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Clinical signs of caprine arthritis-encephalitis and disease-related pathomorphological changes

V. Yu. Koptev, N. A. Shkil, N. Yu. Balybina, I. N. Penkova
Siberian Federal Scientific Centre of Agro-BioTechnologies of the Russian Academy of Sciences (SFSCA RAS), Krasnoobsk, Novosibirsk Oblast, Russia

SUMMARY
Over the past ten years, the small ruminant population in the Russian Federation grew sharply, especially goat population in backyards and on small-scale farms. Alongside with the population growth, clinical signs of some sporadic diseases or diseases that had not been previously registered were detected in animals. Caprine arthritis-encephalitis (CAE) is one of such diseases. It is a chronic infectious disease caused by a small ruminant lentivirus (SRLV) of the *Retroviridae* family, which includes four genotypes, of which genotypes A (maedi-visna – MVV virus) and B (caprine arthritis-encephalitis virus – CAEV) are of epizootic significance. The disease is characterized by long asymptomatic viral transmission and is associated with progressive lesions in the respiratory organs, joints and udder. The disease also affects nervous system in kid goats aged between 2 and 3 months. Clinical signs of caprine arthritis-encephalitis are not pathognomonic; therefore, it is often misdiagnosed, thus, resulting in a barrier to effective treatment. Given the fact, the issue of antemortem and postmortem diagnosis of caprine arthritis-encephalitis is still urgent, because most veterinary specialists have never encountered this disease and the data available in the literature often do not fully cover all clinical details and pathomorphological features. Therefore, the purpose of the work is to study CAE clinical signs and pathomorphological changes. The article describes in detail clinical manifestation of this disease, postmortem lesions in organs and tissues of the sick animals. The results obtained suggest that the destructive changes in the exposed organs are irreversible and, consequently, there is no effective treatment.

Keywords: caprine arthritis-encephalitis, lentivirus, pneumonia, pathomorphological features, small ruminants

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For correspondence: Vyacheslav Yu. Koptev, Candidate of Science (Veterinary Medicine), Leading Researcher, Laboratory of Diseases of Young Animals, Institute of Experimental Veterinary Medicine of Siberia and the Far East SFSCA RAS, 630501, Russia, Novosibirsk Oblast, Krasnoobsk, p/o box 8, *e-mail: kastrolog@mail.ru.*

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Клинические признаки и патоморфологические изменения при артрите-энцефалите коз

В. Ю. Коптев, Н. А. Шкиль, Н. Ю. Балыбина, И. Н. Пенькова
ФГБУН Сибирский федеральный научный центр агробиотехнологий Российской академии наук (СФНЦА РАН), р. п. Краснообск, Новосибирская обл., Россия

РЕЗЮМЕ
Последнее десятилетие на территории Российской Федерации наблюдается резкое увеличение поголовья мелкого рогатого скота, в частности коз, содержащихся в личных подсобных и крестьянских фермерских хозяйствах. При этом все чаще ветеринарные специалисты начали сталкиваться с клиническими признаками заболеваний, ранее не регистрировавшихся в нашей стране либо встречавшихся в виде спорадических случаев. Одним из них является вирусный артрит-энцефалит коз – хроническое инфекционное заболевание, вызываемое лентивирусом мелких жвачных животных семейства *Retroviridae*, включающим в себя четыре генотипа, два из которых имеют эпизоотическое значение: генотип А (вирус маеди-висна – MVV) и генотип В (вирус артрита-энцефалита коз – CAEV). Артрит-энцефалит коз характеризуется длительным бессимптомным вирусоносительством с последующим развитием клинических признаков поражения органов дыхания, суставов конечностей и вымени, а также нервными явлениями у козлят 2–3-месячного возраста. Клинические признаки артрита-энцефалита коз не являются патогномоничными, вследствие чего ветеринарные специалисты, сталкиваясь с данной симптоматикой, часто ставят ложные диагнозы, что приводит к низкой эффективности терапевтических мероприятий. Учитывая вышеуказанный факт, вопрос прижизненной и посмертной диагностики артрита-энцефалита коз до сих пор остается актуальным, так как большинство ветеринарных специалистов никогда не сталкивались с данным заболеванием, а имеющиеся в литературе данные часто недостаточно подробно освещают все нюансы клинической и патоморфологической картины данной патологии. Исходя из этого, целью работы было изучить клинические признаки и патоморфологические изменения при вирусном артрите-энцефалите коз. В статье подробно рассматриваются клинические проявления данного заболевания, описаны патолого-анатомические изменения в органах и тканях больных животных. Полученные результаты указывают на необратимость деструктивных изменений в пораженных органах и, как следствие, на отсутствие эффективных способов терапии.

