Asian Pacific Journal of Tropical Disease

journal homepage: http://www.apjtcm.com

Case report https://doi.org/10.12980/apjtd.7.2017D7-180

Meningeal hyperaemia and myocarditis in a caged rabbit with encephalitozoonosis: Case report and literature review

Davinson Chuka Anyogu*, Shodeinde Vincent Shoyinka, Augustus Uchechukwu Amadi

Department of Veterinary Pathology and Microbiology, University of Nigeria, Nsukka, Enugu State, Nigeria

ARTICLE INFO

Article history:
Received 3 Aug 2017
Received in revised form 30 Aug 2017
Accepted 26 Sep 2017
Available online 29 Nov 2017

Keywords:
Encephalitozoonosis
Meningeal hyperaemia
Myocarditis
Parasite
Rabbits

ABSTRACT

Over the years, encephalitozoonosis in rabbits has raised serious concern owing to the subclinical nature of the infection in most rabbits and the danger of zoonosis in immunocompromised persons. The disease has been diagnosed by clinical signs, histopathological examination and detection of the antibody in serum. The lesions have been described mainly in the brain, kidney and liver of infected rabbits. The present report documented additional lesions seen in a male rabbit presented to the Necropsy Unit of the Department of Veterinary Pathology and Microbiology, University of Nigeria, Nsukka for euthanasia. Following euthanasia, tissue samples from the rabbit were processed and stained with haematoxylin and eosin. The microscopic lesions were comprised of meningeal hyperaemia, myocarditis, chronic nonsuppurative granulomatous hepatitis, and *Encephalitozoon cuniculi* spores in the brain parenchyma. The study showed the importance of reporting new findings in order to elucidate the pathogenic mechanisms for the disease and to renew attention to its zoonotic potential.

1. Introduction

Encephalitozoonosis is the disease caused by *Encephalitozoon cuniculi* (*E. cuniculi*), a single-cell obligate intracellular parasite belonging to the phylum Microspora[1,2]. Although rabbit is the main host, a wide range of mammals are susceptible including rodents, carnivores, monkeys and humans[3-5]. The infection may be subclinical in affected hosts, but immunosuppression is associated with more devastating pathologies in the host. Serological surveys have revealed the occurrence of the infection in apparently healthy rabbits in different countries of the world[6]. Also, several reports have shown the occurrence of the disease in immunocompromised humans with or without HIV infection. Human encephalitozoonosis in people with immunodeficiency such as HIV/AIDS is accompanied by a range of pathologies including brain infection, renal failure, pneumonitis, sinusitis and granulomatous liver necrosis[7-9]. Encephalitozoonosis was classified by the National Institute of Allergy and Infectious Diseases as an emerging infectious disease[10].

In developing countries where rabbits are used for research, the occurrence of subclinical encephalitozoonosis in rabbits may, in addition to posing threat to researchers, interfere with the interpretation of results such as lesions in the tissues. Although lesions of encephalitozoonosis are well documented in literature, it is important to report new findings in order to fully understand the pathogenesis of the disease and to renew attention to its zoonotic potential. This is a case report of atypical central nervous system involvement and cardiac lesions as new findings in encephalitozoonosis in rabbits.

*Corresponding author: Davinson Chuka Anyogu, Department of Veterinary Pathology and Microbiology, University of Nigeria, Nsukka, Enugu State, Nigeria.
Tel: +2347036841871
E-mail: davinson.anyogu@unn.edu.ng
The journal implements double-blind peer review practiced by specially invited international editorial board members.

2. Case report

A 7-month-old male rabbit, weighing 2.4 kg, was presented to the Necropsy Unit of the Department of Veterinary Pathology and Microbiology, University of Nigeria, Nsukka for euthanasia. The rabbit was presented with severe ataxia and head tilt (Figure 1). The clinical signs were observed by the owner about 2 weeks before presentation. The owner isolated the rabbit from the herd immediately after the signs were observed. There were 40 rabbits in the herd including males and females of different ages and sizes.

