Original Article

Clinical findings in lung-digit syndrome in five cats

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Abstract

Clinical studies were carried out in five cats that had disseminated metastases of a primary pulmonary tumor and were suspected of having so-called lung-digit syndrome. In each animal, the primary pulmonary tumor was a solitary nodular lesion. One cat exhibited respiratory symptoms, but the other four animals showed absolutely none of them, even at the time of death. The disseminated metastases were detected in the digits, superficial muscles, skin, lymph nodes and scapula. The median survival time was 60 days (range : 12 ~ 125 days). Except for the animal that died with respiratory symptoms, the animals died suddenly due to unknown causes. These results indicate that a pathological diagnosis based on pulmonary lobectomy for lung-digit syndrome does not have much therapeutic significance, even if it has diagnostic meaning, except in cases with pronounced respiratory symptoms. In addition, the metastatic lesions were spread throughout the body, sometimes in multiple limbs. For that reason, it can be surmised that surgical approaches such as amputation of digits or limbs, which result in functional and organic deficits, are likely to lead to further reduction in quality of life due to the increased burden placed on the remaining digits and limbs without contributing significantly to a cure.

Key word : cat, disseminated metastasis, lung-digit syndrome, primary pulmonary tumor

Introduction

Lung tumors in cats are reported to be rare [2]. Indeed, during the period from April 1985 through March 2008 at Oncology Department, Azabu University Veterinary Teaching Hospital (AUVTH), we diagnosed a total of 1,070 cases of tumors in cats, which included 59 cases of respiratory system tumors, but only 10 of these were pulmonary tumors. Histopathologically, adenocarcinomas are reported to be the most common type of pulmonary tumor in cats [10], followed by squamous cell carcinomas and carcinosarcomas [7]. The etiological factors involved in pulmonary tumors in cats remain unclear, but a case of apparent bacterial involvement has been reported [6]. Metastasis to the bronchial lymph nodes and to other lobes of the lung is common [1], and the prognosis of undifferentiated carcinomas is considered to be worse than that of highly differentiated lesions [9]. In humans and dogs, the cause of death in cases with pulmonary tumors is often respiratory failure brought on by pneumonia or retention of pleural effusion due to pleural infiltration.

In pulmonary tumors in cats, a condition known as lung-digit syndrome has been described, and is characterized by disseminated metastasis of the primary pulmonary tumor to the digits [8]. Only a few reports have been published on the lung-digit syndrome in cats, but it has been reported that the prognosis is very poor, with a median survival of 34 to 104 days [8,15,16]. It is possible reportedly that this syndrome could be associated with various tumors, including adenocarcinomas and squamous cell carcinomas [4,12,14], and that the sites of metastasis include not only the digits but also the skin, kidneys and muscles [4,5,12]. In humans, a possible same pathophysiology is also known in which primary pulmonary tumors show disseminated metastasis to the digits, but much remains unclear regarding this disease condition, and there

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Fig. 1. X-ray image of the hindlimbs of Cat 2. Obvious osteolysis is seen.

Fig. 2. Photograph of the digits of Cat 3 at initial examination. There is no blood flow in the ungual process of the claws of the 2nd, 3rd and 4th digits of the right forelimb. It was thought that this might represent the initial stages of a metastatic digital lesion.

have been few reports concerning its treatment.

In the present study, we report the results of a retrospective analysis of five cats having lung-digit syndrome on the basis of various clinical and laboratory findings.

