

## Case Report

# Clinical evolution of cerebral coenurosis from invasive to chronic infection in sheep and a goat

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### Abstract

This survey describes the evolution *in vivo* of *Coenurus cerebralis* in small ruminants. At presentation, neurological signs and cerebrospinal fluid (CSF) features were suggestive of multifocal or diffuse inflammatory reaction. Magnetic resonance imaging (MRI) captured the transition between the invasive and quiescent phase of the infection, revealing the concurrent presence of meningitis and small cysts. During the quiescent phase, in all animals, neurological symptoms disappeared, and cerebrospinal fluid was unremarkable while cysts grew progressively. Subsequently, the onset of neurological symptoms coincided with MRI signs of diffuse or localized increase of intracranial pressure, as confirmed by direct intracranial pressure measuring. All the animals had an excellent post-surgical recovery. This is the first report describing the evolution of coenurosis *in vivo*. Sequential imaging allowed describing interesting such as the death of some coenuri and different parasite growth rate in the same host.

**Key words:** Coenurosis evolution; small ruminants; MRI; sheep; *Taenia multiceps*

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Cerebral coenurosis is a disease of small ruminants bred with extensive methods [1,2]. The adult worm inhabits the small intestine of canids while the larval stage develops in the central nervous system (CNS) of ruminants [3,4]. The disease occurs in acute, quiescent, and chronic forms [5-7]. Though coenurosis can be controlled by anthelmintic treatment of dogs and by correctly disposing carcasses [8], surgical removal of cysts is the only effective therapy to date. Recent surveys have shown that the correlation between clinical signs and location of the cyst can be limited [9-12]. Magnetic resonance imaging (MRI) and computed tomography (CT) allow for the diagnosis and localization of and the cyst [13] and its surgical removal, with recovery rates of 75%–90% [12-14]. This article describes the clinical evolution of cerebral coenurosis from invasive to chronic infection in three small ruminants who were naturally infected.

Two Sarda sheep and one Maltese goat, all males, 4 months of age, weighting 9–14 kg, were examined because of neurological signs. Physical and neurological examination revealed weight loss, unstable gait, loss of herd instinct, head tremors, obtunded mental status, and bilateral reduction of the menace reaction in all animals. The goat had pyrexia

(40.2°C) and postural reaction deficit in the four limbs. The neuro-anatomic localizations were multifocal (sheep) and diffuse (goat) in the forebrain and brainstem. Complete blood count and biochemistry profile were unremarkable. General and neurological exams, brain MRI, and cerebrospinal fluid (CSF) collection were performed with animals under general anaesthesia (D1) and repeated at days 30 (D30), 90 (D90), 120 (only for the goat) (D120), and 240 (D240). The volume of each cyst prior to its removal was determined using an imaging software as described elsewhere [12], and a morphological and biomolecular identification of the parasites was performed [15].

MRI was performed using a 0.23 Tesla unit (0.23 T MRI scanner, Paramed Medical System, Genova, Italy) over at least two planes of space, from the atlas to the nasal cavity, using a knee coil, with animals in ventral recumbency as described elsewhere [11,12].

CSF was collected by cerebellomedullary cisternal puncture. Macroscopic appearance (color and turbidity), specific gravity, total protein concentration, total nucleated cell count (TNCC), and cytological microscopic examination of CSF were recorded for each animal.

