Autoimmune thyroiditis with systemic idiopathic fibrosis in horses

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Abstract. The article deals with the autopsy materials of the Friesian breed domestic horse (Equus ferus caballus). It presents the research on tissues’ and organs’ histological examination as well as materials from the case record. New nosology for this species and breed has been revealed for the first time for the animal under examination. It was chronic inflammatory thyroid disease of the autoimmune genesis in the hyperthyroid stage which caused the systemic idiopathic fibrosis. Previously this nosology was neither revealed nor described in the Russian and foreign literature sources. The article presents materials from the case record where animal’s clinical condition has been assessed. The description of pathoanatomical and morphological changes in the thyroid tissues in the detected autoimmune thyroiditis and associated pathological processes in the organs and tissues of the studied animal was given. The systemic idiopathic fibrosis associated with thyroiditis condition was described. The features of the blood serum metabolic profile according to the enzymes content, substrates and minerals were presented. The assessment of the thyroid gland endocrine status of total thyroxine (тТ4) and total triiodothyronine (тТ3) has been made. The level of which was 184.0 nmol/l and 7.9 nmol/l respectively. The data indicating the presence of an autoimmune process in relation to thyroid antigens have been traced. The level of antibodies to thyroglobulin and antibodies to thyroperoxidase was 9.7 IU/ml and 98 IU/ml respectively.

1. Introduction
The endocrine system of animal is extremely complex and not all aspects of hormonal regulation have been studied by scientists. Any dysfunction of the hormonal system affects the health of pets very seriously, and in some cases, such pathologies can result in death. Thyroiditis is very dangerous. In veterinary reference books, it is called “thyroid atrophy of idiopathic etiology”. For some unknown reason, thyroid disorders occur and thyroid gland does not produce important hormones [1]. As a result, primary hypothyroidism occurs. Most literary sources agree that with thyroiditis, the normal parenchyma of the endocrine gland is replaced by adipose tissue. Based on this, it can be assumed that the main cause of what is happening is serious poisoning with salts of heavy metals. For such cases, this clinical picture is quite common. In addition, it is typical of autoimmune diseases [2]. The most characteristic disease of domestic animal is lymphocytic thyroiditis. It occurs when gland tissue is infiltrated by lymphocytes, plasma cells and macrophages. In rare cases, the disease can be congenital,
but such animals do not live long. Veterinary practitioners believe that the disease in this case is due to congenital pathologies that lead to the inability of the gland to produce certain types of hormones. The glandular parenchyma remains unchanged, therefore it is not entirely correct to talk about “classical” thyroiditis. In cats, pathology develops after treatment of hyperthyroidism with surgical thyroidectomy or antithyroid drugs. It should be mentioned that cats get sick with thyroiditis extremely rare under normal conditions. Many veterinary endocrinologists believe that the development of this pathology in cats is due to some serious problems with the hypothalamus [3, 4].

The thyroid gland takes a central place among the peripheral glands of internal secretion. Its activity affects almost all key metabolic processes from the regulation of energy and plastic metabolism to the functioning of the reproductive and central nervous system. Its functions violation is revealed as multisystem disorders in the animals’ and humans’ organisms. It can be manifested in different ways. Endocrine disorders of thyroid function can be manifested as hyper- and hypothyroidism, as well as lipid and protein metabolism disorders which are characterized by the decrease or increase in the production of steroid and other hormones [5,6]. Both exogenous and endogenous factors can provoke thyroid dysfunction. Exogenous factors that can cause the development of such thyroid pathologies as microelementos. They can be caused by an insufficient state of essential chemical elements, and excessive intake of such essential and toxic chemical elements as iodine, selenium, cobalt, lead and cadmium. A variety of antigenic factors from viral to bacterial and protozoan infections and infestations also stand for exogenous reasons. Pathology associated with endocrinologic disorders especially humans’ and animals’ thyroid disease is widely detected in the Middle Urals in modern conditions [7,8,9]. This is not only due to iodine deficiency typical of the Ural region but also due to the increasing anthropogenic load. The role of bacteria and viruses inducing the development of autoimmune processes in the body and affecting the endocrine glands has also been proved. In its turn, thyroiditis is a heterogeneous group of thyroid gland inflammatory diseases. Diseases of this group are hardly ever been studied in veterinary practice. There are references to this pathology detection in dogs. The state of hypothyroidism for horses is described in details in scientific literature [10]. However, none is said about hyperthyroidism. There is neither clinical nor morphological description of other pathologies there. All above-mentioned complicates the diagnosis and soothing the pathological conditions directly related to morphological and functional changes of the thyroid gland [11]. This work was aimed to describe pathological changes in the horses’ thyroid glands when hyperthyroidism syndrome and related morphological changes in other parenchymal organs were detected.

