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Original Scientific Paper

PAPILLOMATOSIS IN DAIRY COWS

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Abstract

Bovine papillomatosis belongs to the group of chronic proliferative diseases of viral etiology. Young cattle up to 2 years of age are most often affected. Papillomatosis is caused by the papilloma virus, which forms benign tumors of fibroepithelial properties on the skin and mucous membranes. Usually, the skin form is characterized by the appearance of one or more papillomas, which usually affect the head, neck, shoulders, ears, around the eyes, in the area around the throat, mouth, and udder. As a result, frequent and permanent bleeding may occur.

Key words: papilloma, cow, extensive breeding

INTRODUCTION

Papillomatosis is the appearance of papillomas or warts on the skin. The cause of papillomatosis is a DNA virus from the *Papova*-virus group. The size of this virus is 40-50 nm. It consists of 42 capsomeres. Bovine fetal conjunctival diploid cells, bovine embryonic skin cells, and hamster and mouse embryonic cells are used for the growth of this virus. Also, the virus can adapt to a chicken embryos. According to its characteristics, the virus can easily adapt to different physical and chemical conditions. It does not lose its pathogenicity at 56°C. At a temperature of -70°C, its properties do not change even after 10 months. It is ether resistant. It is sensitive to UV rays (Radojičić et al, 2017; Andrews et al., 2008).

The virus belongs to the *Papova* virus group with several immune types. Infection develops only on superficially damaged skin and mucous membranes. Transmission is possible by direct contact of papillomas, i.e. viruses with damaged skin, as well as by indirect transmission of the virus from a diseased to a susceptible animal through infected instruments (tattooing, marking, castration, and tuberculin testing). The virus is rarely transmitted from the papules of the foreskin or glans penis to the mucous membrane of the

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vagina. Immunity develops after an animal is exposed to diseases (Radojičić et al., 2017; Bojkovski et al., 2007).

Skin growths observed in cattle are benign tumors. The changes that occur are benign and self-limiting. The differentiation of individual virus types is based on histological changes and DNA identification as well as on the application of other molecular techniques. Six types of bovine papillomavirus have been identified in cattle (BPV-1, BPV-2, BPV-5, which are the cause of bovine fibropapilloma, and BPV-3, BPV-4 and BPV-6 are the causes of true epithelial papilloma). Bovine types show some preference for one or more characteristic sites. Papillomatous changes that can occur in the BPV-1 type are fibropapillomatosis on the udder skin and fibropapillomatosis on the penis. In BPV-1 and BPV-2 type of skin fibropapillomas, the changes are observed on the forehead, neck and back.

As ordinary skin warts, they appear in the form of cauliflower around the anus and genital organs, and the abdominal part of the skin. BPV-2 type is also associated with bladder cancer in cattle. BPV-3 type also causes skin papillomas. BPV-4 type also causes papillomas of the esophagus, esophageal groove, mucous membrane of the foregut and small intestine, with the possibility of growing into malignant, especially in animals that are fed with ferns. Type BPV-4 occurs in the anterior parts of the digestive system.

Type BPV-5 causes fibropapillomas with the size of the grain of rice on the skin of the udder. Type BPV-5 actually occurs as a cause of skin warts. Type BPV-6 causes the formation of fern-like epithelial papillomas that occurs on the skin of the udder and breast of cattle. Other papillomas in cattle are located regionally and may have a special antigen identity (oral papillomas, mainly in adult cattle with a high prevalence in some countries, even up to 16 % of cases). BPV-4 type most commonly causes laryngeal papilloma in cattle. The papilloma virus was found in the horny cells of bovine eye cancer (Radojičić et al., 2017; Cvetnić, 2005).

The spread of infection is through direct contact with infected animals when the causative agent enters through skin injuries. When infected animals scratch on the objects in the barn, the virus can survive on those objects. A bunch of warts sometimes appear around the ear shell at the place of marking or around scratches caused by scratching animals on hard objects. The infection can be spread by tattooing, cutting the horns, and by a diagnostic procedure such as tuberculin testing.

A high incidence of perianal warts has been reported in pregnant heifers in whom the infection has spread by rectal examination. Papillomas that spread to the larynx in beef cattle are attributed to an infection caused by viruses in places where the mucous membrane is damaged by bacterial acting (*Fusobacterium nodosus* which causes diphtheria in calves) so that these two diseases can occur in young cattle. An increase in periorbital papillomas in cattle has been reported in relation to other infections in the eyeball area (Radojičić et al., 2017; Jovanović et al., 2012). This disease can affect all age categories of cattle.

It has been recorded in cattle that several animals of the same age may become ill in the barn (Radojičić et al., 2017).

In wild animals, it occurs in deer. Cutaneous papillomas of the head and neck mainly occur in young animals.

The appearance and severity of skin warts can be influenced by factors that cause immunosuppression, so latent infections become clinical diseases. Rarely, the congenital infection has been reported in calves. In cattle, digestive system papillomatosis, as well as udder skin papillomatosis is associated with the BPV-5 type. It can be persistent in all cattle production categories.