Figure 1. Head tilt in rabbit with *E. cuniculi* infection.

The rabbits were kept in wooden house roofed with zinc, partitioned with wood, and the areas left open for ventilation and light were protected with wire mesh. They were fed with commercial pelleted feed (Vital®). The beddings and feeding troughs were in good sanitary condition. The owner had been in the business for 5 years. His customers ranged from high school and college teachers and students who use rabbits for teaching and research, to villagers who use rabbits for food. The present case was the first case with such severe illness in his rabbit farm.

Euthanasia was achieved by dropping the rabbit gently into a chloroform chamber. Euthanasia was smooth and lasted for 13 min. Necropsy was carried out by a ventral midline incision into the carcass from the mandible to the pubis[11]. Most of the visceral organs had no obvious gross lesions. However, there were multifocal pale areas on the liver. The brain was severely hyperaemic with the gyri flattened and sulci widened (indicating brain swelling and compression). Hematoma was found dorsally between the cerebellum and the cerebral hemispheres (Figure 2). Tissues were fixed in 10% neutral-buffered formalin for 48 h and routinely processed, sectioned at 5 μm, and stained with haematoxylin and eosin.

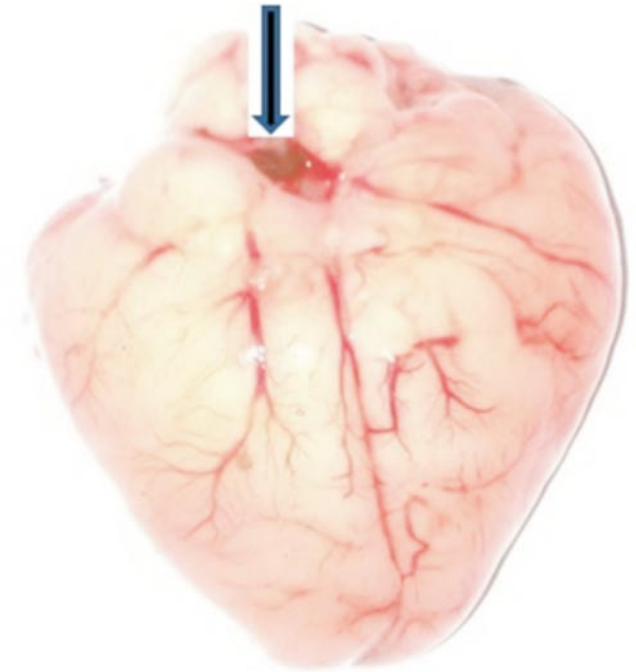

Figure 2. Haematoma (arrow) and severe hyperaemia of cerebral blood vessels.

Microscopically, there was meningeal hyperaemia with a few neutrophils within the meninges. The leptomeninges was lined by numerous mononuclear inflammatory cells (Figure 3A). There were vasculitis with mononuclear leukocytic perivascular cuffing and spores of *E. cuniculi* in the cerebral cortex (Figure 3B). Gliosis and neuronal degeneration/necrosis were evident in the brain section. *E. cuniculi* (parasitophorous vacuole) was identified in the region of a glial nodule amidst severe inflammation (Figure 3C). Lesion in the heart was in the form

