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Formation of cauliflower-like growths on the skin and mucous membrane of rabbits

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Small growths may appear at the anus, epidermis or on the tongue of rabbits. Their origin is not well established for some, by the Shope virus or a rabbit papilloma virus for others.

When examining a rabbit, less attention is paid to the anus. However, this region of the body is just as important as the others and can suffer from many problems. Hard droppings and soft droppings that the rabbit re-ingests pass along the anus. This is called

Figure 1: American cottontail with Shope papilloma on its face, lips and neck (Minnesota, USA). Picture courtesy: Tiffany Adams

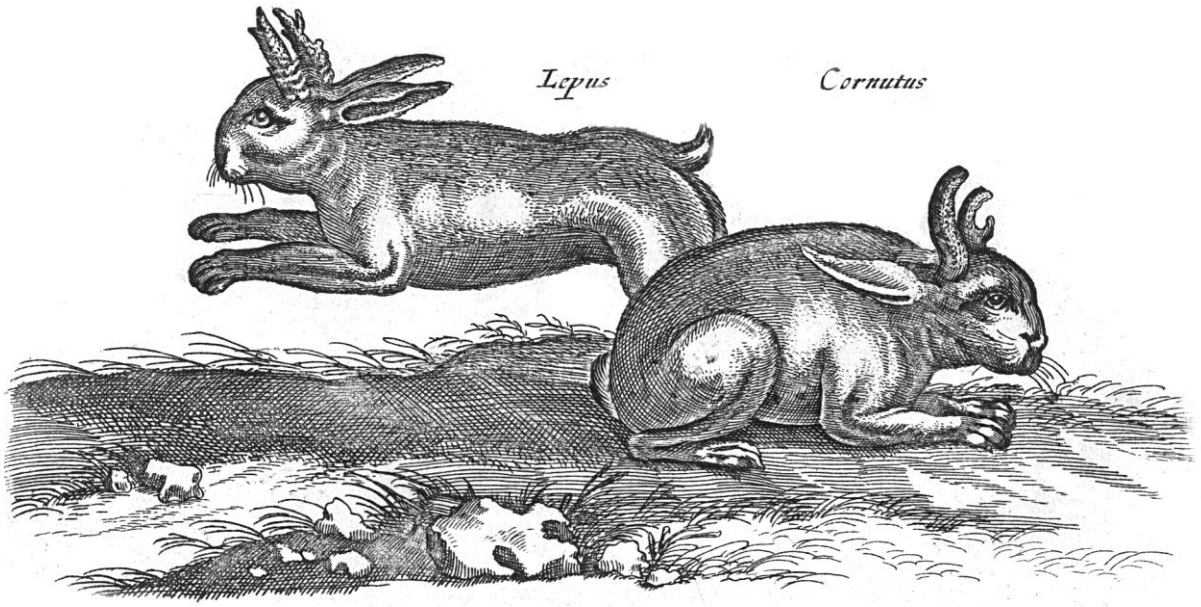

Figure 2: Antique print by Matthäus Merian the Elder (1593 - 1650) showing horned hares.

caecotrophy, which renews the cycle of intestinal bacteria and provides the rabbit with micronutrients, amino acids, vitamins and minerals that are not found in plant food. Sometimes these soft droppings and diarrhea can remain stuck to the fur of the perineal region and form hard crusts whose odor attracts parasitic flies. In other cases, anal glands overflow with odorous secretion and can become infected. Sometimes bleeding from the anus is observed. This is often linked to the presence of a hemorrhoid, polyps or, more frequently, a cauliflower-like growth. Any abnormality in the rabbit's anus should therefore be taken seriously.

Skin papilloma

Skin papillomas are found on the parts of the body where fur is short and less dense: around the nasal openings, eyelids, nose, the inner side of ears and external anal region. They are caused by the Shope papilloma virus, an oncogenic DNA virus that has properties similar to those of Papovaviridae. Its presence causes an exophytic papillary proliferation affecting the squamous epithelium, which leads to the formation of scaly warts or papilloma's.

