jfms

CASE REPORT
Metastatic squamous cell carcinoma in a cat

Ravinder S Dhaliwal DVM, MS, DACVIM (Oncology), DABVP (Canine and Feline)[1]*,
Eric Kufuor-Mensah DVM, PhD, DACVP[2]

[1]*All Care Animal Referral Center, 18440 Amistad Street, Fountain Valley, CA 92708, USA*
[2]*Antech Diagnostics, 17672-A Cowan Avenue, Irvine, CA 92614, USA*

A 7-year-old, spayed female Persian cat was referred for evaluation of progressive paraplegia. The cat was thin, cachectic and paraplegic on presentation. The survey radiographs showed a left caudal pulmonary lesion and lytic skeletal lesions at the right iliac crest and left distal scapula. Due to a poor prognosis for complete recovery, the owner opted for euthanasia. Post-mortem examination revealed bilaterally small and irregular kidneys, lysis of the left iliac crest and left distal scapula and a dilated left ventricular lumen with a thin interventricular septum. Histologically, all the lesions were determined to be squamous cell carcinoma. It appears that the origin or the primary site of the malignancy in this case is pulmonary as cardiac and skeletal tissues are primarily mesenchymal in origin and are less likely to develop a primary epithelial malignancy. To the best of our knowledge, there is no description of cardiac or skeletal metastatic squamous cell carcinoma in a cat.

© 2006 Published by Elsevier Ltd on behalf of ESFM and AAFP.

Squamous cell carcinoma (SCC) is a common oral and integumentary malignancy in cats (Carpenter and Valentine 1992, Anilkumar et al 1994, Rees and Goldschmidt 1998, Bregazzi et al 2001). Biologically, these neoplasms are reported to be locally aggressive and rare to metastasize (Sironi et al 1999, Mukaratirwa et al 2001). Although uncommon feline SCC from other anatomic locations may have more malignant biologic behavior in such cases (Hamilton et al 1984, Anilkumar et al 1994). However, there has been no report on disseminated metastatic SCC in cats. In this study, we describe distant multiple site SCC in a cat with likely lung as a primary site.

A 7-year-old, 1.54 kg, spayed female Persian cat was referred for evaluation of paraplegia. Past medical history included weight loss and anorexia of about 1 month duration. The owner also reported that the cat had been getting progressively weaker on the rear legs and exhibited signs of dyschezia, sneezing and mild dyspnea. A complete blood count, serum biochemical analysis and urinalysis were performed before referral. The complete blood count revealed

mild normocytic normochromic anemia (hematocrit 27%; reference range 29–48%). Results of serum biochemical tests were within reference ranges. The cat was euthyroid and tested negative for retroviruses (feline leukemia and feline immunodeficiency) and coronavirus (feline infectious peritonitis). Urinalysis indicated a urine specific gravity of 1.049 with a 3+ proteinuria, 50–100 red blood cells per high power field and 3+ occult blood. The referring veterinarian was treating the cat for periodontal disease, upper respiratory tract infection, anemia, anorexia and dehydration without clinical improvement. Treatment included routine dental prophylaxis with some extractions, oral antibiotics, an appetite stimulant, an oral multivitamin and an ophthalmic triple antibiotic ointment.

On presentation, the cat appeared thin and cachectic with an unkempt coat. The cat was paraplegic. There was some voluntary movement of the left rear leg but the cat was unable to support weight on the right rear leg, and was dragging that leg. Femoral and sciatic reflexes were hyporeflexive bilaterally and deep pain appeared to be diminished in both rear legs. No obvious spinal hyperpathia was noted. Femoral pulses were

*Corresponding author. E-mail: ravidvm@sbcglobal.net

© 2006 Published by Elsevier Ltd on behalf of ESFM and AAFP.

