Clinicopathologic observations on *Coenurus cerebralis* in naturally infected sheep*

O. Ozmen[1], S. Sahinduran[2], M. Haligur[1], K. Sezer[2]

[1]Department of Pathology and [2]Internal Medicine, University of Akdeniz, Turkey

Abstract

Twelve sheep from 7 different flocks consisting of approximately 150–250 animals each were diagnosed with coenurosis caused by the larval stage of *Taenia multiceps*. Ataxia, incoordination, drowsiness, hind leg paralysis and coma were the most prominent clinical symptoms. Monocytosis and lymphocytosis were observed upon hematological examination. Creatin kinase (CKBB) levels of the animals varied between 421 and 495 U/l. Cysts were commonly localized in the parietal and frontal lobes of the brain and in the cerebellum. In two cases, cysts were found on the lumbar aspect of the medulla spinalis. Symptoms were related to cyst localization. Depression, tilting of the head either to the right or left and head pressing were seen when cysts were located in the cerebrum. Incoordination and hyperexcitability were noted if the cysts were involved with the cerebellum and when located in the spinal cord, hind leg paralysis was the typical clinical sign. On microscopic examination, atrophy was observed in the central nervous system (CNS) organs due to pression by the bladderworms. Nonpurulent meningoencephalitis with perivascular cuffings were the most common histopathological findings. In periodic acid Schiff staining (PAS), positive reaction was observed in protoscoleces. Neurons were the most affected cell type when stained by the Klüver Barrera method. This method also showed that in the CNS, *Coenurus cerebralis* caused a prominent glial reaction. When parasites were localized in the nervous system treatment was impossible. Animals without neurologic sings were treated with praziquantel (Tenikur tablet-Topkim A.S.) 50–100 mg/kg/day for three days.

Keywords: *Coenurus cerebralis*, clinical findings, pathology, treatment, sheep.

Klinisch-pathologische Beobachtungen zu *Coenurus cerebralis* in natürlich infizierten Schafen

Bei 12 Schafen aus 7 unterschiedlichen Herden mit je ungefähr 150–200 Tieren wurde Coenurose verursacht durch Larvalstadien von *Taenia multiceps (Coenurus cerebralis)*, diagnostiziert. Die auffälligsten klinischen Erscheinungen waren Ataxie, Inkoordination, Schläfrigkeit, Nachhand-Lähmung und Koma. Blutuntersuchungen ergaben Monozytose und Lymphozytose. Die Werte der Creatinkinase (CK) der Tiere schwankten zwischen 421 und 495 U/l. Zysten wurden mehrheitlich im Lobus parietalis und frontalis des Grosshirns und im Kleinhirn lokalisiert. In zwei Fällen wurden die Zysten im Rückenmark der Lendenwirbelsäule gefunden. Die klinischen Symptome konnten auf die Zysten-Lokalisationen zurückgeführt werden. So wurde Niedergeschlagenheit, Kopfschiefhaltung nach der betroffenen Seite und Pressen mit dem Kopf bei Zysten im Grosshirn beobachtet. Inkoordination und Überempfindlichkeit auf externe Reize wurden festgestellt wenn die Zysten das Kleinhirn involvierten, während bei Lokalisation in der Wirbelsäule die typischen klinischen Erscheinungen aus Gliedmassen-Paralyse bestanden. Die mikros-kopische Untersuchung ergab eine Atrophie im zentralen Nervensystem (ZNS), die durch Druck der Coenurus hervorgerufen wurde. Histopathologisch war eine nicht-eitrige Meningoen-zephalitis mit perivaskulären Manschetten der häufigste Befund. Mit der PAS (periodic acid Schiff)-Färbung wurde eine positive Reaktion der Protoskolices beobachtet. Neuronen waren der am häufigsten betroffene Zelltyp mit der kombinierten Zell- und Markscheidenfärbung nach Klüver- Barrera. Diese Färbung zeigte auch, dass *Coenurus cerebralis* im ZNS eine erheblich gliale Reaktion hervorruft. Wurden die Parasiten im ZNS vorgefunden, war keine Behandlung möglich. Tiere ohne neurologische Symptome wurden während 3 Tagen mit 50–100 mg/kg KG/Tag Praziquantel (Tenikur®-Tabletten, Topkim) behandelt.

