

Thymomas

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Thymomas are neoplasms of the thymic epithelial cells. They are heterogeneous tumors that include and are sometimes dominated by well-differentiated, nonneoplastic lymphocytes. Well-differentiated lymphoma is a primary differential diagnosis for these tumors. Thymomas are rare tumors in all species. Most reports of thymomas in veterinary medicine are in dogs and cats. Rabbits are also commonly affected (► see Chap. 19), and some reports state that thymomas are one of the most common tumors in older goats.

17.1 Canine Thymomas

Box 17.1. Canine Thymomas in Six Facts

1. Rather rare tumor of dogs
2. Benign growth pattern but clinically malignant due to thoracic mass effect
3. Dyspnea, cranial edema, and cardiac insufficiency as the most common clinical signs
4. Several paraneoplastic syndromes including dermatitis and myasthenia gravis
5. Cytological/histopathologic diagnosis difficult due to lymphocyte dominance in the tumor
6. Surgery as the treatment of choice and associated with a good prognosis

■ Epidemiology and Pathogenesis

Thymomas are rare tumors in dogs but are one of the most common tumors of the cranial mediastinum. They derive from thymic epithelial cells, usually have a *slow and expansive* growth, and only *rarely metastasize*. Nevertheless, due to their delicate location in close proximity to the heart and to the nerves and vessels in the cranial mediastinum, thymomas are often difficult to resect and are a *fatal and clinically malignant disease*. They occur in dogs at a median *age* of 9 years. There is no *gender* or *breed* predisposition. The causes and mechanism of thymoma development in dogs or any other animal species are unknown.

■ Clinical Appearance

Common *clinical signs* in dogs with thymomas are usually related to the mass effect in the thorax. Compression atelectasis of the lung may be associated with *dyspnea, tachypnea, and coughing*. Compression of the cranial vena cava or any other veins draining the cranial region of the body may occasionally be associated with edema of the head and the front limbs. Finally, displacement and encasement of the heart may lead to *moderate cardiac insufficiency*. Exophthalmos is a very common finding in rabbits with mediastinal masses.

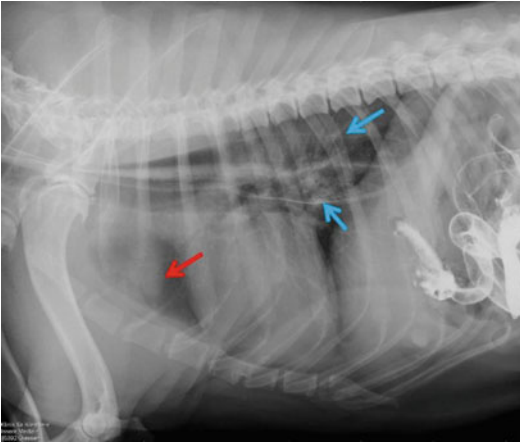
Thymomas are associated with several *paraneoplastic syndromes*, which occur in more than 50% of affected dogs. *Thymoma-associated myasthenia gravis*, an antibody-based autoimmunity against acetylcholine receptors, is the most common paraneoplastic syndrome and may be present in 20–40% of dogs with thymomas. The exact molecular mechanisms of the syndrome are unknown, but a lack of myoid cells in thymomas is suspected, but the exact mechanism is unclear. It is associated with paralysis of the esophagus and leads to megaesophagus, regurgitation, and aspiration pneumonia. *Thymoma-associated exfoliative dermatitis* is more often found in affected cats but has been described in some dogs. It is characterized by a diffuse severe cutaneous erythema and exfoliation (large scales). Again, the underlying molecular mechanisms of the disease are unclear. Finally, autoimmune polymyositis, anemia due to immune-mediated hemolysis, and hypercalcemia due to secretion of parathormone-related peptide have occasionally been described in dogs with thymomas.

Blood work is usually unremarkable in dogs with thymomas.