strong and synchronous and the rear feet were warm to the touch. The remainder of the examination was unremarkable, except for some missing teeth. Differential diagnosis included lumbar spinal cord disease such as intervertebral disk disease, spondylosis, intradural or extradural neoplasia; anemia of chronic disease; chronic infectious or inflammatory disease such as cryptococcosis, histoplasmosis, osteomyelitis; occult metabolic or organic disease such as renal parenchymal disease; or neoplasia. The significance of the proteinuria was not evident at the time because of the presence of occult blood in the submitted sample. Lateral and ventro-dorsal whole body survey radiographs were obtained. Skeletal abnormalities observed included lytic lesions of the right iliac crest (Fig 1) and the distal scapula along with bilateral coxofemoral degenerative joint disease. The left shoulder radiographs were repeated and lysis of the distal scapula was apparent (Fig 2). On the lateral thoracic radiographs (Fig 3), an increased circular, soft tissue opacity approximately 1.5 cm in diameter was apparent in the caudo-dorsal lung field ventral to the descending aorta. Decreased serosal detail was noted in the abdomen because of the lack of peritoneal fat. No obvious mass effect was observed and air filled small and large bowel loops were observed. After reviewing the radiographic findings, the differential

Fig 2. Lateral radiographic projection of the left shoulder of a cat with a lytic lesion (arrow) at the distal scapula.

diagnosis was revised and disseminated malignant disease or fungal osteomyelitis was included. A fine needle aspirate of the left scapular lesion was performed and the slides were submitted for cytologic evaluation. Cytologically, the left scapular lesion revealed a hemodiluted sample. One of the slides, which was less hemodiluted, showed moderate numbers of individually scattered mesenchymal cells. These cells were spindle shaped to polygonal with poor outlines. The cytoplasm was abundant and occasionally microvacuolated. The nucleus was oval, central with homogenously dispersed chromatin and one to three small nucleoli. Atypical cytologic features were mild. A cytologic diagnosis of hemodiluted sample with low number of well-differentiated mesenchymal cells without a definitive diagnosis of malignancy was made.

Fig 1. The ventro-dorsal view of the pelvis of a cat showing the proliferative and likely local bony lysis (arrow) at the right iliac crest.
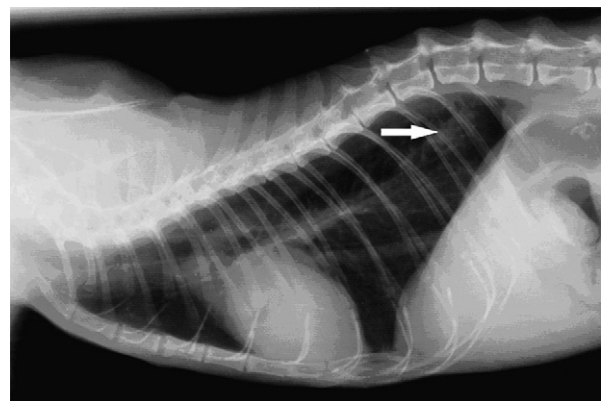

Fig 3. Right lateral thoracic radiograph of the same cat as in Figs 1 and 2 revealed a circular dorso-caudal pulmonary soft tissue opacity (white arrow).

Serologically, the cat tested negative for cryptococcus, histoplasmosis, blastomycosis, coccidiodomycosis and aspergillosis.

Based on the initial clinical, laboratory and radiographic findings a tentative diagnosis of disseminated malignancy was discussed with the owners. An incisional biopsy of the shoulder lesion was recommended. Due to the overall poor prognosis, the owners opted to take the cat home with oral antibiotics. Oral amoxycillin (Amoxi drop; Pfizer), at a dose rate of 25 mg PO bid, was dispensed. The cat's condition deteriorated over the next few days and the cat was re-examined 7 days after the initial examination with no apparent clinical improvement. The weight loss was progressive and disuse muscle atrophy of the right rear leg was apparent. The cat was still paraplegic and unable to support weight on the right rear leg. A dry cough was noted during the examination. No cardiac murmur or arrhythmia was noted. The abdomen was thin on palpation with no apparent organomegaly or mass effect. Due to the poor quality of life and poor prognosis, the owners opted for euthanasia. A complete necropsy was performed.