Schlüsselwörter: *Coenurus cerebralis,* klinische Erscheinungen, Sektion, Behandlung, Schafe

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Introduction

Coenurus cerebralis, the larval stage of a the dog tapeworm Taenia multiceps is the causative agent of the central nervous system (CNS) disease of sheep known as "gid" or "sturdy". The eggs may also infect other herbivorous animals and rarely also carnivores, monkeys and humans. Symptoms in sheep indicating central nervous involvement depend upon localization of the metacestode in the brain or spinal cord and vary from incoordination to paralysis. The larvae wander through the body before localizing in nervous tissue in form of cysts, which reach a diameter of 50 mm or more. Each cyst is filled with clear fluid and contains as many as 500 scolices, visible through the thin walls of coenurus with a germinal layer and the ability to produce many scolices (Blood and Rodostits, 1989; George, 1990; Storts, 1995; Jones et al., 1997). The clinical signs of the disease develop when the CNS of the sheep is invaded by the larval stage or metacestode of the tapeworm *Taenia multiceps* (Edwards and Herbert, 1982). Adult stages of *Taenia multiceps* occur in the small intestine of dogs and wild carnivores, and can reach lengths of up to 1 meter. Sheep become infected by the ingestion of eggs. The oncosphere hatches and penetrates the intestinal wall and is carried by the blood stream to various parts of the body, including the central nervous system, where the coenurus develops. It is filled with fluid and semi-transparent with multiple scolices which burst from the inner surface of the cyst wall. The parasite possesses asexual multiplication, forming hundreds of daughter protoscoleces (Edwards et al., 1979; Willis and Herbert, 1984).

Coenurosis can occur in both an acute and a chronic disease form. Acute coenurosis occurs during the migratory phase of the disease, usually about 10 days after the ingestion of large numbers of tapeworm eggs. Young lambs aged 6–8 weeks are most likely to show signs of acute disease. The signs are associated with an inflammatory and allergic reaction. There is transient pyrexia and relatively mild neurological signs such as listlessness and a slight head aversion. Occasionally the signs are more severe and the animal may develop encephalitis, convulse and die within 4–5 days (Skerrit, 1991). Chronic coenurosis typically occurs in sheep of 16–18 months of age. The incubation time varies from 2 to 6 months. The earliest signs are often behavioral, with the affected animal tending to stand apart from the flock, and to react slowly to external stimuli. As the cyst grows, the clinical signs progress to depression, unilateral blindness, circling, altered head position, incoordination, paralysis and recumbency (Bussell et al., 1997). Unless treated surgically, the animal will die after recumbency (Skerritt, 1991). The aim of this study was to examine clinical and pathological changes on coenurosis in naturally infected sheep.

Animals, Materials and Methods

Twelve sheep from 7 different flocks, each comprising approximately 150–250 animals, were brought to the Veterinary Medical Teaching Hospital with neurological symptoms during the period of February 2001 until February 2004. Because of the poor prognosis, they were presented to Department of Pathology for euthanasia and diagnosis. Ten animals had nervous symptoms such as depression, tilting of the head either to the right or left, head pressing, incoordination, hyperexcitability or paralysis, and two animals were comatose. Blood samples were taken from all animals prior to euthanasia. MS9 blood counting equipment was used for haematological analysis of the blood drawn in EDTA tubes. Creatin kinase BB levels were analysed in serum samples using Vet-Test equipment and reagents.

After euthanasia, the central nervous system organs (especially brain, cerebellum and medulla spinalis) were removed and examined grossly. Tissue samples taken from the CNS during necropsy were fixed in 10% buffered formaldehyde. Using standard methods, tissues were blocked in paraffin and cut to 5µ thickness. Tissue sections were stained with Hematoxylin-Eosin (HE), the Klüver-Barrera method (KBM) and the periodic acid Schiff method (PAS) and examined microscopically (Luna, 1968).