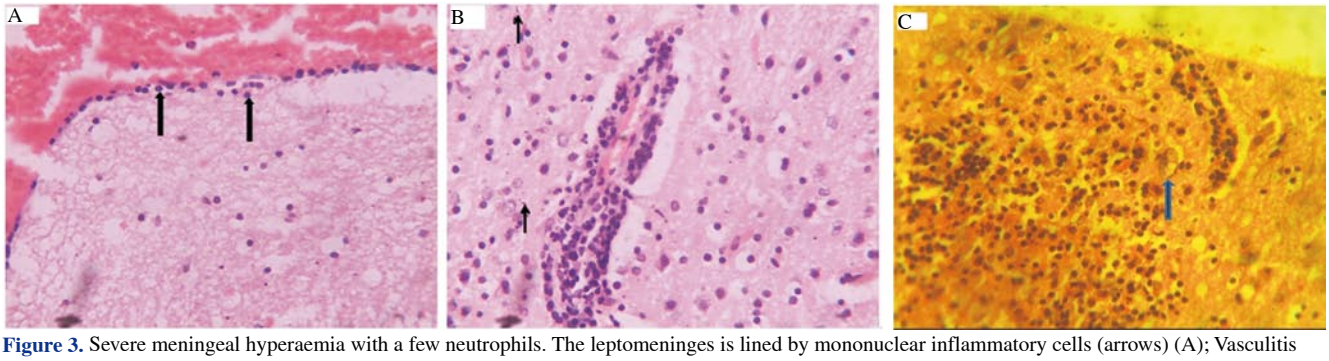

Figure 3. Severe meningeal hyperaemia with a few neutrophils. The leptomeninges is lined by mononuclear inflammatory cells (arrows) (A); Vasculitis with mononuclear leukocytic perivascular cuffing and spores of *E. cuniculi* in the brain parenchyma (arrows) (B); Glial nodule in the cerebral cortex with *E. cuniculi* parasitophorous vacuole (arrow) associated with severe inflammation (C) (H&E, 400×).

of a mild lymphocytic myocarditis (Figure 4). The liver lesions, which were predominantly periportal, included fibroplasia with fibrous connective tissue deposition (Figure 5), and focal areas of granulomatous reaction made up of lymphocytes, macrophages and epithelioid cells (Figure 6).

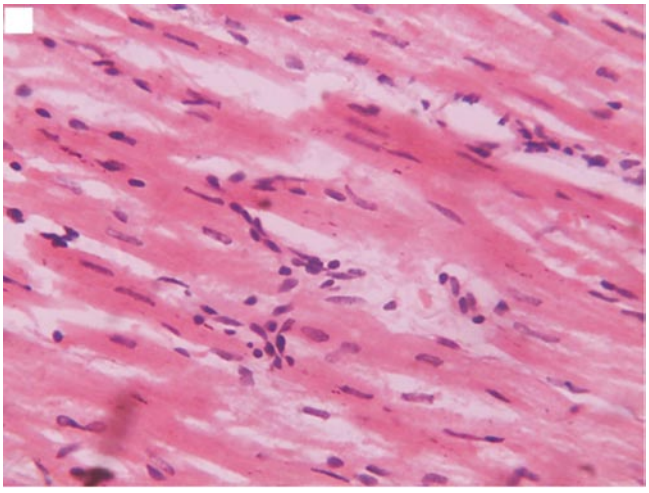

Figure 4. Mild lymphocytic myocarditis (H&E, 400×).

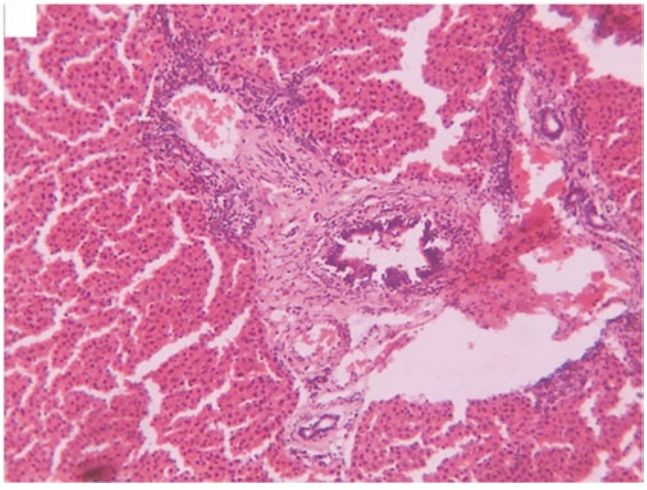

Figure 5. Portal area with perivascular and peribiliary fibroplasia (H&E, 100×).