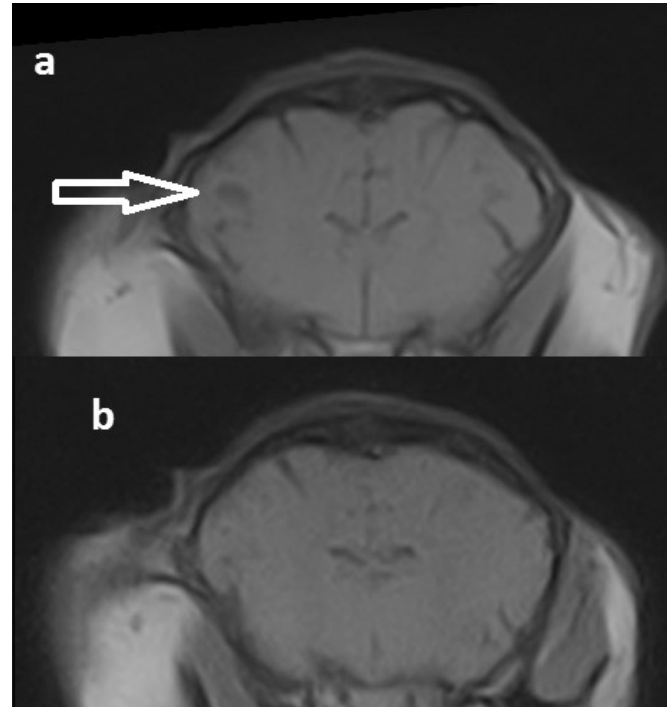
Intracranial pressure (ICP) was measured in each animal before the cysts were removed. Fiberoptic pressure transducer (Codman Microsensor 2005-2011, Codman & Shurtleff, Inc., Raynham, USA) was inserted intraparenchymally through a 0.5 cm burr hole drilled in the parieto-temporal skull opposite the cyst. Even though no experimental survey was carried out on the animals, ethical approval for the study was obtained by the ethical committee of Sassari University, Italy (OPBSA), protocol 14099, 14/09/2014.

Brain MRI revealed rounded and ovoid-shaped cysts, hypointense in T1W and hyperintense in T2W sequences, with different diameters, sharp margins, and not causing mass effect, perilesional edema, or hemorrhage at D1. Cysts lay within or near the meningeal layers, both in the forebrain and in the cerebellum (Table 1). Sheep 1 had four cysts: one in the left parietal lobe, one close to the left side of the falx cerebri, one on the right temporal lobe, and one on the right frontal lobe; the comprehensive cyst volume was 0.48 cm<sup>3</sup>. Sheep 2 had two cysts: one on the left frontal lobe and one on the right temporal lobe; the comprehensive cyst volume was 1.18 cm<sup>3</sup>. The goat had three cysts: one in the right parietal lobe, one in the left side of the cerebellum, and one in the fourth ventricle; the comprehensive cyst volume was 0.3 cm<sup>3</sup>. CSF was in the normal range in sheep 2. TNCC was 28/μL and 39/μL, respectively, in sheep 1 and in the goat; it was characterized by mild mononuclear pleocytosis with 72% lymphocytes, 16% monocytoïd/macrophage cells and 12% eosinophils in the sheep, and mild mononuclear pleocytosis with 80% lymphocytes and 20% monocytoïd/macrophage cells in the goat. CSF total protein, specific gravity value, and Pandy test

results were in the normal ranges in all the examined animals.

Based on the clinical anamnesis and examination, MRI, and CSF findings, coenurosis by *T. multiceps* was diagnosed in the three examined animals. At D30, all the animals showed a marked improvement of neurological signs. Brain MRI revealed that cysts increased in volume without mass effect, perilesional

**Figure 1.** Transverse T1W images from sheep 2 at day 1 (a) and day 30 (b).



Note the cyst in the right temporal lobe (white arrow) and its disappearance in the subsequent study.