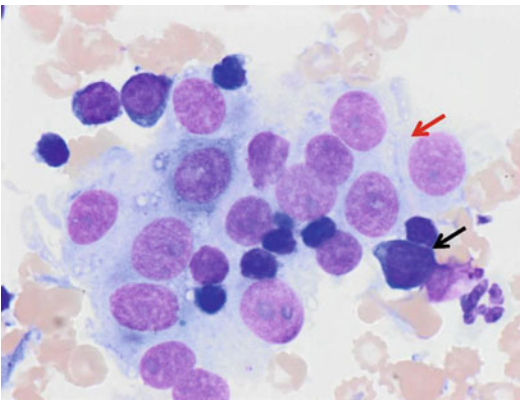
Thoracic radiographs and particularly *computed tomography (CT)* are usually helpful to identify cranial masses and to evaluate the extent of replacement and invasion of the surrounding structures (■ Fig. 17.1). *Ultrasound* is also commonly used to identify and confirm mediastinal masses. Final diagnosis requires *ultrasound- or CT-guided fine needle aspiration* or biopsy.

■ Cytology and Histopathology

Cytology of *fine needle aspirates* of the tumor mass and pleural fluids obtained by *thoracocentesis* usually contain a high fraction of small,



■ **Fig. 17.1** Thoracic radiograph, right lateral recumbency, thymoma (red arrow), and megaesophagus (blue arrow) due to subsequent myasthenia gravis (With permission of Dr. N. Bauer, Faculty of Veterinary Medicine, Justus Liebig University, Giessen, Germany)



■ **Fig. 17.2** Cytology, thymoma dog (the same dog as in ■ Fig. 17.1), May-Grünwald-Giemsa, 1000x. Note the small cluster of slightly spindle-shaped to polygonal epithelial cells (red arrow) surrounded by small- to medium-sized mature lymphocytes (black arrow) (With permission of Dr. N. Bauer, Faculty of Veterinary Medicine, Justus Liebig University, Giessen, Germany)

mature, well-differentiated lymphocytes, and fewer medium-sized lymphocytes interspersed between a few neoplastic thymoma cells (■ Fig. 17.2). The lymphocytes often cover the actual epithelial spindle-shaped and occasionally plump polygonal epithelial tumor cells. Well-differentiated mast cells and macrophages can also be present. *Cytological preparations may be misdiagnosed as a well-differentiated lymphoma.*

A homogenous population of one type of lymphocyte and the absence of other cell types are indicative of lymphoma, while a mixed cellular population is suggestive of thymoma even in the *absence of epithelial cells.*

Histopathology of biopsies or surgically excised tumors can be a good diagnostic tool. Diagnosis is often complicated by the presence of numerous well-differentiated lymphocytes covering the actual tumor cells. *Hassall's corpuscles*, concentric eosinophilic masses, are specific structures of thymic tissues and are usually also present in thymomas. *Immunohistochemical detection of cytokeratin* improves the detection and evaluation of cellular morphology of the positive tumor cells.

■ Therapy

Surgery is the most commonly used treatment modality for canine thymomas. Radiographs and CT must be used to determine how resectable the tumor is, but a lot depends on the skills and experience of the surgeon. In the few studies available, it is stated that surgical excision is associated with median survival times of 2–3 years in almost 50% of patients. There is a 20% recurrence rate, but secondary surgery is associated with a *good prognosis.*

Prednisone and doxorubicin are used as *primary and adjuvant chemotherapy*; chemotherapy is associated with partial remission and shrinking of the tumor. Shrinkage is however thought to be caused by a reduction of the non-neoplastic lymphocyte population in the tumor rather than directly targeting the thymoma cells.

Radiation therapy may also be associated with a partial or complete response and survival times of up to 8 months, but more studies are required to confirm its efficacy.

