Note

Genital microsporidiosis in women with AIDS: A post-mortem study

Griselda Torres², Fernando Izquierdo³, Virginia Capó²,∗, Ledy X. López², María C. López², Daniel Limonta², Soledad Fenoy², Carmen Del Águila³, Fernando J. Bornay-Llinares⁴

² Department of Pathology, Institute of Tropical Medicine Pedro Kouri, Havana, Cuba
³ Department of Virology, Institute of Tropical Medicine Pedro Kouri, Havana, Cuba
⁴ Laboratory of Parasitology, Faculty of Pharmacy, University San Pablo-CEU, Madrid, Spain
⁵ Department of Parasitology, University Miguel Hernández, Alicant, Spain

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A B S T R A C T

Background: Microsporidiosis is a life threatening opportunistic infection of AIDS patients. The infection is usually restricted to specific anatomical areas, but could become systemic depending on the involved species. Genital microsporidiosis in female patients is rare.

Objective: To report genital microsporidiosis in female AIDS patients.

Methods: Tissues samples from the genital tract (ovary, fallopian tubes and uterus) of eight deceased women who died of wasting syndrome associated to AIDS and disseminated microsporidiosis at the Institute of Tropical Medicine Pedro Kouri were collected between 1997 and 2005. Using an indirect immunohistochemistry assay the microsporidia species involved in those cases were identified.

Results: We report several cases of microsporidal infection of the female genital tract. Six out of eight women with the disseminated form of the disease showed the presence of microsporidia in the genital tract. Encephalitozoon cuniculi and Encephalitozoon hellem were identified in the internal lining epithelium of the fallopian tubes and endometrium.

Conclusions: Microsporidia species could disseminate to other organs and become systemic in severe immunocompromised cases. To our knowledge this is the greatest number of female genital tract microsporidiosis cases so far reported in humans.

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R E S U M E N

Antecedentes: La microsporidiosis es habitualmente una enfermedad oportunistica fatal para los pacientes con sida y puede producir una infección localizada o sistémica en función de la especie infectante. La infección del tracto genital femenino por microsporidios ha sido escasamente reportada en la literatura.

Objetivos: Describir las especies de microsporidios en el tracto genital femenino.

Métodos: Se analizaron muestras de tejidos provenientes del aparato reproductor (ovario, trompa uterina y útero) de ocho mujeres fallecidas con síndrome de desgaste asociado al sida y microsporidiosis diseminada, en el periodo de 1997 a 2005 en el Instituto de Medicina Tropical Pedro Kouri. Para la identificación de las especies de microsporidios se utilizaron anticuerpos específicos mediante la técnica de inmunohistoquímica indirecta.

Resultados: Se describe la infección por microsporidios en el tracto genital femenino. De las ocho mujeres estudiadas con la forma diseminada de estos parásitos, seis presentaron microsporidios en el tracto genital. Se identificaron Encephalitozoon cuniculi y Encephalitozoon hellem en el epitelio de revestimiento de la luz de trompas de Falopio y en endometrio.

* Corresponding author.
E-mail address: vcapo@ipk.sld.cu (V. Capó).

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**Results**

Microsporidiosis is an opportunistic and life-threatening infection in AIDS patients and in severely immunocompromised patients. Microsporidiosis has been described in several anatomical locations. However, only one report of this infection affecting the female genital tract has been so far diagnosed. Microsporidia species are obligate intracellular parasites recently placed within the Kingdom Fungi. However, the available data are not conclusive and more analyses have to be conducted to validate those claims. Four species have been frequently reported infecting humans (i.e., *Enterocytozoon bieneusi, Encephalitozoon intestinalis, Encephalitozoon cuniculi*, and *Encephalitozoon hellem*). Microsporidiosis can be diagnosed using histological preparations, but monoclonal antibodies or molecular methods are required for the species identification. The proper identification of microsporidia species is essential to indicate the treatment.

**Materials and methods**

Between 1997 and 2005 eight women out of sixty evaluated patients were diagnosed *post-mortem* with disseminated microsporidiosis at the Institute of Tropical Medicine Pedro Kouri (IPK). These women had died with wasting syndrome and disseminated microsporidiosis associated to AIDS. *Post-mortem* tissues samples from ovary, Fallopian tubes and uterus were analysed and processed following standard histological techniques for the identification of microsporidia species described elsewhere. Rabbit polyclonal antibodies anti-*E. intestinalis, E. cuniculi* and *E. hellem*, at 1:1600 dilution and mouse monoclonal antibodies anti-*E. bieneusi* and anti-*E. intestinalis* at 1:1000 dilution were used as primary antibodies. Microsporidial IHC positive controls involved paraffin-included human tissues previously studied by transmission electron microscopy. Negative controls comprised both, necropsy tissues samples from immunocompetent subjects who died of causes other than microsporidiosis, and tissues samples of the eight evaluated women omitting the primary antibody to detect background staining. The presence of human cytoqueratine was used as an internal control to prove the good tissue condition after the fixation process.

**Discussion**

In this study, microsporidia spores were observed inside macrophages in several organs including the lymph nodes and vascular endothelium. The location of the spores at these specific sites suggests that this could be related with their propagation, as previously reported. Some authors proposed that mononuclear phagocytes may play an important role in the dissemination of the pathogen, by escaping from the intracellular degradation within naïve macrophages. Macrophages require activation signs of Th1 cells to increase their intracellular microbicidal effects. This has been shown to be hindered in AIDS patients, who have significantly low numbers of CD4+ T cell lymphocytes. Thus, it has been suggested that the infected macrophages may induce a cytokine gradient for the recruitment of additional macrophages that would become proliferating stores and vehicles for the dissemination of pathogenic microbes.

Another factor that may have influence in the dissemination of pathogens is the type of infecting microsporidia species. The two species found in this study, *E. cuniculi* and *E. hellem*, are related to the disseminated form of the infection. Although a crossed reactivity of the polyclonal antibodies used cannot be discarded, the possibility of co-infection with two microsporidia species may be possible as reported by others.

Only one case of microsporidia affecting the ovaries has been found in the revised literature. According to a report, microsporidia infection in HIV/AIDS patients has a moderate incidence in Cuba. Once antiretroviral therapy (ART) was supplied to AIDS patients in 2001, microsporidiosis has almost disappeared as cause of death. This impact can be attributed to the restoration of T cell-mediated immunity and to the possible direct antiparasitic activity of some components of ART (i.e., protease inhibitors).

Microsporidiosis have rarely been considered in the differential diagnosis of opportunistic infections in AIDS. However, an explanation to the relatively high number of cases found in our series may be related to the fact that autopsies are performed in our institution in 75% of all deceased patients. Therefore, the probability of finding microsporidia spores in this type of samples greatly increased the probabilities.
Conclusion

These findings suggest that microsporidia could disseminate to other organs in cases of severe immunodeficiency. The six studied patients represent the larger number of females with tubular genital tract involvement, so far reported.

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References

4. del Aguila C, Croppo GP, Moura H, Da Silva AJ, Leitch GJ, Moss DM, et al. Ultrastructure, immunofluorescence, western blot, and PCR analysis of eight isolates of Encephalitozoon (Septata) intestinalis established in culture from sputum and