**Table 1.** Cyst progression in each animal.

Subject	Cyst number, distribution	Day 1	Day 30	Day 90	Day 120	Day 180	Day 240
Sheep 1	Cyst number	4	4	4		4	
	Cyst on left parietal lobe (cm <sup>3</sup> )	0.17	0.7	2.4		6	
	Cyst on left side of falx cerebri (cm <sup>3</sup> )	0.15	1.3	5.5		9.3	
	Cyst on right temporal lobe (cm <sup>3</sup> )	0.15	1.08	5.1		46.7	
	Cyst on right frontal lobe (cm <sup>3</sup> )	0.0075	0.09	0.3		1.1	
	Comprehensive cyst volume (cm <sup>3</sup> )	0.48	3.17	13.3		63.1	
Sheep 2	Cyst number	2	1	1		1	1
	Cyst on left frontal lobe (cm <sup>3</sup> )	0.06	0.19	2.3		6.63	16.61
	Cyst on right temporal lobe (cm <sup>3</sup> )	1.12	0	0		0	0
	Comprehensive cyst volume (cm <sup>3</sup> )	1.18	0.19	2.3		6.63	16.61
Goat	Cyst number	3	3	3	3		
	Cyst on right parietal lobe (cm <sup>3</sup> )	0.1	0.6	5.55	7.4		
	Cyst on left side cerebellum (cm <sup>3</sup> )	0.06	0.3	1.5	1.75		
	Cyst in the fourth ventricle (cm <sup>3</sup> )	0.13	0.7	2.7	3.62		
	Comprehensive cyst volume (cm <sup>3</sup> )	0.3	1.6	9.8	12.8		

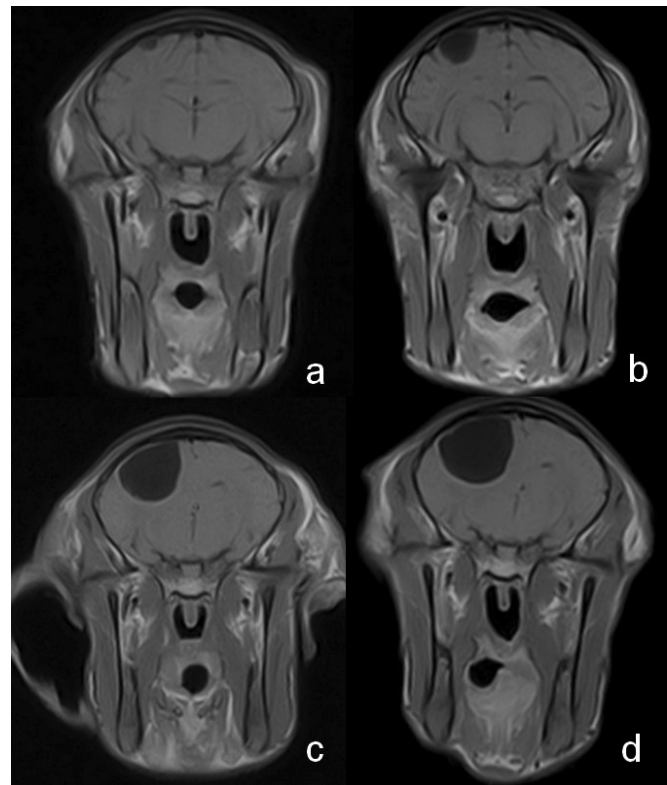
edema, or contrast enhancement (Table 1); the comprehensive cyst volume was 3.17, 0.19, 1.6 cm<sup>3</sup>, respectively, in sheep 1, 2, and the goat. The complete disappearance of the cyst located in the right temporal lobe was observed in sheep 2 (Figure 1). CSF cytological examination was in the normal range in all the subjects. At D90, neurological examination was unremarkable in all ruminants. Brain MRI showed even larger cysts causing mild to moderate mass effect: the comprehensive cyst volume was 13.3, 2.3, 9.8 cm<sup>3</sup>, respectively, in sheep 1, 2, and the goat. Neither perilesional edema nor contrast enhancement were observed (Table 1). CSF cytological examination from both sheep was in the normal range. CSF was not performed in the goat due to the presence of the growing cysts in the caudal fossa. A deterioration of neurological signs was observed in the goat at D120. Stuporous mental status, menace reaction reduction on the left eye, and postural reaction deficit in the four limbs were observed in the goat. On brain MRI, the cyst localized in the cranial fossa caused mild deviation of the falx cerebri and mild compression of the lateral ventricle. The caudal fossa cysts caused severe obstruction and secondary dilatation of the fourth ventricle as well as severe compression and deviation of the brain stem and cerebellum (Figure 2). The comprehensive cyst volume was 12.8 cm<sup>3</sup> (Table 1). The surgical removal of the cysts was performed soon after the MRI examination. At D180, neurological evaluation was in the normal range in sheep 2, while sheep 1 showed obtunded mental status and postural reaction deficit in the four limbs. Brain MRI showed that the four cysts had increased in volume, causing effacement of the sulci, severe mass effect, ventricle system compression, and bilateral mild dilatation of the olfactory recesses. Moreover, the cyst initially located in the right temporal lobe passed below the tentorium, reaching the caudal fossa, causing severe compression and deviation of the cerebellum; the comprehensive cyst volume was 63.1 cm<sup>3</sup> (Table 1). MRI suggested severe high ICP, and hence CSF was not collected. The animal underwent surgical therapy soon after MRI examination.