Necropsy findings consisted of thin body condition with numerous gross and microscopic abnormalities as described below. Grossly, the heart weighed 13 g; base to apex length was 4 cm; left ventricle free wall measured 0.5 cm; right ventricle diameter was 1.0 cm, and the interventricular septum was 0.4 cm. The left ventricular lumen was increased in size, dilated, with wall of interventricular septum slightly thinned. Both kidneys grossly appeared small and irregular with no other obvious significant lesion. The lobes of the lungs were firm and appeared slightly red in color, and failed to collapse. The left caudal lung lobe contained a solitary 1 cm diameter, raised, whitish-yellow, firm, circular lesion. The spleen was enlarged and had several variable sized reddish superficial nodules; its consistency was firmer than normal. The cut surface of the spleen revealed small white areas within the splenic pulp. The lesions in the right iliac crest and left distal scapula consisted of uniformly soft, white or tan, friable partially necrotic tissue with small focal areas of irregular ossification, hemorrhage and necrosis noted on the cut surface. The abnormal tissue expanded the medullary cavities and sometimes perforated adjacent cortical and cancellous bone. No other significant gross lesions were observed.

Representative sections of the visceral tissues and bone were fixed immediately in 10% neutral-buffered formalin, processed routinely, and embedded in paraffin. Tissue sections were cut to 4 μm thickness and stained with hematoxylin and eosin. Microscopically, the sections of the heart examined (Figs 4 and 5) had neoplastic proliferation of epithelial cells which formed irregular cords and variable sized nodules effacing the myocardium with associated marked desmoplasia. The neoplastic cells had round ovoid to elongate hyperchromatic nuclei with finely stippled chromatin and centrally located nucleoli. The cytoplasm was scant to moderate, pale eosinophilic, granular or occasionally vacuolated with intercellular bridges. Histologically the presence of intercellular bridges is a unique diagnostic feature of SCC. Mitoses range from 0 to 4 hpf. In spleen, 90% of the section examined was effaced by neoplastic process. The neoplastic cells formed irregular cords, fronds, and sheets alternating with variably sized cystic cavitations, which contained necrotic cellular debris. The cells had round ovoid hyperchromatic nuclei with finely stippled chromatin and prominent centrally located nucleoli. The cytoplasm was moderate, pale eosinophilic with intercellular bridges. The sections of the lung examined was also characterized by neoplastic proliferation of epithelial cells which formed variably sized nodules, fronds and cords within the alveoli, blood vessels and lymphatics, effacing the normal architecture. Microscopically, it appears that the pulmonary lesions were extensive, suggesting local micrometastasis. The cytoplasmic findings were similar to that noted in the cardiac parenchyma. The decalcified sections of the scapular
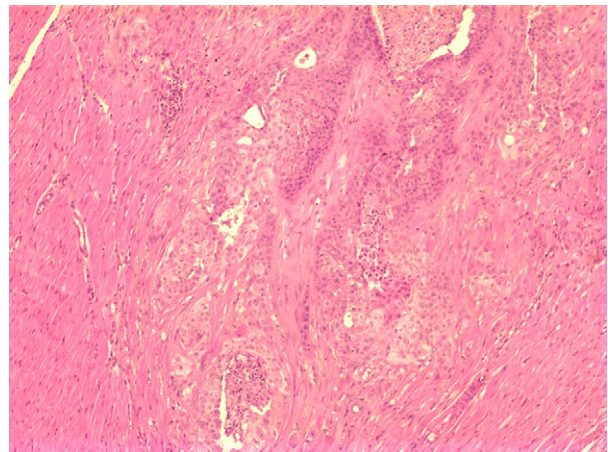