Warts on the udder often disturb the milking process in lactating cows, especially if the papillomas are located on the udder teats (Radojičić et al., 2017).

The virus attacks basal keratinocytes, causing excessive cell growth that is characteristic of wart formation. The virus infects epithelial and connective tissue through the injured skin. In the following period, the viral DNA infects the cell nucleus and integrates into the cell genome. Due to the wrong activation of an undefined enzyme that is responsible for the regulation of cell growth, intensive proliferation begins. Fibroplastic proliferation is followed by the period without significant morphological changes.

Papilloma develops in three phases (proliferative, stationary, and involutional), (Radojičić et al., 2017). According to some authors, the incubation period lasts between 3.5 and 4 months in natural conditions. This is one of the reasons why this disease rarely develops into clinical manifestations in beef cattle. According to the anatomical localization, some authors divided the disease into the skin, genital and esophageal papillomatosis. The skin form is characterized by one or more papillomas that are usually located in the head, neck, shoulders, ears, around the eyes, in the area of pharynx, on the lips, and udder.



Figure 1. The clustered shape on the udder (photo orig. Kosovčević, 2017)

Large papillomas can be often traumatized, and permanent bleeding can lead to anemia. Cases like clinically manifest papillomatosis that caused anorexia, reduced weight gain, and provoked even death in the animal, have been described in the literature. It has been recorded that the disease lasts, on average, between 30 and 50 days. Most of the diseased animals recovered without therapy. The genital form of papillomatosis affects both male and female animals. In male animals, changes occur on the glans penis or nearby in the form of individual papillomas.

If the papillomas progress, the bull will not be capable of providing semen. There are cases of papilloma in female animals in the area of the vulva and vagina. In the case of traumatized papilloma, vaginitis can develop. Esophageal papillomatosis, which is detected in a negligible percentage, is characterized by the formation of one or more papillomas on the esophageal mucosa surface. In very rare cases, esophageal obstruction can occur (Radojičić et al., 2017). The whole course of the disease (incubation, growth, papilloma regression) in young infected cattle can last from 1 to 3 months. In older and immunosuppressed animals, papillomas cease in a few weeks. At places that are more exposed to small skin damage (head, neck, shoulders, abdomen, udder, and teats), an infection caused by the virus causes the formation of papillomas, which are initially smooth and hairless and then develop into different shapes and sizes. Initially, the size of the pinhead gradually reaches the size of a walnut (sometimes in few months) and then spread through the surface and increases in size. With a wide base on the skin, they can grow into intensively cornified, cauliflower-like formations with a pronounced furrows. Others grow into hanging papillomas. Cauliflower-looking papillomatosis is named the fungiform form, and that on the stalk is named as the pendular form. Papillomas on the udder and teats are conical, small, are called filiform papillomas and sometimes appear enzootic in heifers and young cows. Mechanical injuries can cause bleeding and bacterial infections, especially in large papillomas (large papillomatous masses), and may cause resorption of decomposed tissue and even septic conditions. Such papillomas have a putrid odor, and the spread of papillomatosis over the skin negatively affects the general appearance of the animal and can also cause disturbed growth of young animals. Filiform papillomas on the skin of the udder and teats during mechanical injuries can bleed. Fungiform papillomas more commonly, and others less frequent, gradually decrease during the withdrawal of the disease, then dry up, and the dried remains fall off. There are no scars at the site of fallen papilloma. Extremely large papillomas fall off very slowly or do not have a tendency to dry out. Papillomas on the mucus membrane of the foreskin, glans penis, vagina, udder cistern, mouth and pharynx cause mechanical disorders in these organs. Warts are growths on the epidermis, that can be with the root or on the stem. They appear on any part of the body, but if a large number of animals in one group is affected then they usually attack the same part of the body. Usually, in cattle up to 2 years old, skin papillomas appear on the head, especially around the eyes, on the neck, shoulders, but they can also spread to other parts of the body. They vary in size, from 1 cm and up, are most often like cauliflower, and withdraw spontaneously. However, the growths can be presented for five to six months, and, in the