At D240, sheep 2 shown depressed mental status and menace reaction reduction in the right eye. At MRI, the cyst had increased in size (16.61 cm<sup>3</sup>), causing moderate to severe mass effect on the left frontal lobe, suggesting localized increase of intracranial pressure (Figure 3) (Table 1). CSF was not collected, and the cyst was surgically removed.

ICP values measured were 10, 32, and 5 mmHg, respectively, for the goat, sheep 1, and sheep 2 (normal

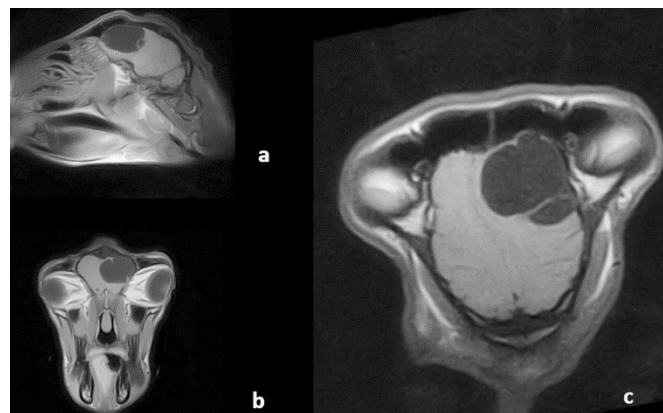
range 1–12 mmHg). Each cyst was grasped, the cystic fluid aspirated, and the collapsed cyst removed through gentle traction of its wall. Suture was performed as routine. Animals received antibiotic and anti-inflammatory therapy for the following 7 days. The neurological outcome was considered excellent at days 8, 12, and 30 post-surgery, respectively, for sheep 1, the

**Figure 2.** Transverse T1W images from the goat at day 1 (a), day 30 (b), day 90 (c), and day 120 (d).



An example of the growth of the cyst over time.

**Figure 3.** Sagittal (a), transverse (b), and dorsal (c) images from sheep 2 at day 240.



Note the cyst on the left frontal and parietal lobes. Images suggest localized increase of intracranial pressure.

goat, and sheep 2. The morphometrical features of the parasites were consistent with those of *T. multiceps* described by Leske in 1780, also confirmed by DNA sequencing of the *cox1* gene [15].