Results

The age of the affected sheep ranged from 1–5 years (mean 2 years) and all flocks had a history of more than one year of disease. Mortality rate varied among flocks from 8%–15%. Clinically, ataxia, drowsiness, hind leg

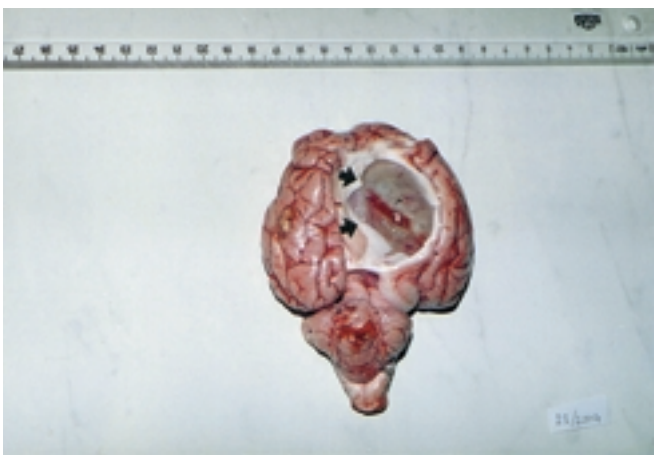

Figure 1: Parietal lobe localization of Coenurus cerebralis.

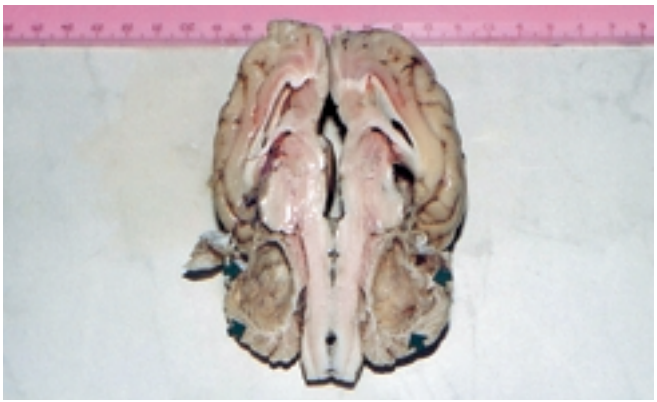

Figure 2: Cerebellar localization of lesions due to Coenurus cerebralis.

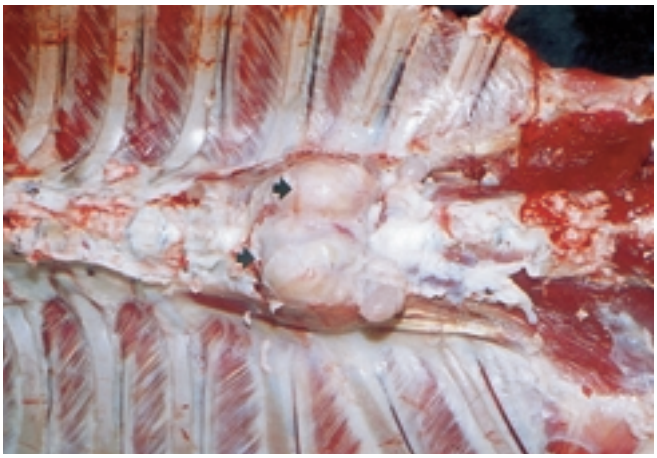

Figure 3: Localization of metacestode at the lumbal part of the medulla spinalis.

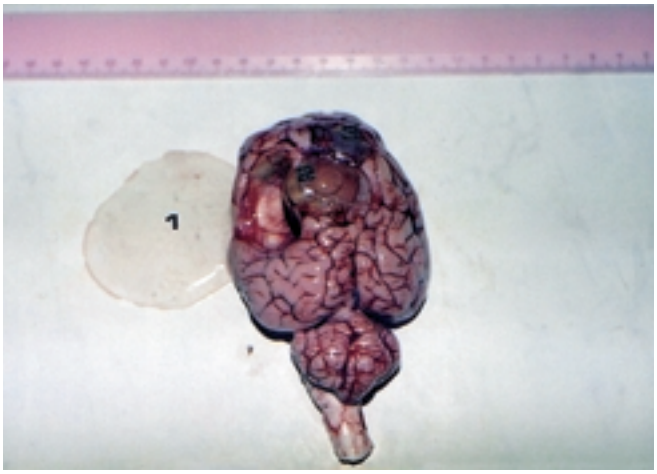

Figure 4: Three specimens of Coenurus cerebralis in the brain.