Ключевые слова: артрит-энцефалит коз, лентивирус, пневмония, патоморфологическая картина, мелкий рогатый скот

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Для корреспонденции: Коптев Вячеслав Юрьевич, кандидат ветеринарных наук, ведущий научный сотрудник лаборатории болезней молодняка ИЭВСиДВ СФНЦА РАН, 630501, Россия, Новосибирская обл., р. п. Краснообск, а/я 8, *e-mail: kastrolog@mail.ru.*

INTRODUCTION

Easy and relatively cheap handling of backyard goats resulted in a sharp increase in their population in the Russian Federation, thus, forcing veterinarians to deal with clinical manifestations of the diseases that either had not been previously registered in the country, or occurred sporadically. The primary reason behind it is that, until recently, there has been no veterinary control over import of animals from Russia's near and far abroad and their movements between the regions of the country. Poor veterinary control arose from imperfect laws and outright negligence of some goat breeders.

Under these circumstances, veterinarians working with small ruminants (in particular with goats) have to deal with a growing number of lesions in respiratory tract, musculoskeletal system, as well as with mastitis that do not respond to standard therapy. The progeny produced by animals with these clinical signs can develop such neurological conditions as loss of coordination and head tilt. In most cases, a combination of the clinical features is indicative of caprine arthritis-encephalitis.

Caprine arthritis-encephalitis (CAE) is a chronic infectious disease of goats caused by a small ruminant lentivirus of the *Retroviridae* family. The family includes four genotypes, of which genotypes A (maedi-visna virus, MVV) and B (caprine arthritis-encephalitis virus, CAEV) are of epizootic significance [1, 2]. The virus can easily cross the species barrier between sheep and goats, causing a pathological process with similar clinical signs [3–8]. The disease is characterized by a long asymptomatic virus transmission, followed by development of lesions in the respiratory tract, joints and udder, as well as by neurological disorders [9]. At the same time, genotype A lentivirus is believed to affect respiratory organs, while genotype B causes a set of lesions in musculoskeletal system.

The disease is reported in all countries with well-developed goat farming, including Russia [10–12].

CAE clinical signs are not pathognomonic, therefore, it is often misdiagnosed by veterinary specialists, thus, resulting in a barrier to effective treatment.

Currently, CAE diagnosis can be confirmed only by serological and molecular biological methods, including enzyme-linked immunosorbent assay (ELISA) of blood sera for antibodies to CAE virus, or real time polymerase chain reaction (PCR) used to detect proviral DNA in pathological samples from animals [13–15].

No medicinal products for CAE specific prevention and therapy have been developed so far. Preventive measures are mainly technical, i.e. segregation of seropositives and seronegatives, kidding under sterile conditions and early weaning of kid goats, followed by feeding with pasteurized milk or whole milk substitute [16, 17]. Regular serological monitoring of herds for seropositive animals with the following culling is one of the main preventive measures [18, 19].

The situation is complicated by the fact that the Ministry of Agriculture of the Russian Federation has not so far developed any legal framework to regulate preventive measures in the field. It means that, if seropositive animals are detected, there is either no response on behalf of the state veterinary services, or they take hasty, often illegal, measures to eliminate the sick animals as soon as possible.

Despite a wide range of publications, the issue of antemortem and postmortem diagnosis of CAE is still urgent, because most veterinary specialists have never encountered this disease and the data available in the literature often do not fully cover all clinical signs and pathomorphological features [20–22].

Thus, the purpose of the work was to study clinical signs and pathomorphological changes caused by caprine arthritis-encephalitis.

MATERIALS AND METHODS

The following data are required to diagnose CAE antemortem: the anamnesis, clinical examination of animals and the results of serological tests.

Bodywin vacuum tubes (China) with coagulation activator and EDTA were used for blood sampling.

The antibodies in blood serum was detected using ID Screen® MVV/CAEV Indirect Screening Test (IDVet, France) and CAEV/MVV Antibody Test Kit (IDEXX B.V., the Netherlands) for indirect ELISA. The results were read with a semi-automated microplate absorbance reader Infinite® F50 (TECAN, Austria).

