Cutaneous lymphoid proliferative diseases in domestic animals

In cutaneous lymphoid proliferations, reactive and neoplastic proliferations can be differentiated. Most proliferations are of T-cell origin. In most cases, those of B-cell origin are plasma cell tumors. A cutaneous involvement is seen in less than 10% of canine lymphomas and 2% of feline lymphomas. The existence of tumors of the natural killer cells is thought likely, but there are no reliable markers available at the moment.

In cats, the meaning of feline leukemia virus (FeLV) in the tumor genesis is well known, whereas in dogs, there is no evidence of retroviral involvement. In sheep and cattle retroviruses are known as a cause of lymphomas.

The histologic differences between reactive and neoplastic proliferations may be very subtle or even impossible to find. Even immunohistology is not a completely safe tool in distinguishing between neoplastic and reactive lesions, but can be helpful to determine the populations. If the populations are positive for a T-cell and not for a B-cell, or vice versa, this gives an indication of the type of population found and can be helpful when choosing treatment.

For scientific purposes, PCR-techniques are used to determine the clonality of the lymphoid populations (poly- or monoclonal). Even if the existence of a reactive monoclonal population is thought possible, this clonality is a strong hint towards a tumor and the proof of the origin of the cells.

Cutaneous plasmacytoma

Cutaneous plasmacytomas are common tumors in dogs, mainly aged between 4 and 13 years. Male dogs are predisposed and a breed predilection is discussed for the Cocker Spaniel. Common sites are pinnae, lips, digits, chin, oral cavity, trunk and rectum. The superficial epidermis is intact in most cases and the diameter is usually less than 2cm. The B-cell marker CD79a is positive in 80% of cases.

A possible aetiology could be that plasma cell tumors develop as a result of a chronic immunostimulation, for example, at the pinna after chronic otitis, or at the gingival with chronic gingivitis. Most extramedullary plasmacytomas are benign and can be cured with surgery. Tumors from the oral cavity, the digits or subcutaneous tumors may be more aggressive. Plasmacytomas in cats are rare, more commonly affecting older male cats.

Although the histologic features are more or less the same as in dogs, the expression of CD markers is not examined in detail. The aetiology should be the same as in dogs. Not much is known concerning plasmacytomas in other animals, although it has been suggested that in horses, the nodular cutaneous amyloidosis might be a plasma cell tumor with excessive deposition of amyloid.

Cutaneous lymphocytosis

The incidence of cutaneous lymphocytosis in dogs and cats is not known in detail. They are characterized by a slow progression and their T-cell origin. Local lymphoid proliferations can develop in other animals as well. Histologically well differentiated lymphocytic lesions with a low mitotic index are found. It has been suggested that the lesions could be caused by chronic antigenic stimulation as found in chronic infections. The T-cell populations are monoclonal, usually indicating a tumor. It is possible that it starts as a reactive lesion which develops towards a slowly progressive lymphoma. In cats it is known that primary lesions can last up to two years, in some cases waxing and waning. In all cases lesions seem to come back sooner or later and become progressive.
Internal organs can also be affected. Cats that are affected are aged between 6 and 15 years. In dogs, very few cases are described. There have been published cases of cutaneous lymphocytosis in horses, but surgery often cures these.

**Epitheliotropic lymphoma**

As in human medicine, there are four different classified subtypes. The most common one is “classical mycosis fungoides” (MF). This strain often involves the lymph nodes and regularly spreads to other organs, although the leukemic form (“Sezáry-syndrome”) is very rare. In all cases, epitheliotropic lymphoma is a T-cell lymphoma.

Dogs are the most commonly affected domestic species. There are three clinical stages: patch, plaque and tumor stage. Patch and plaque may occur at the same time, and older animals are predisposed.

Clinically, MF is subdivided into 4 principal categories:

1. Exfoliative erythroderma: generalized erythema, scales, loss of pigment, alopecia.
2. Mucocutaneous lesions such as loss of pigment, erosions and ulcerations.
3. Solitary or multiple plaques or nodules.
4. Ulcerative alterations of the oral mucosa.

The histopathologic key feature is the tropism of the lymphocytic tumor cells for the epidermal, mucosa-associated or follicular epithelium. In the epithelium, the distribution of the tumor cells may be diffused or in microaggregates (“Pautrier’s microabcesses”). Single lesions may regress spontaneously, but the overall disease is progressive with a survival time of up to 2 years.

Chemotherapeutical protocols do not influence the disease significantly. Although the aetiology is not known, in dogs, a relation to retroviruses has not been found. A persistent antigenic stimulation leading to chronic T-cell activation is discussed. Epitheliotropic lymphoma in cats is rare, usually affecting older animals, with lesions most commonly found on the head. Here the aetiology is not known either, although an infection with FeLV seems to be the exception. Epitheliotropic lymphoma is known to occur in rabbits and horses, although in ferrets only one case has been described.

**Cutaneous non-epitheliotropic lymphoma**

Primary cutaneous non-epitheliotropic lymphomas may occur or it may occur as a cutaneous manifestation of the generalized lymphoma. As well as the classical forms, vasotrophic and vasoinvasive tumors are also possible. The large majority is of T-cell origin, B-cell lymphomas being very rare. The non-epitheliotropic cutaneous lymphomas are rare, even compared to the epitheliotropic lymphomas. The average age of dogs affected is between 9 – 11 years old. The classical forms show solitary or multiple nodules or infiltrative plaques in all locations.

**Chronic lymphatic leukemia with cutaneous lesions**

Very few cases have been published involving cats and dogs, with leukemia developing cutaneous involvement in later stages.