paralysis, torticollis, loss of balance, twirling and coma were the most prominent findings. A relationship was observed between cyst location and clinical symptoms. Depression, tilting of the head either to the right or left, and head pressing were seen when cysts were located in the cerebrum. Incoordination and hyperexcitability were seen if the cysts were involved with the cerebellum. When cysts were located in the spinal cord, hind leg paralysis was the typical clinical sign. Creatin kinase (CKBB) levels varied between 421 and 495 U/l. Hematological observations revealed monocytosis and lymphocytosis. Monocytes of the affected animals were 9.2%–9.7% and lymphocytes between 79% and 87%.

In all but two cases, the Coenurus was localized in the parietal and frontal lobes of the brain and in the cerebellum (Fig. 1 and 2). The parasite was localized on the lumbar medulla spinalis in two cases (Fig. 3) while in others multiple Coenurus could be observed (Fig. 4). The main clinical symptom was hind leg paralysis, if the parasite was in the medulla spinalis. Cysts were mostly located in the cerebral cortex and in one case they were found in the cerebellum. The diameters of the bladderworms ranged from 2–7 cm, with a mean of 4 cm. Microscopically, protoscolices were found to be alive and in some cases purulent exudate was seen in the bladder. Microscopically, atrophy was observed in CNS organs due to metacestodes. Histopathology revealed severe inflammation around the cysts. Usually, nonpurulent meningoencephalitis with perivascular cuffings were observed. The reaction was chronic and the most prominent inflammatory cells were lymphocytes and monocytes. Foreign body giant cells (Fig. 5)

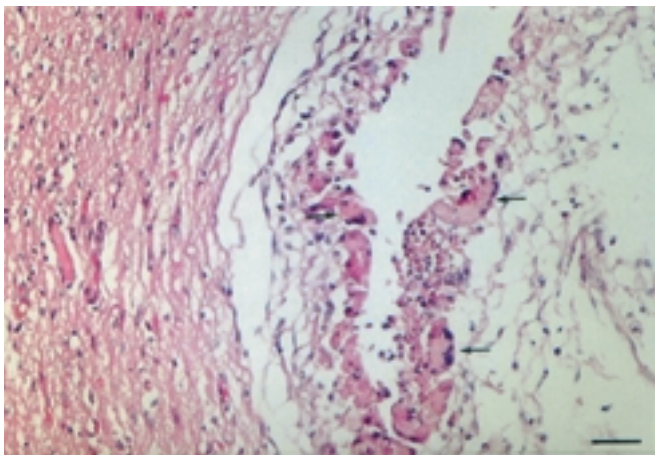

Figure 5: Foreign body giant cells around the metacestode (Hematoxylin-Eosin, bar = 60 µ).

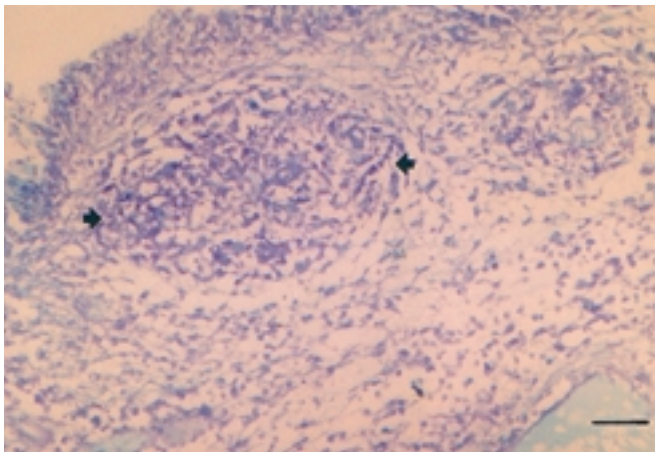

Figure 6: Glial reaction in the brain (Klüver-Barrera, bar = 60 µ).