CAE virus was detected in blood with a set of reagents produced by "RealBest-Vet DNA CAEV (caprine arthritis-encephalitis virus)" (Vector-Best, Russia), on Bio-Rad (USA) amplification system.

The animals were autopsied using a generally accepted method of G. V. Shor [23]. Pathological material for histological studies was fixed in a 10% formalin solution. Histological preparations were stained with hematoxylin and eosin according to the standard procedure.

RESULTS AND DISCUSSION

Clinical manifestations and anatomical and morphological changes caused by caprine arthritis-encephalitis were described in two backyard animals of different age.

Example 1. A crossbreed kid goat of 2 months old. As the history taking shows, the animals at the age of 1.5 months have such neurological signs as head tilt, "circling". The animal clinical status deteriorated over time, as evidenced by the animal owners.

Fig. 1. Clinical manifestations of central nervous system lesions in a 2-month-old CAE infected kid goat

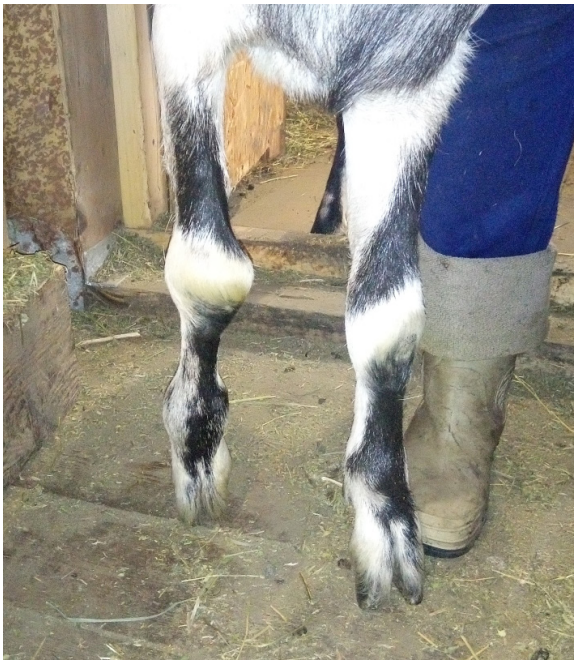

Fig. 2. Enlargement of carpal joints in a CAE-infected goat (5 years old)

The external examination demonstrated that the kid constantly tilted rightward. The animal starts circling and often gets lost in space. Coordination is bad, feed intake becomes difficult (Fig. 1).

To confirm the preliminary diagnosis of "caprine arthritis-encephalitis", a blood sample was taken from the mother goat to obtain serum and to test it in ELISA for antibodies to the disease agent. The test results revealed antibodies to CAE virus with S/P% – 603% (positive result according to the instruction for the kit: S/P% ≥ 60%).

Since the kid goat was fed with mother's milk since birth, he could have colostral antibodies to CAEV in sera. Therefore, in order to exclude a false-positive ELISA result, his blood sample was tested in PCR, which revealed a proviral DNA of CAE virus.

The analysis of clinical signs together with the laboratory diagnosis made it possible to ultimately diagnose "caprine arthritis-encephalitis". The animal owner decided to cull and destroy the baby goat and the mother goat.

Example 2. A Nubian goat, 5 years old. It was bought at the age of 2 months. As the history taking shows, a 3-year-old animal demonstrates low mobility, lameness, refused from mating.

As revealed by clinical examination, hock and carpal joints are enlarged. The animal finds it difficult to walk and weight-bearing lameness is observed (Fig. 2). During palpation, the affected joints were stiff and painless.

To confirm the CAE pre-diagnosis, a blood sample was taken from a goat after examination. An ELISA test for CAEV antibodies in sera showed S/P% of 592% (in accordance with the kit instructions, S/P% ≥ 60% stands for a positive result), which resulted in ultimate diagnosis of "caprine arthritis-encephalitis".

The goat's condition significantly deteriorated the following year. The animal practically did not walk and such respiratory signs as wheezing and dyspnea were seen.

After the emergency slaughter, the animal was autopsied and pathological material was sampled for histological tests, i.e. samples from different brain regions, medulla oblongata, meninges, lungs, articular capsule, and surface of the articular cartilage of the affected joint.

The autopsy and subsequent histological examination showed the following results.