same cases, up to 18 months when, consequently, weight loss occurs. Udder warts are present in different forms depending on the type of papilloma virus. There is a possibility that the warts will be pulled out of the roots. The flat and round type usually multiplies, always rooted up to 2 cm in diameter. The third shape has a structure like a grain of rice. Perianal warts are aesthetically uncomfortable, but it seems that they do not affect the activity of production abilities of animals. Warts that are located on genitals (vulva and penis) prevent mating because they are large, fragile, and bleed easily. They are usually easily infected and get dirty. They occur on the mucous membrane of the penis in young bulls and can be in a single form or in clusters with stems. They often withdraw spontaneously. There is a high prevalence in cattle in some localities. Papillomas appear on the lateral and dorsal part of the tongue, soft palate, esophagus, esophageal groove, and in the foregut. Papillomas mostly appear in the esophageal groove, and in the reticulum. A less common manifestations of bovine papillomatosis include changes in the bladder, which do not show clinical signs but maybe a predisposition to enzootic hematuria. Papillomas caused by the BPV-4 virus are located in the anterior parts of the digestive system of cattle that are feed with ferns, and they are the foci for the transformation of horny into cancerous cells. In cattle fed by ferns, immunosuppression occurs and the mutagenic action of ferns causes a neoplastic transformation of papilloma cells. Morphologically, the neoplasm resembles a rough mass that is similar to cauliflower. They can be of different sizes and uneven shapes, raised above the surface of the skin or mucous membranes, They can be tied to the base with their entire width, and in some cases only with thin stump. Papillomas on the mucous membrane are characterized by a strong proliferation of connective tissue elements with a slight swelling of the surrounding epithelium. Epithelial loss and secondary bacterial infections create a predisposition for leukocyte infiltration and the appearance of edema. According to its clinical signs, the disease is clearly visible, so the diagnosis is made on its basis. The histological examination can confirm the disease with certainty. It is necessary to distinguish malignant skin tumors (if they are formed in the breeding cattle and have the ability to infiltrate the surrounding tissues). They metastasize to other organs in a high percentage. Pathological and histological analysis is recommended. The prognosis is unfavorable for widespread papillomatosis, and especially with putrefactive and foul-smelling tumor decay, if tumors are not removed in time.

In milder cases, ligation of papillomas, their termocauterization, freezing with liquid nitrogen, application of keratolytic (usually salicylic acid) can be performed. Vaccine therapy in mild cases shortens the course of the disease by a few weeks. It is recommended to make an autogenous vaccines due to the existence of different types of viruses. One of the possible procedures is the following: a piece of papilloma, the size of a walnut to a pigeons' egg, is washed well with a soap brush, rinsed with water, cut into small pieces, and ground into a porridge. Porridge is then diluted with a 12 to 15 times higher amount of 0.5 percent carbolic acid in physiological sodium chloride solution, strained through the gauze, and kept closed for several days. The obtained amount is then divided into three

parts that are injected subcutaneously at intervals of 8 to 14 days. It is sometimes noticed that the removal of a large mass of papillomas accelerates the disappearance of the remaining ones (Radojičić et al., 2017; Mc Gavin et al., 2008).

Lately, it is recommended to make a porridge from the tumor mass and dilute it with the physiological solution in a ratio of 1:10. The resulting mass should be frozen and thawed 5 to 7 times. The obtained mass is used for the immunization of animals by application to the subcutaneous tissue (Radojičić et al., 2017).

MATERIALS AND METHODS

A clinical case of cow udder papillomatosis

The animal affected by papillomatosis was about 27 months old. A month to two months before that, the cow aborted two fetuses. Hygienic conditions in the facility were satisfactory and there were three more animals in the facility that were not infected. There was intensive pain when touching the udder and papilla. The milking was done mechanically. The animal had a normal metabolism, appetite, with a normal body temperature. Papillomas appeared in the area of the abdomen around the navel, and mostly on the udder, which can be seen in figure 2.

Udder papillomatosis affects the aesthetic appearance but also the milking process. Infectious papillomatosis is interesting. Warts can be imposing. The predilection site is the skin under the udder and the skin of the udder. In practice, it has been noticed that animals up to 2 years of age usually get sick. In older animals, this disease is rare, since there is a possibility that those animals were immunized, after recovering from illness, at a younger age. It has also been noticed in the literature that papillomas and warts appear on the skin of the udder and teats in older cows (Marković, 1982).



Figure 2. Filiform papillomas on the udder, conical small ones located on teats (photo orig. Kosovčević, 2019)

There is no satisfactory treatment for bovine papillomatosis. In some cases, the vaccine is also successful. In this case, we made the vaccine by sampling a couple of large warts, the size of a hazelnut, from the udder. After cleaning with a brush and soap, warts were crushed into porridge and diluted with 10 to 20 times more physiological solution, then filtered through gauze and mixed with 2 to 3% formalin solution and left to stand for several days. The application was done subcutaneously using 1/3 in 2 to 3 occasions at intervals of 8 to 14 days.

RESULTS AND DISSCUSION

In this study, the effect of the vaccine was examined, which gave favorable effects in the treatment of papillomatosis in this animal. The first visible effects occurred after the third administration of the vaccine on day 35, and the final effect appeared after the fifth application of the vaccine on day 55. This can be seen in figure 3. and 4.



Figure 3. The appearance of the udder after the third application of vaccine, 35th day of application of the vaccine (photo orig. Kosovčević, 2019)



Figure 4. The appearance of the udder after the fifth application of the vaccine, 55th day (photo orig. Kosovčević, 2019)

CONCLUSION

The results of this study confirmed the successful effect of the vaccine made from the own papillomas of the animal included in this study. The vaccine stimulates the individual's immune response until the papilloma completely disappears or is cured.

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