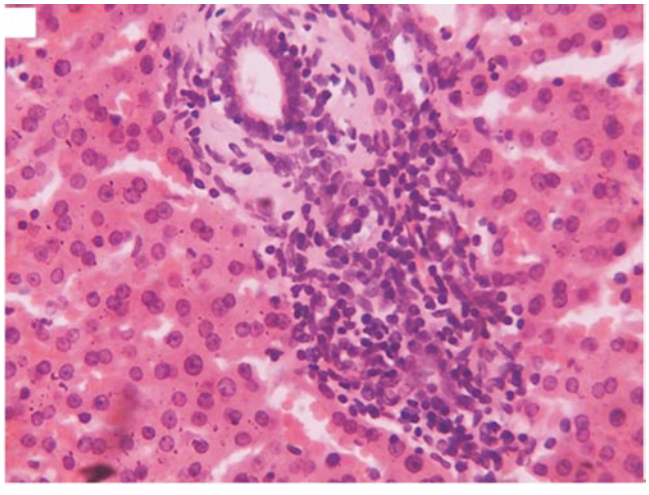

Figure 6. Granulomatous hepatitis in the portal area (H&E, 400×).

3. Discussion

E. cuniculi infection in rabbits could be transmitted via transplacental transmission, inhalation of spores, or ingestion of feed contaminated with infected urine[12]. In the case reported here, subclinical infection may have been present in the pen and later progressed to a full blown encephalitozoonosis. The infection could also have been originated from wild rats which enter the pen in search of feed pellets that drop off the troughs, thereby the open troughs and floor of the pen are contaminated with *E. cuniculi* spores shed in their urine and feces. Antibodies to *E. cuniculi* have been detected in wild rodents, indicating their role as reservoir hosts for this infection[13]. The spores of the parasite are also able to survive in the environment for a long period, facilitating their transmission between hosts[14].

Head tilting, ataxia, and granulomatous meningoencephalitis are the central nervous system alterations that are mostly reported in encephalitozoonosis in rabbits[15,16]. The occurrence of haematoma, vascular and meningeal hyperaemia in the present study may be due to the inflammation of the brain and meninges as well as vascular thrombosis caused by the parasite[17], or due to physical cranial trauma self-inflicted by the rabbit in response to the nervous disturbances. Occurrence of gliosis and glial nodules in the cerebral cortex was initiated by neuronal degeneration and necrosis and consequent recruitment of the glial cells for neuronophagia. The identification of the parasite in the brain section is one of the diagnostic methods for this disease[17].

Myocarditis has not been consistently reported in encephalitozoonosis. Its occurrence in the present study may suggest tissue penetration of the parasite via vascular damage. *E. cuniculi* has been detected in the intima of blood vessels suggesting its ability to penetrate vessel walls into tissues eliciting inflammatory response in the perivascular and interstitial areas[17].

Granulomatous hepatitis is a frequent occurrence in encephalitozoonosis in rabbits[17]. It has also been reported in human cases in AIDS patients[3]. The liver lesions in rabbits are associated with signs of hepatic failure[15]. The hepatic granulomatous reaction is usually periportal in location and also mostly characterized by lymphocytes, plasma cells, epithelioid and giants cells[18]. In this report, the periportal lesions included fibroplasia which depicted the chronic nature of the infection. This suggested that the rabbit may have been struggling with subclinical infection with chronic inflammatory

reaction prior to the dominance of the neurological manifestation of the disease.

In conclusion, encephalitozoonosis is a chronic devastating disease in rabbits. Its subclinical nature in most infected rabbits poses serious threat to immunosuppressed animals and humans. In the absence of serological and molecular diagnoses, clinical signs of paralysis and head tilting and the typical histopathological lesions in tissues, in addition to identification of the parasitophorous vacoule and spores in tissues, may be sufficient to diagnose the disease. Meningeal hyperaemia and myocarditis in this study were presented as additional features of this disease in rabbits.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgments

The authors are grateful to Mr. Obioma Egonu and all who assisted in necropsy and tissue processing.

References

[1] Abu-Akkada SS, El Kerdany EDH, Mady RF, Diab RG, Khedr GAE, Ashmawy KI, et al. *Encephalitozoon cuniculi* infection among immunocompromised and immunocompetent humans in Egypt. *Iran J Parasitol* 2015; **10**(4): 561-70.