The central nervous system. The dura mater has no visible changes. The brain vessels are injected; the petechial hemorrhages can be seen. Brain convolutions are smoothed (Fig. 3).

Histological analysis of the cerebral cortex, medulla oblongata and cerebellum revealed similar pathomorphological changes: hyperemia, pericellular and perivascular edema in brain tissue, mononuclears clusters around

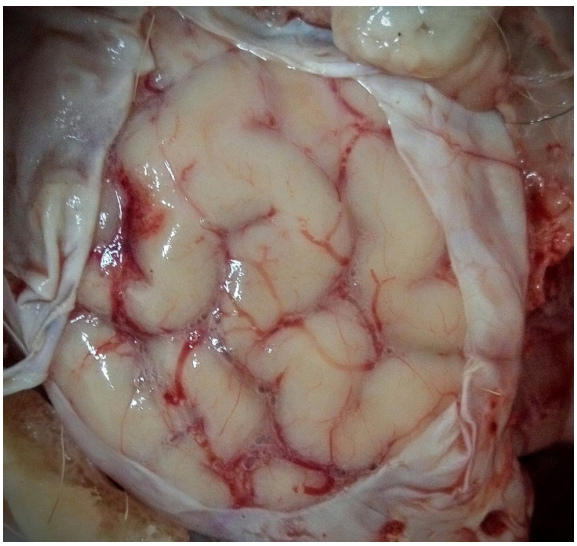

Fig. 3. Brain of a CAE-infected goat

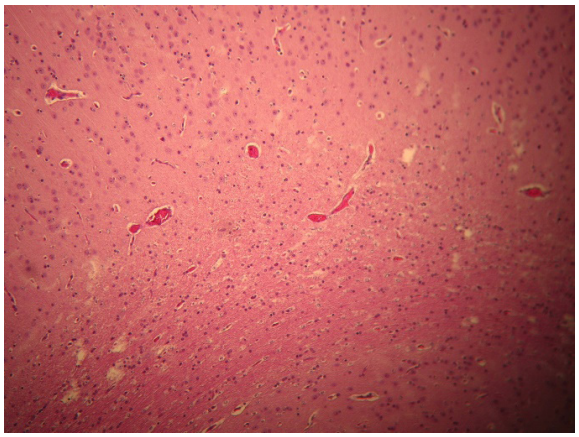

Fig. 4. Brain cortex of a CAE-infected goat. Histological section. Hemostasis. Hematoxylin and eosin stain (magnification 100×)

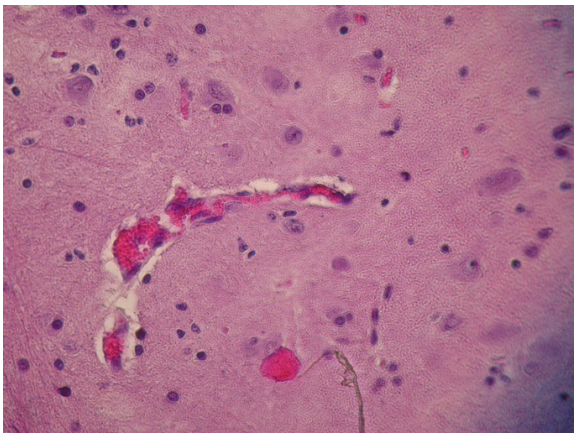

Fig. 5. Cerebellum of a CAE-infected goat. Histological section. Hemostasis. Hematoxylin and eosin stain (magnification 400×)

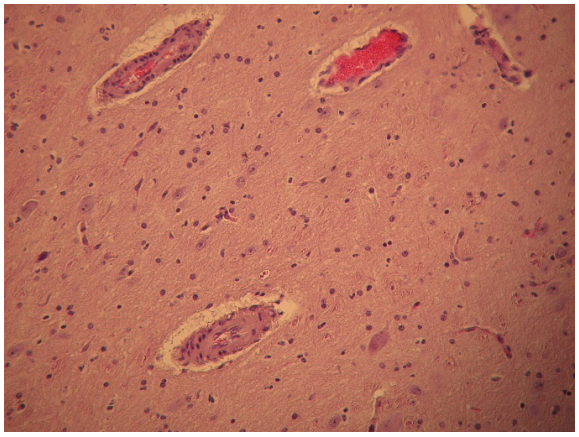

Fig. 6. Medulla oblongata of a CAE-infected goat. Histological section. Perivascular edema, hemostasis, mononuclear clusters. Hematoxylin and eosin stain (magnification 100×)

