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AIDS-related Zoonotic Pathogen, *Enterocytozoon bieneusi*

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Abstract

Microsporidia in humans emerged with the AIDS epidemic. *Enterocytozoon bieneusi* is the most significant species and causes chronic diarrhea, wasting, papillary stenosis, acaculous cholecystitis, bile duct dilatation and sclerosing cholangitis and is responsible for 30-50% of all cases of in people with AIDS. Microsporidiosis has been reported in immunosuppressed, and in immunologically normal individuals. Variety of study has revealed the mode of transmission and possible reservoir of *E. bieneusi*. Its sites of infection suggest that transmission occurs by ingestion. Transmission has been speculated to occur via infected animals to human, person to person. There is evidence that *E. bieneusi* occurs in pigs, monkeys, and possibly other animals such as cattle, dogs, cats, llamas and rabbits. *E. bieneusi* from infected humans has been transmitted experimentally to macaques and to pigs. These observations reflect indirectly the zoonotic nature of *E. bieneusi* and indicate that cross species transmission is a real possibility. Meanwhile, In recent report, thirty-two percent of the pigs were found to be positive with rates higher over the summer months in US.

Introduction

Microsporidia are obligate intracellular protozoan parasites that cause opportunistic infections in animals and humans, specially in AIDS patients. They are sufficiently unique to be classified in a separate phylum. The phylum Microspora contain nearly 100 genera and more than 1000 species of microsporidia that infect a wide range of invertebrate and vertebrate hosts (4). They form environmentally resistant spores. These organisms are defined by a nucleated sporoplasm, a coiled polar tube, and an anchoring disk, and absence of several eukaryotic characteristics such as lacks of mitochondria, Golgi membranes and eukaryotic ribosomes (15, 29). Microsporidian species infecting animals and humans measure approximately 1.0 to 2.0 by 1.5 to 4.0 μm and are easily misidentified as bacteria and small yeast (4, 24). Diagnosis of microsporidiosis can be made by detecting spores in fecal samples with trichrome, brightening, or fluorescent stains (6, 8, 28). Species identification is usually performed by these chemical methods in conjunction with molecular assays such as use of the PCR (12, 14, 17, 27).

Enterocytozoon bieneusi and its transmission to human

Several species are becoming increasingly recognized in association with significant diseases among AIDS patients. *Enterocytozoon bieneusi* is the most common microsporidian associated with AIDS. This species primarily infects enterocytes of the small intestine and causes chronic diarrhea and also causes significant wasting and malabsorption (3, 13). *Encephalitozoon intestinalis* and *Encephalitozoon hellem* both cause diarrhea, sinusitis, nephritis, pneumonia, and keratitis (20, 24, 29). *Encephalitozoon cuniculi, Vittaforma corneae, Nosema ocularum,* and *Pleistophora* spp. have been detected less frequently in the patients (2, 5, 7, 9).

The prevalence of microsporidial infection as a cause of HIV-associated diarrhea is uncertain. Since *E. bieneusi* was first recognized in biopsy specimens in persons with AIDS in 1985 (13) this parasite has been identified in 30 to 50% of AIDS patients with chronic diarrhea (18, 25, 29). Moreover, *E. bieneusi* has been recently reported to be associated with hepatobiliary and pulmonary infections and to cause papillary stenosis, acaculous cholecystitis, bile duct dilatation and sclerosing cholangitis (1, 19, 22, 30). The sources of microsporidia infecting humans and transmission routes are not clearly defined. Animals are, however, most likely the major sources of human infections as this organism from the infected animals is released into the environment via animals stool, urine, and respiratory secretions and people can easily be infected by these contaminated materials. Since detection of *E. bieneusi* in fecal samples of pigs was described in 1996 (11), occurrence of *E. bieneusi* in several other animals such as pigs, dogs, cats, rabbits, monkeys and cattle have been reported (10, 17, 18 23).

At least one animal species infected with *E. bieneusi* experimentally exhibited similar clinical sings to human infection (26). Two monkeys immunosupressed by simian immunodeficiency virus were inoculated with *E. bieneusi* spores from an AIDS patients. Both animals began shedding spore within a week post-inoculation. One monkey became wasted and developed AIDS-related illness, and the other one developed acute septicemic illness and was near death. *E. bieneusi* from AIDS patients and from macaques monkeys with AIDS were also successfully transmitted to immunosuppressed gnotobiotic piglets (16).

In a recent report fecal and bile samples collected from 202 pigs over 18 months at a slaughterhouse in Massachusetts, USA were analyzed by PCR for *E. bieneusi* infection (31). Thirty-two percent of the pigs were found to be positive with rates higher over the summer months. Sequence analysis of *E. bieneusi* ribosomal internal transcribed spacer (ITS) from selected positive samples revealed that isolates from 3 different pigs were identical in their ITS sequence to the human *E. bieneusi* type D listed in Genbank. Further, *E. bieneusi* spores purified from these samples successfully infected 4 gnotobiotic piglets, which reflect the viability of these spores. The study confirms the zoonotic potential of *E. bieneusi,* and the

possibility of swine as reservoir for human infection. The polymorphism analysis within and between each of humans, pigs, cat and cattle also indicated a close relationship between *E. bieneusi* strains from humans and these animals (23). This result suggested that various animals provide a plausible source of human infections with *E. bieneusi.*

요약

*Enterocytozoon bieneusi*는 특히 AIDS환자에게 치명적인 질병을 초래하는 세균과 원충 중간단계의 병원체로서 현재 30%~50%의 발생률로 AIDS환자로부터 가장 많이 발생되는 병원체로 알려지고 있다. 하지만 이 병원체는 1980년 후반에서야 비로소 학계의 주목을 받기 시작했으며 환자에게 심한 만성 설사, 기력 쇠진, 악성 영양 결핍 등을 주 임상증상으로 하고 있다. 이렇게 다양하고 심각한 질병을 일으킴에도 불구하고 현재까지 이 병원체에 대한 연구가 미흡하였다. 현재 이 병원체에 대한 가장 중요한 연구 중 연구 중 하나는 이 병원체에 대한 AIDS환자로의 전파 경로이다. 최근 여러 각도의 동물야외 조사 및 실험동물을 이용한 연구를 토대로 AIDS환자에 대한 이 병원체의 전파가능성은 감염동물에서부터 전파가 가장 중요한 경로가 될 거라 보고되고 있다.

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