This virus is native to the United States, where it affects white-tailed cottontails (Figure 1). Large brownish papillomas develop on the face, on the outer lip and on the neck. During the 16th century, trade increased between the North American continent and Europe; travelers could have been passive carriers of the Shope papilloma virus. First accounts of horned rabbits and hares in Europe do, indeed, correlate with the increase in trade. In addition, there are no known accounts or illustrations of "horned" hares or rabbits in Europe before the 16th century (Figure 2). Naturalists of the time studied the horned hare and gave it the Latin scientific name *Lepus cornutus*.

Transmission

Although most Shope papilloma tumors are free of the infectious virus, contact transmission between rabbits is suspected.

Figure 3: Papilloma on the right lip of a female rabbit. It did regress and ultimately disappeared after several months. Picture courtesy: Arie van Praag

The virus can also be transmitted by blood-sucking insects such as fleas, mosquitoes, reduvid bugs or rabbit ticks.

Clinical signs and treatment

Once present in a skin cell, the virus induces the formation of warts covered with scales and papillomas. The first signs are a reddish and swollen area, followed by the growth of a rounded papilloma. Over time, papillomas turn into pedunculated and horned warts and corneal warts (Figures 3, 4). Pigmentation of the tumors is sometimes observed.

One third of the papillomas seen in rabbits regress within 6 months after their appearance, if left untreated. Nevertheless, the Shope virus is more aggressive in the European rabbit than in the American cottontail. Benign tumors can become malignant and progress into carcinoma with metastasis in the lymphatic and pulmonary tissue. Metastatic cells often migrate to the lymph nodes and lungs and, as the disease progresses, in the spleen, kidneys and liver.

Surgical removal of the tumor is recommended, even though papillomas and warts tend to regress over time when left untreated. Ablation methods include traditional surgical excision or elimination of the tumor by laser, electro-desiccation or liquid nitrogen. Administration of pain relievers for at least 24 hours after surgery is necessary.

Anal papilloma

When examining the perineal area, a reddish cauliflower-like growth is sometimes observed at the junction of the rectum and anus, at the level of the anal canal or anal margin (Figure 5). Benign anorectal papilloma's develop from the Malpighian

Figure 4 : Papilloma at the base of the ear in a rabbit. After a few months, a horn appeared. Picture courtesy: Arie van Praag

layer of the skin, one of the 4 layers forming the epithelium composed of keratinocytes. This is why papillomas are never found in the intestine, at most they are found as deep as 1 cm into the anal canal. These growths are comparable to warts seen in other areas of the body. Like warts, the structure of papilloma's is well differentiated, which is typical of benign tumors. Cells that compose the mass preserve their normal epithelial structure and function. The major difference is a greater and faster division of cells. No pain is associated with their presence.

Transmission

The origin of these tumors has not been established to date. A papilloma virus has been suspected in the past, but has never been proven. Indeed, attempts to transmit an anal papilloma from one rabbit to another have failed. In summary, papilloma may not be caused by a papilloma virus, nor are they transmitted to other rabbits, for example during mating.

Clinical manifestations

The size and appearance of a papilloma vary from one individual to another (Figure 5). In some, the size of the growth is that of a pinhead, in others it can reach a centimeter in diameter. Most continue to proliferate over the years and a cancerous transformation cannot be ruled out. If the rabbit develops a strong immune response against the causing agent, the papilloma regresses and disappears naturally a few months later.

Treatment

These growths are very vascular. The tissue is fragile. Any slight trauma will lead to easy and profuse bleeding. When the papilloma reaches a certain size, begins to ulcerate and/or prevents defecation (tenesmus), it is removed surgically by electrocoagulation

Figure 5: Anal papilloma have different presentations in each rabbits. Picture courtesy: Patrick Jacquaz, Julie Smith.

with an electric scalpel or laser, to avoid excessive bleeding. In this case, it is important to remove the whole papilloma tumor and its peduncle, to avoid recurrence. The final diagnosis will be confirmed after a microscopic analysis of the tissue from the removed growth. Prognosis for recovery is good.

An anorectal papilloma must be differentiated from an anal polyp, inverted rectum, tumor of the anus, inflammation of the anus, or growth of scar tissue at the anus as a result of a bite (anal imperforation).