Cases

Cat 1 was an 8-year-old, castrated male Scottish Fold. One month prior to being brought to AUVTH, a hard mass, 1.8 cm in diameter, was palpated intramuscularly in the left thigh. The mass rapidly increased in size, attaining a diameter of 3.0 cm in approximately 2 weeks. The animal was then taken to the referring veterinary hospital, and incision biopsy performed at that time led to a diagnosis of adenocarcinoma based on histopathology. The owner was recommended to consider extensive surgery, including limb amputation, and subsequently brought the animal to our hospital. An initial examination revealed the mass in the left thigh to have a diameter of 3 cm and to be wedged into the underlying muscle. In addition, a 7-mm mass was detected in the buccal skin and a 5-mm mass was detected on the left side of the larynx. Cytology of both lesions showed cell clusters with a high degree of atypia, and they were considered to be epithelial in origin. Chest X-rays showed an isolated 3-cm nodular shadow in the median region of the pulmonary posterior lobe. These findings were consistent with lung-digit syndrome, and therapy consisted mainly of symptomatic treatment for ulceration. On Day 28, the general condition of the animal was favorable, but each of the tumors had nevertheless grown larger. Thereafter, the general condition gradually worsened, and on Day 60, the patient died suddenly of unknown causes. The animal had shown an appetite until the day before death, and there had been no respiratory symptoms accompanying the pulmonary tumor.

Cat 2 was a 10-year-old, spayed female American Shorthair. The cat had been taken to the referring veterinary hospital with the chief complaint of bleeding from the claws. Chest X-rays performed at that time revealed an isolated mass in the pulmonary right posterior lobe. At the time of examination, histopathology of the desquamated nail bed lesion led to a diagnosis of carcinoma, and the animal was brought to AUVTH. In our examination the digital tumor showed a clear increase in size, and ulceration, decomposition (Fig. 3) and osteolysis (Fig. 1) were observed. Chest X-rays during our initial examination revealed an isolated mass in the right posterior lobe that was 4 cm in diameter and had not increased in size. Symptomatic and supportive therapies were initiated with no anticancer therapy. The animal died suddenly of unknown causes on Day 104.

Cat 3 was a 14-year-old, spayed female American Shorthair, which was brought to AUVTH with the chief complaints of digital lesions and an isolated pulmonary mass. The digital lesions were located on multiple digits, and there was clear swelling and ulceration involving multiple digits on the right hindlimb, along with marked lameness. Cytology of this lesion

Fig. 3. Photograph of the right hindlimb of Cat 2. Swelling, ulceration and decomposition are seen to involve multiple digits.

Fig. 4. X-ray image of the scapula of Cat 3. Swelling of the soft tissues and osteolysis are seen.

Fig. 5. X-ray image of the tail of Cat 4. Osteolysis of a tail vertebra is seen.

yielded epithelial cell clusters showing atypia. The right forelimb did not show any swelling, but there was no blood flow in the ungual process of the claw (Fig. 2). We considered that this might represent the initial stages of a possible metastatic digital lesion. Chest X-rays confirmed the presence of an isolated, 4×3-cm mass in the right posterior lobe. Subsequently, the animal developed disseminated lesions of the facial skin and scapula (Fig. 4). The animal died suddenly of unknown causes on Day 125. Even at the time of death, the animal did not exhibit any respiratory symptoms.

Cat 4 was a 12-year-old, castrated male American Shorthair. It had been taken to the referring veterinarian with the chief complaint of bleeding from the digits. Swelling of the digits was noted, and histopathology of the desquamated nail resulted in a diagnosis of a carcinoma. Because the animal also had lesions on multiple digits, the tail and lymph nodes, it was brought to AUVTH. The second digit on the right hindlimb was enlarged to 2 cm with accompanying tenderness and ulceration, and obvious osteolysis was noted. The tail lesion also exhibited tenderness and osteolysis (Fig 5). The lymph nodes below the right knee were swollen to 1.5 cm, and epithelial cell clusters accompanied by similar atypia were obtained from the lesions at the three sites noted above. Chest X-rays confirmed the presence of an isolated, 2-cm mass in the left posterior lobe. Subsequently, symptomatic therapy was administered, but the metastatic lesions of the digits increased in size, and the quality of life (QOL) of the animal worsened due to pain. On Day 42, the animal died due to deterioration of its general condition caused by respiratory symptoms.