Fig 4. Heart; cat. The cardiac tissue is infiltrated by the population of proliferative neoplastic epithelial cells forming irregular cords and sheets. Hematoxylin and eosin (10×).
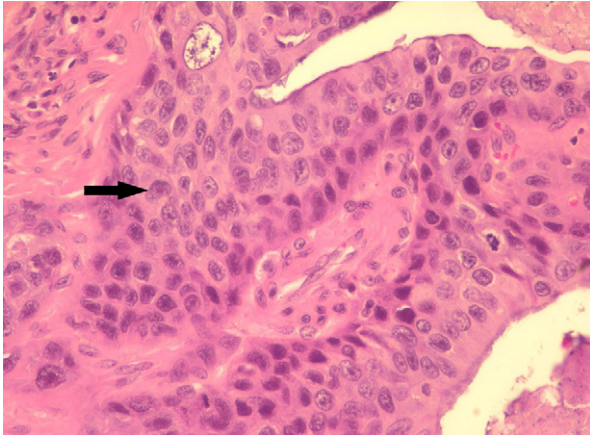
Fig 5. Heart; cat. Higher magnification of the same section as in Fig 3, noticeably the neoplastic process (arrow) appears to be effacing the myocardium. Hematoxylin and eosin (40×).

and right iliac crest showed an infiltrative neoplastic process of epithelial cells with invasion and destruction of bone. The histologic description of lung, spleen, heart and skeletal lesions was consistent with a diagnosis of SCC.

Microscopic findings of the sections of the intestine and liver revealed marked diffuse lymphoplasmacytic enteritis and marked diffuse hepatocellular cloudy swelling with mild multifocal lymphoplasmacytic and suppurative portal hepatitis, respectively. The sections of both kidneys examined had marked chronic inflammation characterized by variable sized wedge shaped areas of infiltration by lymphocytes and plasma cells. The final microscopic diagnosis of renal parenchyma was chronic fibrosing lymphoplasmacytic nephritis with hyalinization of glomeruli and severe tubular and collecting duct proteinosis. The cavity of the renal pelvis contained a large mineralized calculus. The sections of liver, kidneys and intestines showed no evidence of malignancy. The final microscopic diagnosis was metastatic SCC.

The present report documents an unusual case of widespread visceral and skeletal SCC in a relatively young, 7-year-old Persian cat. Clinical abnormalities such as paraplegia, weight loss, and anorexia in this cat were referable to disseminated SCC. Paraplegia was likely due to generalized weakness and skeletal lesion at the right iliac crest. No apparent spinal cord abnormality was evident on physical, radiographic and necropsy examination. We were unable to determine the origin of the primary tumor; therefore, we established a post-mortem diagnosis of

widespread visceral and skeletal SCC metastasis likely pulmonary in origin or from an unknown primary site. We believe that the primary origin is pulmonary because neither cardiac nor spleen or skeletal tissue is embryologically epithelial in origin. However, one may also argue that this may be a case of metastatic SCC with an unknown primary or multicentric SCC. The term multicentric seems inappropriate because of the reasons explained earlier. The etiologies for disseminated visceral and skeletal osteolytic lesions have not been well described in the cat. Infectious diseases such as disseminated bacterial, fungal, and parasitic diseases are reported causes of osteolytic lesions in cats but were considered unlikely in this case, because these organisms were not detected serologically or microscopically (Wolf 1987, Greene and Troy 1995). The cardiac SCC in this case is a unique and unusual presentation of metastatic site. To the best of our knowledge primary or metastatic cardiac SCC in cats have not been previously reported. Carcinoma of unknown primary site is not a well-documented clinical syndrome in veterinary medicine. In our experience the diagnosis is a recurrent challenge, treatment is often times difficult and prognosis is still poor. With the increasing availability of advanced imaging techniques such as computed tomography, magnetic resonance imaging and positron emission tomography scanning, our ability in detecting tumor localization in cases with complex anatomical sites and carcinoma of unknown primary site will substantially improve in future. However, false positive findings have to be considered (Culine et al 2003).