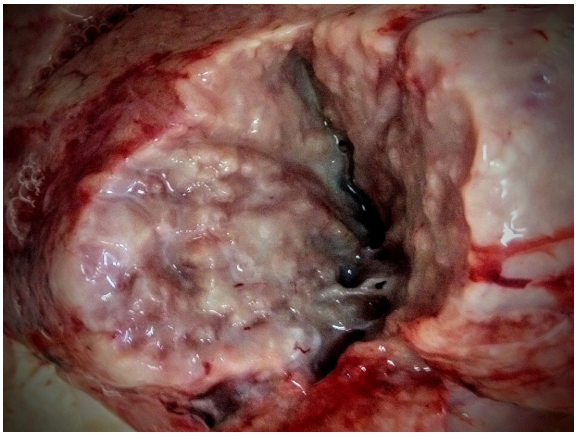

Fig. 7. Lung of a CAE-infected goat

blood vessels (lymphocytes and monocytes) – perivascular cellular sheaths, as well as scattered foci of cellular accumulations (Fig. 4–6).

Respiratory organs. Lungs are enlarged, become airless. The edges are rounded, the surface is rough. Fibrinous exudate is observed on the visceral pleura, local hemorrhages are found. Advanced fibrosis can be seen (Fig. 7).

The sections demonstrate broken lung architectonics. Lung parenchyma is dense, of "rubber" consistency, lobulated with local hemorrhages and extensive fibrosis.

Histological analysis of the lung tissue revealed signs of inflammation, the lumen of the alveoli is filled with exudate – reticulated fibrin masses and leukocytes. In some parts of the section, the exudate does not fit tightly

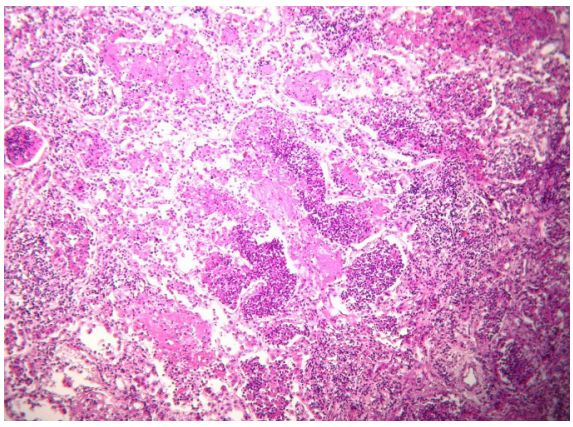

Fig. 8. Lung of a CAE-infected goat. Histological section. Croupous pneumonia. Hematoxylin and eosin stain (magnification 100×)

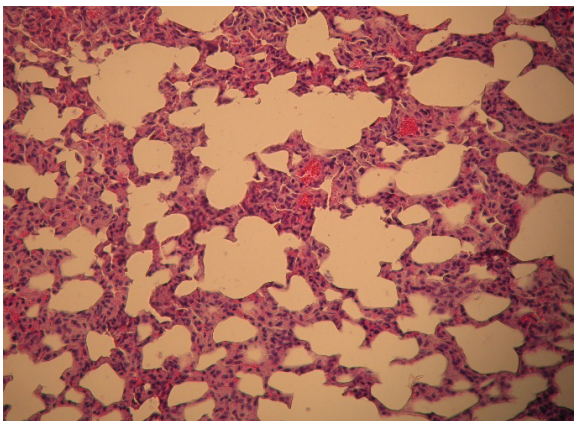

Fig. 9. Lung of a CAE-infected goat. Histological section. Croupous pneumonia. Hematoxylin and eosin stain (magnification 400×)