Cat 5 was a 12-year-old, spayed, mixed-breed female. The animal was examined at the referring veterinary hospital with the chief complaint of sudden enlargement of a neck mass. The neck mass was 3 cm in size and was firmly attached to the underlying tissue. Facial palsy was observed, and was thought to be associated with tumor infiltration. Chest X-rays were performed and confirmed the presence of a 2-cm, isolated mass in the left lung posterior lobe. When the animal was referred to and examined at AUVTH, the cervical mass was found to have increased in size to 5 cm, and was surrounded by edema. We also observed mass lesions accompanied by pain in the nail bed of multiple digits of both the right

Table 1

	Cat 1	Cat 2	Cat 3	Cat 4	Cat 5
Breed	Scottish Fold	American Shorthair	American Shorthair	American Shorthair	Mixed
Age at Onset (y)	8	10	14	12	12
Survival (d)	60	104	125	42	12
Cause of Death	Unclear (sudden death)	Unclear (sudden death)	Unclear (sudden death)	Respiratory symptoms	Unclear (sudden death)
Presence of Respiratory Symptoms at Death	No	No	No	Yes	No
Initial Symptom	Thigh skin mass	Digital lesions	Digital lesions	Digital lesions	Digital lesions
Sites of Disseminated Metastasis	Thigh, neck, cheek	Multiple digits	Multiple digits	Multiple digits, tail, lymph nodes	Multiple digits
Site of Pulmonary Mass	Right posterior lobe	Right posterior lobe	Right posterior lobe	Left posterior lobe	Left posterior lobe
Size of Pulmonary Mass at Discovery at X-ray (cm)	3×2	4×4	4×3	2×2	2×2
Histopathological Specimen	Skin punch biopsy	Desquamated digital lesion	None	Desquamated digital lesion	None
Histopathological Diagnosis	Adenocarcinoma	Carcinoma	None	Carcinoma	None

forelimb and the left hindlimb. Cytology of those lesions yielded epithelial cell clusters showing atypia. The pulmonary mass was 2 cm in size and thus had not grown. Symptomatic therapy was initiated, but the general condition worsened and the patient died on Day 12. This animal had not exhibited any respiratory symptoms.

Discussion

It has been reported that the primary lung lesion in lung-digit syndrome is usually a solitary nodular lesion that is asymptomatic in the initial stages [15]. The five cats that we examined in this study were characterized by having a solitary pulmonary nodular lesion, and in all cases, the reason for the visits to the referring veterinarians was the presence of metastatic lesions of the digits (Table 1). Moreover, no respiratory symptoms accompanying the pulmonary mass were observed at the time of the initial examination.

The metastatic lesions in lung-digit syndrome are generally lesions of the digits [3,5], and in four of the five cats we analyzed, the lesions were in the nail bed. Nail-bed lesions are sometimes initially noted as caused by poor circulation in the blood vessels of the nail (Fig. 2), and as the condition worsens, obvious swelling and osteolysis occur, and ulceration and necrosis are observed (Fig. 1, Fig. 3). The metastatic lesions consisted only of nail lesions in two of our cats, whereas the other three animals also had lesions at other sites (facial skin, thigh muscles, tail (Fig. 5), lymph nodes, and scapula (Fig 4)). The literature also documents lesions disseminated to other organs and tissues, including the brain, heart, kidney, spleen, diaphragm, thoracic vertebrae and eyeball. [4,11–13]

In lung-digit syndrome, dissemination from the primary pulmonary tumor occurs as a result of migration of malignant cells via a pulmonary vein and then the aorta, thereby spreading systemically. Accordingly, there is a possibility that cancer cell dissemination may occur throughout the body, particularly to organs and tissues that have a rich blood supply, such as the kidneys and heart. Lesions disseminated to such sites are difficult to detect in comparison with those of the nail bed, and as a result they are not reported very often. This indicates the need for more thorough examination of cats with lung-digit syndrome by necropsy.