[2] Hollyer JA, McGuinness E, Browers LC, Didier ES, Giudice C, Perl DP, et al. *Encephalitozoon cuniculi* - associated equine encephalitis: a case report. *J Equine Vet Sci* 2014; **34**(11-12): 1348-51.

[3] Didier ES. Microsporidiosis: an emerging and opportunistic in fection in humans and animals. *Acta Trop* 2005; **94**(1): 61-76.

[4] Abu-Akkada SS, Ashmawy KI, Dweir AW. First detection of an ignored parasite, *Encephalitozoon cuniculi*, in different animal hosts in Egypt. *Parasitol Res* 2015; **114**(3): 843-50.

[5] Meng X, Zheng J, He X, Jia H, Zhang Y. First characterization in China of *Encephalitozoon cuniculi* in the blue fox (*Alopex lagopus*). *J Eukaryot Microbiol* 2014; **61**(6): 580-5.

[6] Harcourt-Brown FM, Holloway HK. *Encephalitozoon cuniculi* in pet rabbits. *Vet Rec* 2003; **152**(14): 427-31.

[7] Weber R, Deplazes P, Flepp M, Mathis A, Baumann R, Sauer B, et al. Cerebral microsporidiosis due to *Encephalitozoon cuniculi* in a patient with human immunodeficiency virus infection. *N Engl J Med* 1997; **336**(7): 474-8.

[8] Levine DJ, Riley DJ, Jorgensen JH, McClain WD, Tio F, Visvesvara GS, et al. Key diagnostic features of granulomatous interstitial nephritis due to *Encephalitozoon cuniculi* in a lung transplant recipient. *Am J Surg Pathol* 2013; **37**(3): 447-52.

[9] Carhan A, Ozkan O, Ozkaya E. The first identification of *Encephalitozoon cuniculi* infection in an animal care worker in Turkey. *Iran J Parasitol* 2015; **10**(2): 280-5.

[10] Khan IA, Moretto M, Weiss LM. Immune response to Encephalitozoon cuniculi infection. *Microbes Infect* 2001; **3**(5): 401-5.

[11] King JM, Roth-Johnson L, Dodd DC, Newson ME. *The necropsy book: a guide for veterinary students, residents, clinicians, pathologists, and biological researchers*. 7th ed. New York: Cornell University; 2013, p. 1-259.

[12] Kunzel F, Joachim A. Encephalitozoonosis in rabbits. *Parasitol Res* 2010; **106**(2): 299-309.

[13] Meredith AL, Cleaveland SC, Brown J, Mahajan A, Shaw DJ. Seroprevalence of *Encephalitozoon cuniculi* in wild rodents, foxes and domestic cats in three sites in the United Kingdom. *Transbound Emerg Dis* 2015; **62**(2): 148-56.

[14] Moretto MM, Khan IA, Weiss LM. Gastrointestinal cell mediated immunity and the microsporidia. *PLoS Pathog* 2012; doi: 10.1371/journal.ppat.1002775.

[15] Meredith AL, Richardson J. Neurological diseases of rabbits and rodents. *J Exot Pet Med* 2015; **24**(1): 21-33.

[16] Leipig M, Matiasek K, Rinder H, Janik D, Emrich D, Baiker K, et al. Value of histopathology, immunohistochemistry, and real-time polymerase chain reaction in the confirmatory diagnosis of *Encephalitozoon cuniculi* infection in rabbits. *J Vet Diagn Invest* 2013; **25**(1): 16-26.

[17] Nast R, Middleton DM, Wheler CL. Generalized encephalitozoonosis in a Jersey wooly rabbit. *Can Vet J* 1996; **37**: 303-5.

[18] Fuentealba IC, Mahoney NT, Shadduck JA, Harvil J, Wicher V, Wiccher K. Hepatic lesions in rabbits infected with *Encephalitozoon cuniculi* administered per rectum. *Vet Pathol* 1992; **29**(6): 536-40.