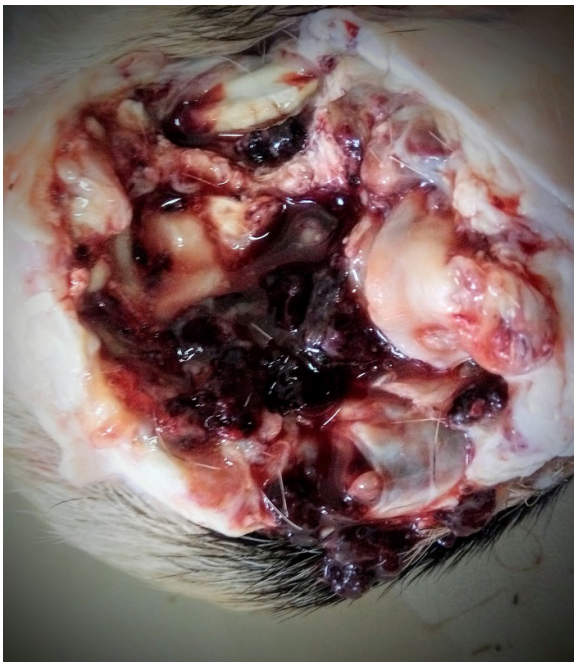

Fig. 10. Carpal joint of a CAE-infected goat.

to the alveoli walls – slit-like lumen can be seen. In the interalveolar septa, inflammation is not pronounced, vascular hyperemia, stasis and stroma edema are observed. Blood clots are visualized in the lumen of some small vessels. The whole combination of morphological changes observed in the micropreparation suggests croupous pneumonia in the animal (Fig. 8, 9).

Carpal joint. The carpal joint demonstrates a 1.5–2 times increase in size. The joint capsule edema with petechial hemorrhages is observed. A great number of blood clots is detected in the autopsied articular cavity (Fig. 10).

The synovial membrane is loose and blood-soaked. The surface of the articular cartilage of the radial and metacarpal bones is yellowish, matte, with degenerative sites.

The histological analysis revealed eroded surface of the articular capsule in the sick animal, which means degenerative changes and destruction of the joint surface due to arthritis (Fig. 11, 12).

The data obtained indicate that morphological changes in the CAE-affected tissues are irreversible, which can be a basis for animal culling and slaughter without any therapeutic support.

CONCLUSION

Caprine arthritis encephalitis is a chronic viral disease when infected goats remain asymptomatic carriers for a long time. The disease occurs in all the countries with well-developed goat farming. The main CAE clinical signs include arthritis of hock and carpal joints, respiratory lesions in the form of interstitial pneumonia, mastitis of one or both mammary glands. Clinical signs observed in animals younger than 3 months include lesions of the central nervous system, i.e. incoordination and head tilt. The symptoms manifest themselves only at the end stage at the age of 3–5 years, in young animals – within the first 2–3 months after birth. Due to poor awareness and taking into account the fact that CAE clinical manifestations are non-specific, the disease is often misdiagnosed, thus, resulting in a barrier to effective treatment.

CAE clinical manifestations and post-mortem lesions were studied during the research.

Necropsy of the CAE-infected animal revealed the following lesions in central nervous system: injection of vessels and petechial hemorrhages on the brain surface. The histological features included hyperemia, pericellular and perivascular edema of brain tissue, as well as accumulation of mononuclear cells (lymphocytes and monocytes) around blood vessels.

The lung edges are rounded, the surface is rough with advanced fibrosis. Fibrinous exudate is observed on the visceral pleura and local hemorrhages are found. Histological examination revealed that the lumen of the alveoli is filled with exudate – reticulated fibrin masses and leukocytes.

The joint capsule edema with petechial hemorrhages is observed. A great number of blood clots is detected in the articular cavity. The synovial membrane is loose. There were degenerative sites on the surface of the articular cartilage.

The histological microscopy revealed eroded surface of the articular capsule, which means there are arthritis-related degenerative changes of the joint surface.

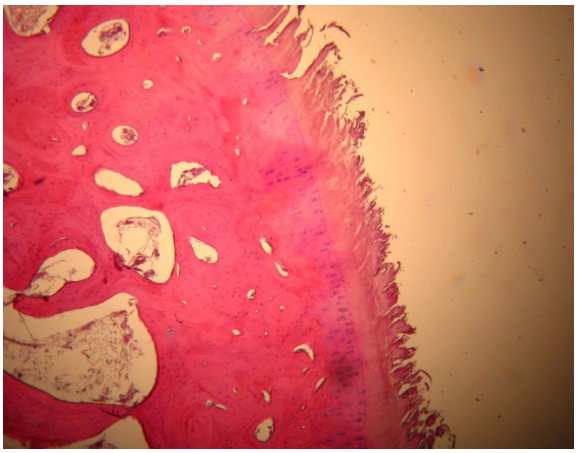

Fig. 11. Articular surface. Histological section. CAE-caused erosion of the articular surface. Hematoxylin and eosin stain (magnification 100×)