Oral papilloma

White or pinkish cauliflower-like papillomas are also observed on the mucosa of the oral cavity (Figures 6, 7). They are mainly observed on the ventral side of the tongue, more rarely on gums, palate or the internal mucous side of the lips. These papillomas are caused by a rabbit oral papilloma virus (ROPV), which is different from the Shope virus. Unlike the latter, the virus responsible for oral papillomas primarily affects European rabbits and, to a lesser extent, other lagomorphs.

Transmission

The virus that causes oral papillomas can be spread to other rabbits, from a nursing doe to her offspring, or between adult rabbits. Since saliva contains cells that have slough off from the papilloma, it is possible that these cells allow transmission of the virus to another rabbit, e.g., during a grooming session. Laboratory experiments in New-Zealand rabbits have concluded that the mucous membranes of the genitals, such as the penis sheath and the vulva, are also susceptible to the oral papilloma virus, with the growth of small tumors. Such a natural transmission of the virus to the genitals never seems to have

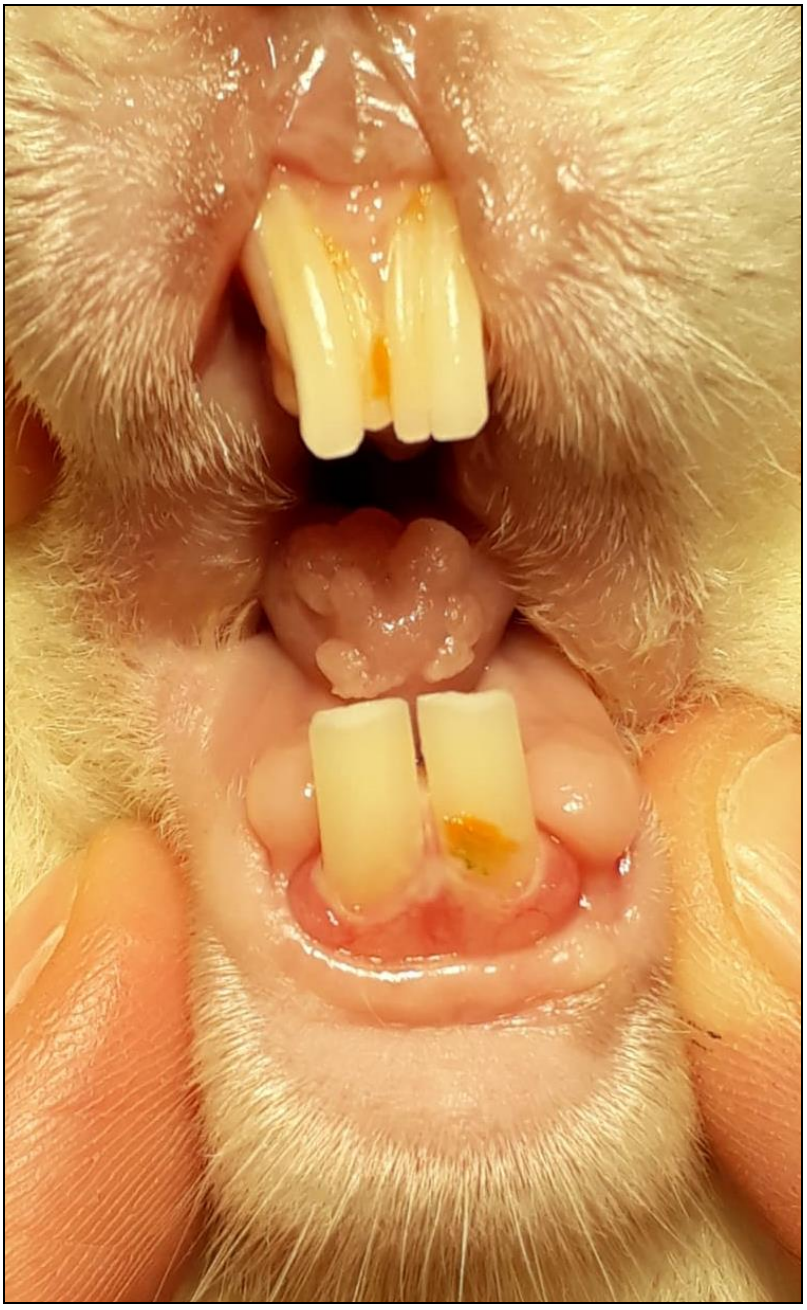

Figure 6: Oral papillomas on the tongue of a rabbit, diagnosis confirmed by a biopsy. Picture courtesy: Marjorie Panchaud

Figure 7: Oral papillomas on the tongue of a rabbit, diagnosis confirmed by a biopsy. Picture courtesy: Marjorie Panchaud

occurred naturally, even if an affected rabbit licks regularly its perineal area. The natural presence of 3 oral papilloma's on the nictitating membrane has, however, been demonstrated in a 3-year-old Flemish Giant rabbit.