For a definitive histopathological diagnosis of lung-digit syndrome, it is necessary to perform tissue diagnostics on both the pulmonary mass and the metastatic lesion(s), and the findings must be in agreement. In addition, it has been reported that identification of the primary lesion can be achieved on the basis of the periodic acid-Schiff reaction and/or immunohistochemical staining for keratin 8 [15]. Histopathological studies were not conducted on the pulmonary mass of any of the five cats reported here because of danger, and only the metastatic lesions of three animals were examined (desquamated nail bed in two cats; core biopsy of intramuscular mass in one cat) histopathologically. For this reason, we were unable to rule out the possibility of primary tumor in the digit or at other locations to have metastasized to the lung or others, or the possibility of having multiple tumors in the body. However, solitary nodular lesions having a size of 2 cm or greater are highly likely primary lung tumors. In addition, diagnosis of carcinoma was made in all five cases, either cytologically or histologically, with the body surface lesions. Also, it has been reported that 87.5% of tumors in the digits of cats are

metastatic lesions [15]. On the basis of these, we surmise that these five animals were consistent with lung-digit syndrome.

There have been few reports published regarding the treatment of lung-digit syndrome, and to our knowledge there have been absolutely no reports of successful therapy. It has been reported that respiratory symptoms due to the pulmonary mass in lung-digit syndrome exert little effect on the duration of survival or QOL [8]. Cytology of an asymptomatic pulmonary mass by highly invasive lobectomy has diagnostic value, but it has little benefit in terms of therapy. Metastatic lesions spread throughout the body, including multiple limbs. For that reason, surgical approaches such as amputation of digits or limbs, which result in functional and organic deficits, have the potential to further reduce QOL. Accordingly, careful consideration should be given to these factors when deciding whether surgical approaches are indicated. To date, there have been few reports published regarding chemotherapy or radiotherapy for lung-digit syndrome; therefore, these approaches need to be investigated in the future.

None of the published reports has identified any cat breed that is particularly susceptible to lung-digit syndrome, but it is noteworthy that three of the five cats we analyzed were American Shorthairs. Although the number of animals was obviously small, the present tendency for American Shorthairs to be predominant indicates the need for a larger number of cases, with the objective of investigating whether certain cat breed(s) are particularly susceptible to this syndrome.

The median survival of cats with lung-digit syndrome has been reported to be 34 to 104 days [8,15,16], and the median survival of our cases, although small in number, was also very short as 60 days (12–125).

If a tumor is discovered in a digit in a cat, it is necessary to perform a careful examination of the whole body, including chest X-rays, at an early stage. If lung-digit syndrome is suspected, it is important to explain to the owner that the prognosis is very poor and that there is a possibility of sudden death. In addition, we believe that any decisions regarding indications for surgery should take into careful consideration the possibility that such surgical approaches as pulmonary lobectomy and amputation of digits or limbs may not translate into longer survival or an improved QOL. In the future, we hope to accumulate a larger number of cases of lung-digit syndrome in cats and to perform necropsies with the objectives of elucidating the developmental morphology of this syndrome and of investigating the efficacy of chemotherapy and radiotherapy in its treatment.

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肺指症候群の猫5例の臨床所見

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和文要約

肺指症候群と考えられた猫5例の臨床所見について検討を行った。肺原発巣に伴う呼吸器徴候は5例中1例のみで見られ、ほかの4例では呼吸器症状は全くみられなかった。播種転移部位は、主に、指、体表部筋肉、皮膚であった。5例の中央生存期間は60日（12～125日）であり、呼吸器徴候を伴い死亡したものは1例のみであった。これらの臨床所見から、本病態における治療として、肺葉切除は意義が低いことが示唆された。また、転移病変は全身に存在することから、断指をはじめとする外科的治療は残存する指や肢の負重増加により動物の生活の質をさらに低下させる可能性が示唆された。

Key word : cat, disseminated metastasis, lung-digit syndrome, primary pulmonary tumor

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