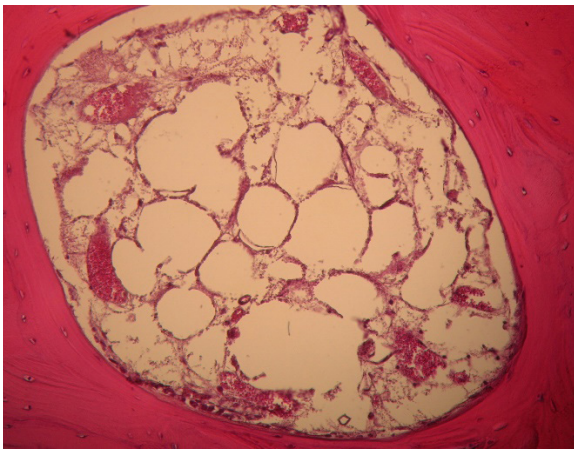

Fig. 12. Articular surface. Histological section. CAE-related hemostasis. Hematoxylin and eosin stain (magnification 100×)

In general, the results obtained significantly add to the earlier published data on CAE pathomorphological changes [17].

The disease symptoms are not pathognomonic, which may be a significant barrier to a correct diagnosis, if it is based only on history taking and clinical analysis. Consequently, the main diagnostic methods include ELISA for antibodies to CAE virus in the animal sera or real-time PCR for detection of proviral DNA.

Caprine arthritis-encephalitis clinically manifest itself only at the end stage. At the same time, pathological processes in tissues is irreversible. This fact makes it pointless to treat animals with obvious clinical signs; therefore, veterinary specialists should make the animal owners focus on the on-farm disease prophylaxis and prevention of the pathogen escape from the CAE-affected areas.

It is noteworthy that the Russian Federation has currently no regulations on CAE prevention approved by the Ministry of Agriculture.

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INFORMATION ABOUT THE AUTHORS / ИНФОРМАЦИЯ ОБ АВТОРАХ

Vyacheslav Yu. Koptev, Candidate of Science (Veterinary Medicine), Leading Researcher, Laboratory of Diseases of Young Animals, SFSCA RAS, Krasnoobsk, Novosibirsk Oblast, Russia; *https://orcid.org/0000-0003-0537-6659, e-mail: kastrolog@mail.ru.*

Nikolay A. Shkil, Doctor of Science (Veterinary Medicine), Professor, Head of Laboratory of Diseases of Young Animals, SFSCA RAS, Krasnoobsk, Novosibirsk Oblast, Russia; *https://orcid.org/0000-0002-5124-2208, e-mail: shkil52@mail.ru.*

Natalya Yu. Balybina, Researcher, Laboratory of Diseases of Young Animals, SFSCA RAS, Krasnoobsk, Novosibirsk Oblast, Russia; *https://orcid.org/0000-0001-8786-3738, e-mail: n.balybina@alumni.nsu.ru.*

Izabella N. Penkova, Postgraduate, Laboratory of Diseases of Young Animals, SFSCA RAS, Krasnoobsk, Novosibirsk Oblast, Russia; *https://orcid.org/0000-0001-6328-2509, e-mail: penkova_izabella@mail.ru.*

Коптев Вячеслав Юрьевич, кандидат ветеринарных наук, ведущий научный сотрудник лаборатории болезней молодняка СФНЦА РАН, р. п. Краснообск, Новосибирская обл., Россия; *https://orcid.org/0000-0003-0537-6659, e-mail: kastrolog@mail.ru.*

Шкиль Николай Алексеевич, доктор ветеринарных наук, профессор, заведующий лабораторией болезней молодняка СФНЦА РАН, р. п. Краснообск, Новосибирская обл., Россия; *https://orcid.org/0000-0002-5124-2208, e-mail: shkil52@mail.ru.*

Балыбина Наталья Юрьевна, научный сотрудник лаборатории болезней молодняка СФНЦА РАН, р. п. Краснообск, Новосибирская обл., Россия; *https://orcid.org/0000-0001-8786-3738, e-mail: n.balybina@alumni.nsu.ru.*

Пенькова Изабелла Николаевна, аспирант лаборатории болезней молодняка СФНЦА РАН, р. п. Краснообск, Новосибирская обл., Россия; *https://orcid.org/0000-0001-6328-2509, e-mail: penkova_izabella@mail.ru.*