amplification products were cloned and sequenced as previously described (10).

Genotyping of *P. carinii* f. sp. *hominis* DNA, extracted from BAL fluid at the mt LSU rRNA, identified the same genotype in two independent PCR products from the mother and in two PCR products from the infant. Each of the sequences had C at position 85 and C at position 248, which is equivalent to genotype 1 reported by Beard et al., one of the most common types in the United States (2) (Table 1). At DHPS the same genotype was identified in three independent PCR products from the mother and two PCR products from the infant. Each sequence had A at position 165, equivalent to threonine at residue 55, and C at position 171, equivalent to proline at residue 57. This sequence corresponded to the wild-type DHPS sequence (8) and is consistent with the absence of prior sulfa exposure in both mother and infant (6). At the ITS locus, the genotype of all seven clones from the infant was B_1a_3 (corresponding to Eg as described by Lee et al. [9]). This genotype occurs in 16% of United Kingdom samples (11) and in up to 27% of samples from the United States and Denmark (9). The genotype B_1a_3 was also found in 8 of 10 clones from the mother, while Ca_3 (corresponding to Fg) was found in one clone and B_1b_1 (corresponding to Eb) was found in another clone (Table 1), indicating that the infection was not clonal.

These data suggest that the infant was infected with a single type of *P. carinii* f. sp. *hominis* that was identical to the majority type infecting the mother. From the time course of the clinical symptoms, it is highly probable that the mother had *P. carinii* infection before the time of delivery. By analogy with the experiments on transmission of *P. carinii* infection in animal models (3, 5), the airborne transmission of *P. carinii* from the mother to the infant is the most probable explanation, especially in view of their very close proximity. An alternative explanation, but less probable considering the time course of the clinical symptoms, was that both mother and infant acquired the infection from a common exogenous source. Transmission of this fungus via the placenta, via blood during delivery, or via breast milk is less likely (1, 12).

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