The present study describes, for the first time, the clinical evolution *in vivo* of cerebral coenurosis from invasive to chronic infection, documented with MRI and CSF findings. History and clinical signs suggested a multifocal or diffuse inflammatory reaction ascribable to the acute phase of coenurosis. Transient pyrexia and nervous dysfunction have been related to the migration of immature metacestode in the brain [16]. MRI and CSF revealed the concurrent presence of meningitis and small cysts, highlighting the transition from acute to the early quiescent phase. Sequential MRI showed the growing pattern of the metacestode. During first MRI, all the cysts were located near or in the meningeal layers. Indeed, oncosphere migrates through the meningeal bloodstream and then reaches different sites, where it develops into a mature cyst [17]. The predilection of coenuri for the subarachnoid space seems to facilitate the nourishment of the cyst by cerebrospinal fluid [18]. Between the first and the second MRI (D1–D30), one cyst (0.06 cm<sup>3</sup> in diameter) disappeared without leaving residual lesions as hemorrhage or scar tissue. Post-mortem examinations in acute coenurosis have demonstrated necrotic lesions in the brain characterized by immature metacestode, 2 to 4 mm diameter, surrounded by hemorrhagic foci up to 2 mm wide [17]. The principal immune response against taeniid cestodes in their intermediate hosts is antibody and complement mediated lysis of the early developing oncosphere [19-21]; these features have been used to develop recombinant antigens for vaccination against *T. multiceps* in sheep [5,6]. However, complete cystic resorption is described here for the first time. During the quiescent phase of infection, neurological symptoms disappeared in all animals, while a silent, progressive enlargement of the cysts was highlighted in MRI by the absence of perilesional edema, hemorrhage, and peripheral enhancement [22]. At this stage, CSF cytological examination was also in the normal range. As previously reported [23], normal CSF does not always allow the exclusion of the presence of chronic coenurosis. Different authors report that this is due to the isolation created by the coenuri against host tissues and immunity system within the nervous system [8,15].

Coenuri were found mainly in the cortex (80.6%), cerebellum (7.3%), and thalamus (5.7%) [7], while coenuri in other localizations were sporadic [7]. The cortex distribution can be a consequence of its higher

biomass with respect to other CNS structures, particularly in the middle cortex. The different growth rate observed in the same animal probably reflects both the relative opportunity for the parasite to reach these regions and the different ability to get nourishment [7]. Parasitic cysts behave as slow-growing and low-pressure lesions in brain tissue, allowing the adjacent structures to adapt to the slowly increasing pressures [12]. In this way, the parasite may reach considerable volumes before clinical signs appear [24]. Other authors [14] have suggested a correlation between symptomatology and raised ICP caused by the size of the cyst. The same correlation has been reported in humans with cerebral hydatid cysts [25]. In all the animals, the onset of neurological symptoms coincided with MRI signs of diffuse or localized increase of ICP. Specifically, in sheep 1, both MRI and direct ICP findings suggested a diffuse ICP increase in the forebrain. In sheep 2 and in the goat, MRI and direct ICP features were suggestive of localized increase of ICP in the forebrain and the caudal fossa, respectively. The presence in ruminants of a clear bony division between cranial and caudal fossa may explain why the changes in pressure in one cavity may not be reflected on the ones nearby. Neurological signs were observed between 120 and 240 days from the first clinical examination. As has been previously reported, the deterioration of the clinical condition seems to change more rapidly when the cyst is localized in the caudal fossa [14,26]. Given that the growing cyst can determine bone adaptive morphological modification, it is likely that these changes are less effective when the cyst is located in the caudal fossa [12]. The rapid clinical recovery after surgical removal of the cyst suggests that symptomatology could depend mainly on diffuse or localized increase in ICP.

The present survey, thanks to the sequential use of MRI, unveiled some interesting aspects and details of the clinical evolution of coenurosis in sheep and goats. The complexity of the clinical pictures above suggests that MRI, CSF, and ICP should be taken into account prior to surgical treatment of coenurosis.

#### Authors' Contributions

MAE, MLM, and AV conceived the study and drafted the manuscript. ESP, VM, RD, and LM performed the animal surgery, and RZ performed the CSF study. CT, APP, and AS collected parasites after surgery and performed the morphological and biomolecular identification. All authors read and approved the final version of manuscript.

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**Conflict of interests:** No conflict of interests is declared.