2. Experimental

The 14 years horse of the Friesian breed’s corpse has been examined. According to the owner, the horse was imported from the Netherlands. The animal was kept in the appropriate for this breed conditions. Horse has been set all the necessary preventive vaccination. Horse’s euthanasia was held by the attending physician according to the owner’s decision immediately before the study. The owner provided a complete medical record for the period of the disease from August 2014 to January 2015 which included the results of serological, hematological and biochemical studies as well as the results of abdominal cavity ultrasound examination. Animal’s blood samples were taken for hematological, biochemical and enzyme immunoassay with the help of vacuum blood collection systems before euthanasia. Clinical, biochemical and enzyme immunoassay of blood plasma was performed on an automatic biochemical and enzyme immunoassay analyzer ChemWell 2910 (Sombi) by Awareness (USA) with the help of reagents recommended by the international Federation of the clinical chemistry of DIALAB GmbH (Austria) company. Enzyme immunoassay was performed by sets of LLC ‘Hema Medica’ (RF) having modified the method for horses in order to reveal the number of thyroid hormones and antithyroid antibodies. Visual examination of the animal’s body was performed indoors under artificial light (incandescent lamps) in accordance with the guidelines of P. I. Kokurichev (1977), A. V. Zharov (2001) and D. G. Latypov (2014). Samples were taken from the animal’s corpse for further histological examination. Histological study was conducted at the Department of morphology, examination and surgery of the Ural State Agrarian University. Fixation of the material was carried out
in a 10% solution of neutral buffered formalin. The filling of the material for histological examination was carried out manually according to Romeis. Sections were cut from the blocks by microtome with microprocessor control ‘MZP-01 TEKHNOM’ (RF). The sections were stained with hematoxilin and eosin according to Van Gieson. Visual assessment of tissue sections was performed by means of a direct light microscope model Leica DM750 with digital image processing system Leica ICC50HD company Leica Microsystems GmbH (Germany).

3. Results and considerations
The first symptoms of the animal’s disease revealed in August 2014 were the following: weight loss, severe anxiety, sweating, and refusal from feed, intolerance to loads, colic attacks, and intermittent fever. Serum samples were twice examined during the period from August 2014 to January 2015. Infectious diseases like SAP, brucellosis, horses’ infectious anemia and case disease were excluded. Patient’s blood biochemical analysis throughout the follow-up from August 04, 2014 to December 15, 2014 had a number of features that reflect the development of various systemic pathologies. According to the data of patients’ blood clinical analysis of biochemical markers during the observation period, it can be concluded that the animal’s body was exposed to severe hypoxic phenomena at the tissue level. It is likely due to a decrease in the hemoglobin level in the red blood cells. Hypoxic phenomena led to chronic myocardial damage which was indicated by the high level of creatine kinase myocardial band isoenzyme in the blood plasma. The animal showed depletion of the key electrolytes pool which is associated with the presence of stress reaction provided by steroid hormones accompanied by the disfunctioning of the renin-angiotensin-aldosterone system. At the same time stress reactions caused by steroid and thyroid effects provoked the development of hepatobiliary pathology manifested in a hepatocytes volume decrease. It was indicated by a transaminase level decrease when other markers of hepatobiliary diseases increased. In its turn, this process could be marked by an increase of glucose level in the blood plasma due to the decrease in its capture by hepatocytes. Also, increased glucose levels could be caused by increased gluconeogenesis due to the increased levels of steroid and thyroid hormones. The hyperlipidemia was noted during the visual assessment of animal’s blood plasma which is associated with the lipolysis activation against the high levels of thyroid hormones and hepatobiliary pathologies. A study of thyroid hormones was conducted according to the clinical picture as well as a number of other signs identified by clinical biochemical analysis. The state of hyperthyroidism was revealed, the level of total thyroxine was 184.0 nmol/l, and triiodothyronine was 7.9 nmol/l.