were also seen around the cysts. Protoscoleces were seen as slight eosinophilic granular structures, but they were prominent in PAS staining sections. Protoscolices were a bright pink color, and PAS positive. Glial cells were found to be the most sensitive CNS cells to Coenurus infection by Klüver-Barrera method staining (Fig. 6). This technique also indicated that glial cell reaction was more prominent than lymphocytic reaction. Protoscoleces were stained purple by KBM. When parasites were localized in the nervous system treatment was impossible. Animals without neurological sings were treated with praziquantel (Tenikur tablet-Topkim A.Ş.) 50–100 mg/kg/day for three days. New Coenurus cases were not observed in these flocks during the six month period.

Discussion

Coenurus occurs in sheep and is usually localized in the brain or spinal cord forming a large cyst filled with liquid and many floating scolices. It may reach 5cm or more in diameter. The intermediate hosts comprise a number of herbivorous species, in which the cysts develop in the brain and spinal cord. This causes a disease called 'staggers', which affects the balance of the animals (Edwards et al., 1979; Willis and Herbert, 1984; Blood and Rodostits, 1989; George, 1990; Storts, 1995; Jones et al., 1997). Bussell et al. (1997) reported posterior paralysis due to *Coenurus cerebralis* in the lumbar spinal cord. Paralysis caused by lumbar localization of the bladderworms was also seen in two animals in the present study. Because similar clinical symptoms can be seen in different CNS diseases such as Listeriosis, differential diagnosis in this study was made by necropsy and histopathological findings. Typical cysts were seen in all sheep with neurological symptoms. Gogoi et al. (1992) reported a relationship between cyst localization and clinical symptoms, similar what was also found in our study. Acute meningoencephalitis in lambs may occur as a consequence of migration of large numbers of immature stages of the parasite. Chronic symptoms develop as a result of increased destruction of brain and spinal cord tissue as the Coenurus grows (Edwards and Herbert, 1982). In this study all of the animals were at least one year of age without any signs of an acute reaction.

In the literature there are no reports on blood parameters with Coenurus infection. Monocytosis and lymphocytosis observed in this study may have been caused by a chronic inflammatory reaction of the CNS. Creatine kinase BB is a specific enzyme marker for CNS lesions and the highly elevated serum levels found in all sheep examined are attributable to CNS damage. Histopathological examination of the lesions was consistent with a chronic nonpurulent infection. Marked tissue reactions were observed around the metacestode. PAS- positive staining was also observed in protoscolices and the Klüver-Barrera method proved very suitable for studying CNS tissue and neuronal reactions. In agreement with results of Storts (1995), we also found the neurons in the cerebrum, cerebellum and medulla spinalis to be the most sensitive cells to *Coenurus cerebralis*.

In some countries *T. multiceps* is very rare. For example coenurosis has not been reported in sheep in the United States for several decades (Jones et al., 1997). In Jordania, for example, Abo-Shehada et al. (2002) reported a prevalence of the disease between 3–10%. *T. multiceps* has an indirect cestode life cycle. Gravid proglottides shed by dog faeces burst and the eggs are disseminated in the environment and will contaminate pastures and water supplies as well. When ingested by sheep (or other ruminants), the eggs hatch and the hexacanths develop into metacestodes, which penetrate the intestinal wall and enter the blood stream. Only those parasites that reach the nervous system will become fully developed Coenurus in 7 to 8 months (Edwards et al., 1979; Willis and Herbert, 1984). The feeding of sheep carcasses to dogs may cause a new infection thus perpetuating the life cycle. Unfortunately, many owners in Turkey still feed their dogs infected sheep carcasses and contribute to the frequent occurence of this disease. However, the real prevalence of coenurosis is difficult to assess, because farmers as well as veterinary surgeons often send all animals with central nervous symptoms for slaughter without any confirmation of the diagnosis made.