■ Prognostic Factors and Molecular Markers

The prognosis for canine thymomas very much depends on resectability and surgical treatment. Complete resection is associated with a good prognosis for long-term survival. Vascular invasion is negatively correlated with prognosis, whereas the amount of lymphocytic infiltrate is positively correlated with prognosis.

Studies do not show a correlation between survival time and hypercalcemia and the presence of myasthenia gravis or megaesophagus at the time of thymoma diagnosis, histopathological thymoma subtype, or tumor development at a later date.

■ Suggested Further Reading

(Aronsohn et al. 1984; Atwater et al. 1994; Day 1997; Hunt et al. 1997; Hylands 2006; Marx et al. 2015; Moffet 2007; Robat et al. 2013; Smith et al. 2001; Tepper et al. 2011; Turek 2003; Yoon et al. 2004; Zitz et al. 2008)

17.2 Feline Thymomas

Box 17.2. Feline Thymomas in Six Facts

1. Rather rare tumor of cats
2. Benign growth pattern but clinically malignant due to thoracic mass effect
3. Dyspnea, cranial edema, and cardiac insufficiency as the most common clinical signs
4. Paraneoplastic syndromes less common than in the dog
5. Cytological/histopathologic diagnosis difficult due to lymphocyte dominance in the tumor
6. Surgery as the treatment of choice and associated with a good prognosis

■ Epidemiology and Pathogenesis

Thymomas are very rare tumors of the cranial mediastinum. Mediastinal lymphomas by far outnumber thymomas in the cat (▶ see Chap. 6). There is significantly less literature on feline thymomas than on canine thymomas, but they seem to be similar in most aspects of their biology, clinical signs, and response to treatment. Feline thymomas derive from *thymic epithelial cells*, usually have a slow and expansive growth, and only *rarely metastasize*. Nevertheless, due to their delicate location in close proximity to the heart and to the nerves and vessels in the cranial mediastinum, thymomas are often difficult to resect and are a *fatal and clinically malignant disease*. They occur in cats at a median age of 10 years. There is no

gender or *breed* predisposition. The causes and mechanism of thymoma development in cats or any other animal species are unknown.

■ Clinical Appearance

The common *clinical signs* in cats are in almost all aspects similar to those in dogs with the exception of the incidence of paraneoplastic syndromes. Clinical signs are usually related to the mass effect in the thorax. Compression atelectasis of the lung may be associated with *dyspnea*, *tachypnea*, and *coughing*. Compression of the cranial vena cava or any other veins draining the cranial region of the body may be associated with edema of the head and the front limbs. Finally, displacement and encasement of the heart may lead to *moderate cardiac insufficiency*.

Thymomas are associated with several *paraneoplastic syndromes*. *Thymoma-associated myasthenia gravis*, an antibody-based autoimmunity against acetylcholine receptors, is occasionally described as a paraneoplastic syndrome in cats. The exact molecular mechanisms of the syndrome are unknown. It is associated with paralysis of the esophagus and leads to megaesophagus, regurgitation and aspiration pneumonia, and generalized weakness. *Thymoma-associated exfoliative dermatitis* (■ Fig. 17.3) is rare but has been well described in the literature. It is characterized by a diffuse severe non-pruritic, cutaneous erythema and exfoliation (large scales). Again, the underlying molecular mechanisms of the disease are unclear.

Blood work is usually unremarkable in cats with thymomas.

Thoracic radiographs and particularly *computed tomography (CT)* are usually helpful to identify cranial masses and to evaluate the extent



■ Fig. 17.3 Exfoliative dermatitis in a cat with a thymoma

of replacement and invasion of the surrounding structures. *Ultrasound* is also commonly used to identify and confirm mediastinal masses. Final diagnosis requires *ultrasound- or CT-guided fine needle aspiration* or biopsy.