Three-dimensional tumor was found on the left in the inguinal region in the colon projection, ascites, and the small intestine atony during the abdominal cavity ultrasound examination. It was decided to euthanize the animal on the basis of the general clinical record in January 2015 for the final diagnosis postmortem and further studies. Homogeneous mass of dense consistency with multiple cystic cavities from 0.5 cm to 4 cm in diameter was found in the abdominal cavity. Spleen was tightly adjacent to the right of the mass (gray-red free end of the large omentum sized 10×60 cm with sharply injected vessels). Homogeneous mass was closely adjacent to the square lobe in the area of the liver. The stomach was located in the left hypochondrium, in the region of the xiphoid cartilage. It was limited in mobility due to the omentum ingrowth into the tumor. The pancreas was completely immersed in a homogeneous mass which makes its visualization impossible. Two-thirds of the duodenum, jejunum and two-thirds of the small colon were completely hidden in the homogeneous mass. The free part of the intestine was mixed into the pelvic cavity. Homogeneous mass acquires the consistency of cartilage in the aorta and portal vein. The thyroid gland was slightly increased in size, the right and left lobes were rounded-elongated, of dense consistency, the lobes were covered with a dense matte capsule. Discission color was heterogenic from red to yellowish-white. Thyroid gland histological examination revealed diffuse infiltration of the parenchyma by lymphocytes. Macrophages foci, plasma cells as well as lymphoid follicles with embryonic centers were found among them. Most thyroid follicles were destroyed, their basal membrane being damaged. Oxyphilia was detected in the follicular epithelium of some cells cytoplasm. Such cells were arranged in groups. There were felt-like structures of the cells. Fibrosis with
significant loss of colloid in the follicles was observed. These structural changes are typical for autoimmune thyroiditis.

Table 1. The content of iodothyronines and autoantibodies to thyroperoxidase in autoimmune thyroiditis

| Indicator                  | unit     | healthy   | value     | diseased   |
|----------------------------|----------|-----------|-----------|------------|
| triiodothyronin            | nmol/l   | 1.2-12.4  | 18,6±2.2  |
| thyroxine free             | nmol/l   | 11.5-18   | 5.7±0.9   |
| tiotropy hormone           | ME/l     | 0.01-0.1  | 0.4±0.02  |
| antibody to thyroperoxidase| titer    | 0-20      | 60±4      |

Hyalinosis of the renal tubules, sclerosis of the glomeruli, productive lymphadenitis and systemic fibrosis of the abdominal organs were also revealed along with the deep pathological processes found in the thyroid gland. Titers of antibodies to thyroglobulin and thyroperoxidase were determined in the serum taken before euthanasia (table 1). There was an autoimmune pathological process in respect of thyroid antigens.

4. Summary

The materials of clinical, biochemical blood tests, pathoanatomical dissection and histological examination presented in the work allow concluding that the studied animal suffered from autoimmune thyroiditis with the phenomenon of systemic idiopathic fibrosis. This horses' pathology revealed is being described for the first time. An autoimmune process against the thyroid gland is confirmed by high titers of antibodies to thyroglobulin and thyroperoxidase.

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