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Observations clinico-pathologiques de *Coenurus cerebralis* chez des moutons naturellement infectés

Des cas de coenurose causés par des stades larvaires de *Taenia multiceps (Coenurus cerebralis)* ont été diagnostiqués chez 12 moutons provenant de 7 troupeaux différents, troupeaux comprenant chacun 150 à 200 animaux. Les symptômes cliniques les plus marquants étaient l'ataxie, l'incoordination, la somnolence, la paralysie de l'arrière train et le coma. Les examens sanguins montraient une monocytose et une lymphocytose. Les valeurs de la créatinekinase (CK) oscillaient entre 421 et 495 U/l. Les kystes ont été localisés principalement dans les lobes pariétaux et frontaux du cerveau ainsi que dans le cervelet. Dans deux cas, les kystes ont été trouvés dans la moelle épinière en région lombaire. Les symptômes ont pu être mis en relation avec la localisation des kystes; ainsi l'abattement, le port de tête penché en direction du côté affecté et le fait de pousser au mur avec la tête ont été observés lors de kystes situés dans le cerveau. L'incoordination et l'hypersensibilité face aux stimuli externes ont été constatés lorsque les kystes touchaient le cervelet alors que les localisations médullaires entraînaient les signes typiques de paralysie des membres. L'examen microscopique révélait une atrophie du système nerveux central causé par la pression. Une méningo-encéphalite non purulente avec formation de manchettes péri-vasculaires était la constatation histopathologique la plus fréquente. Une réaction positive à la coloration PAS des protoscolex a été observée et les neurones étaient les cellules les plus fréquemment touchées sur la base de la coloration combinée de Klüver-Barrera. Cette coloration montrait aussi que *Coenurus cerebralis* cause une réaction gliale importante. Lorsque les parasites étaient présents dans le système nerveux central, aucun traitement n'était possible. Les animaux ne présentent pas de symptômes neurologiques ont été traité pendant 3 jours avec 50–100 mg/kg PC/jours de Praziquantel (Tenikur® Topkim).

Osservazioni clinico-patologiche riguardanti il *Coenurus cerebralis* in pecore infettate in modo naturale

In 12 pecore provenienti da differenti greggi di ognuno circa 150–200 animali è stata diagnosticata una cenurosi causata dallo stadio larvale della *Tenia multiceps (Coenurus cerebralis)*. Le manifestazioni cliniche appariscenti erano atassia, scoordinazione, sonnolenza, paresi degli arti posteriori e coma. Le analisi sanguigne mostravano monocitosi e linfocitosi. I valori della creatinchinasi (CK) degli animali si aggiravano tra 421 e 495 U/l. Nel lobo parietale e frontale del cervello e nel cervelletto sono state riscontrate delle cisti. In due casi sono state pure riscontrate nel midollo spinale delle vertebre lombari. I sintomi clinici potevano essere ricondotti alla localizzazione delle cisti. Sono stati osservati abbattimento, testa ruotata dalla parte colpita e spintoni con la testa quando le cisti erano localizzate nel cervello. Scoordinazione e ipersensibilità agli stimoli esterni sono stati riscontrati se erano implicate le cisti del cervelletto mentre se erano implicate quelle localizzate nella colonna vertebrale i tipici sintomi clinici comportavano paralisi degli arti. Dall'analisi microscopica risulta un'atrofia del sistema nervoso centrale (SNC) provocato dalla pressione del cenuro. Il risultato più frequente dell'analisi istopatalogica è stato una meningoencefalite non purulenta con infiltrazioni perivascolari che fasciano i vasi sanguigni. Con la colorazione PAS (periodic acid Schiff) è stata osservata una reazione positiva del protoscolice. I neuroni erano i tipi di cellula più frequentemente riscontrati con la colorazione combinata di Klüver-Barrera per cellula e guaina di mielina. Questo metodo di coloraziona indica che il *Coenurus cerebralis* nel SNC causa una forte reazione gliale. Se nel SNC erano presenti parassiti nessuna cura era possibile. Animali senza sintomi neurologici sono stati curati durante 3 giorni con 50–100 mg/kg KG/giorno con Praziquantel (Pastiglie di Tenikur®, Topkim).

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Corresponding address

Dr. Ozlem Ozmen, PhD, Akdeniz University, Veterinary Faculty, Department of Pathology, 15100 Burdur, Turkey
Phone: + 90 248 234 45, Fax: + 90 248 234 45 05, E-Mail: oozmen@akdeniz.edu.tr.

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