■ Cytology and Histopathology

Cytology of fine needle aspirates of the tumor mass and pleural fluids obtained by *thoracocentesis* usually contains a high fraction of small mature, well-differentiated lymphocytes, and a few well-differentiated mast cells and macrophages interspersed between a few neoplastic thymoma cells. The lymphocytes often cover the actual epithelial spindle and occasionally plump polygonal epithelial tumor cells. Cytological preparations may be misdiagnosed as well-differentiated lymphomas. A homogenous population of one type of lymphocyte and the absence of other cell types are indicative of lymphoma. A heterogeneous cellular population is suggestive of thymoma.

Histopathology of biopsies or surgically excised tumors can be a good diagnostic tool. Diagnosis is often complicated by the presence of numerous well-differentiated lymphocytes covering the actual tumor cells. *Hassall's corpuscles*, concentric eosinophilic masses, are specific structures of thymic tissues and are usually also present in thymomas. There is an uncommon, feline-specific cystic thymoma subtype, which is associated with a better prognosis than solid thymomas. *Immunohistochemical detection of cytokeratin* improves the detection and evaluation of cellular morphology of the positive tumor cells.

■ Therapy

Surgery is the most commonly used treatment modality for feline thymomas. Radiographs and CT must be used to determine how resectable the tumor is, and success very much depends on the skills and experience of the surgeon. In the few studies available, it is stated that surgical excision is associated with survival rates of 89% at 1 year and 75% at 3 years and a median survival of 5 years.

Prednisone and doxorubicin have been tested as *primary and adjuvant chemotherapy* in a few studies and may be associated with partial remission and shrinking of the tumor. Shrinkage is thought to be caused by a reduction of the non-

neoplastic lymphocyte population in the tumor rather than directly targeting the thymoma cells.

Radiation therapy may also be associated with a partial or complete response and survival times of up to 2 years, but more studies are required to confirm its efficacy.

■ Prognostic Factors and Molecular Markers

The *prognosis* for feline thymoma very much depends on the resectability and surgical treatment. Complete resection is associated with a good prognosis for long-term survival. Vascular invasion is negatively correlated with prognosis, whereas the amount of lymphocytic infiltrate is positively correlated with prognosis. The recurrence and presence of paraneoplastic syndromes have no influence on prognosis.

■ Suggested Further Reading

(Cavalcanti et al. 2014; Day 1997; Hill et al. 2013; Patnaik et al. 2003; Shilo et al. 2011; Singh et al. 2010; Smith et al. 2001; Spadavecchia and Jaggy 2008; Turek 2003; Yoon et al. 2004; Zitz et al. 2008)

17.3 Thymomas of Goats

Box 17.3. Thymomas of Goats in Three Facts

1. Common tumor in old goats
2. Benign growth, often incidental necropsy finding
3. No reported treatment modality in this species

■ Epidemiology and Pathology

Thymomas in the goat are tumors of thymic epithelial cells. The few epidemiologic studies on tumors in goats indicate that thymoma may be the *third most common tumor* in this species after lymphoma and squamous cell carcinomas. There seems to be a predisposition for dairy goats. Up to 25% of all tumors in *Saanen goats* are thymomas, suggesting a *breed disposition* for these animals. Thymomas are usually a tumor of middle-aged to old goats, appearing at an *age* of 4–10 years. Thymomas in the goat are usually *incidental find-*

ings found on necropsy. Clinical signs including *dyspnea* or esophageal compression with *megaesophagus* and regurgitation have been described in a few rare cases. Caprine thymomas are usually slowly and *expansively growing tumors*. Metastatic thymic carcinoma has been described in one case report in a goat with pulmonary metastases. *Cytologically and histopathologically*, the cytokeratin-positive cells are often hidden by abundant mature lymphocytes. There are no reports on treatment modalities or prognostic factors for caprine thymomas.

■ Suggested Further Reading

(Braun et al. 2009; Hadlow 1978; Lohr 2013; Olchowoy et al. 1996; Parish et al. 1996; Rostkowski et al. 1985)

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