Clinical manifestations

Over time, the growths take on a rougher, even pedunculated appearance. Depending on their stage of development, they can reach between 3 and 10 mm thick (Figure 6). Early stage tumors have mostly normal cells. Maturation of the tumor leads to a clear demarcation of the tissues surrounding the tumor, and shows parakeratosis and hyperkeratosis. The cells take on an irregular polyhedral shape. Numerous cell divisions are observed in the basal layer.

The tumors are benign and no cancerous transformation takes place. Their growth is

slow and lasts between 6 and 9 months, after which they disappear naturally within a few weeks. They mainly affect young rabbits up to the age of 2 years after which a lifelong immunity develops against this virus. The immune response causes the inflammation of the papilloma, accompanied by its ulceration, its resorption, and regeneration of the mucosa.

Treatment

When papillomas become a source of trouble in the rabbit's feeding, they can be removed by surgical excision. Administration of antibiotics helps prevent secondary bacterial infections. Analgesic should be given for at least 24 hours after surgery, to relieve pain

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References

EMBL-EBI. Viruses Genomes – Cottontail rabbit papillomavirus. Cottontail rabbit papillomavirus was the first mammalian papillomavirus to be discovered. ebi.ac.uk/2can/genomes/viruses/Cottontail_rabbit_papillomavirus.html

Hagen KW. Spontaneous papillomatosis in domestic rabbits. Bull Wildl Dis Assoc 1986;2:108-110.

Kidd JG, Rous P. Cancer deriving from virus papillomas of wild rabbits under natural conditions. J Exp Med 1940;71:469-493.

Kreider, JW, Bartlett GL. The Shope papilloma-carcinoma complex of rabbits: A model system of neoplastic progression and spontaneous regression. Adv Cancer Res 1981;35:81-110.

Larson CL, J.E. Schillinger JE, Green RC. Transmission of rabbit papillomatosis by the rabbit tick, *Haemaphysalis leporispalustris*. Biol Med 1936;33:536-538.

Munday JS, Aberdein D, Squires RA, Alfaras A, Wilson AM. Persistent conjunctival papilloma due to oral papillomavirus infection in a rabbit in New Zealand. J Am Assoc Lab Anim Sci. 2007 Sep;46(5):69-71.

Phelps WC, Leary SL, Faras AJ. Shope papillomavirus transcription in benign and malignant rabbit tumors. Virology 1985;146:120-129.

Pokorny E. Herrlich Wild – Höfische Jagd in Tirol. Wien, A: Kunsthistorisches. Museum

Robert J. ParsonsRJ., Kidd JG. Oral papillomatosis of rabbits: a virus disease. J Exp Med. 1943; 77(3): 233–250.

Rous P, Beard JW. The progression to carcinoma of virus-induced rabbit papilloma. J Exp Med 1935;62:523-548.

Shope RE. A transmissible tumor-like condition in rabbits. J. Exp. Med 1932;66:793.

Shope RE. Serial transmission of the virus of infectious papillomatosis in domestic rabbits. Proc Soc Exp Biol Med 1935;32:830-832.

Shope RE, Hurst EW. Infectious papillomatosis of rabbits. J Exp Med 1933;58:607-624.

von Bomhard W, Goldschmidt MH, Shofer FS, Perl L, Rosenthal KL, Mauldin EA. Cutaneous neoplasms in pet rabbits: a retrospective study. Vet Pathol 2007;44:579-588.

Weisbroth SH, Scher S: Spontaneous oral papillomatosis in rabbits. J Am Vet Med Assoc. 157:1940–1994, 1970.