Primary pulmonary SCC in cats is a rare histologic diagnosis. Development of clinical signs associated with SCC in cats varies depending on the anatomic location. In cats, SCC has been reported to occur at various anatomic locations such as the oral cavity (Hutson et al 1992, Tannehill-Gregg et al 2001), the esophagus (Gualtieri et al 1999), the nasal planum (Lana et al 1997, Fidel et al 2001), the eye (Sironi et al 1999), the nasal and paranasal sinuses (Mukaratirwa et al 2001) and the thymus (Carpenter and Valentine 1992, Anilkumar et al 1994). Other less common forms include cutaneous horn and SCC in situ or Bowen's disease (Rees and Goldschmidt 1998). Bowen's disease or multicentric cutaneous SCC in situ is a diffuse cutaneous malignancy in cats. Clinically these cats are presented with multiple, crusted lesions in haired-pigmented regions of the skin, including the trunk, limbs, feet, head,

and neck. These lesions are unrelated to exposure to sunlight. These neoplasms do not recur locally after surgical excision; however, similar lesions can develop at other anatomic sites (Baer and Helton 1993, Rees and Goldschmidt 1998). Biologically, SCC is locally aggressive and slow to metastasize, however, this may not be true for patients with visceral or metastatic SCC. Treatment for squamous cell carcinoma is tailored according to the anatomic location of the lesion. Commonly used treatment modalities include surgery (Hutson et al 1992), external beam radiation therapy (Hutson et al 1992, Theon et al 1995, Bregazzi et al 2001, Fidel et al 2001), photodynamic therapy (Magne et al 1997, Frimberger et al 1998, Lucroy et al 1999, Stell et al 2001) and cryotherapy (Lana et al 1997). Very few cats with metastatic SCC have been identified to allow for thorough characterization of this disease in this species.

Our literature review revealed few case reports of metastatic SCC in cats; thymic SCC with metastasis to the sternal lymphoid tissue and to the left lung (Anilkumar et al 1994) and intraocular metastatic SCC from primary pulmonary SCC (Hamilton et al 1984). Metastasis of primary pulmonary neoplasm to other sites can also occur (Hahn and McEntee 1997). To the authors' knowledge, this is the first report of metastatic skeletal and cardiac SCC in a cat. From this single case report, nothing can be gained regarding the treatment of disseminated SCC in cats. In the current case the only way that an early diagnosis could have been established is if a routine survey of thoracic and abdominal radiographs would have been performed. For primary pulmonary neoplasms pneumonectomy is still the treatment of choice, with distant metastasis still being a possibility. The efficacy of chemotherapy for primary pulmonary carcinoma is not well documented. Vinorelbine tartarate (Navelbine Benvenue laboratories, Bedford, OH 44146), a new semisynthetic vinca alkaloid, has shown partial response in dogs with metastatic bronchoalveolar carcinoma (Poirier et al 2004). In general majority of solid malignancies, especially once distant metastasis has developed, are not very chemosensitive. This can be explained by the fact that anticancer drugs kill cells by first order kinetics meaning higher dosage will induce more cell death, however, due to concurrent toxicities to normal cells the antineoplastic drugs have very narrow therapeutic index. Therefore, clinically it is merely impossible to achieve a complete remission with conventional dosing regimen, for a patient with bulky regional disease and

associated metastasis. Newer developments in tumor vaccines and small molecule drugs will enhance the remission and survival rates in future.

The conclusions that can be drawn from this report is that unlike in the oral cavity or skin, the feline SCC at other anatomic locations such as pulmonary parenchyma in the current case, is more metastatic. Secondly, although rare, it is possible that in some cats distant visceral and skeletal metastasis can occur due to SCC. Necropsy examination of additional affected cats may confirm or refute this hypothesis.

References

Anilkumar TV, Voigt RP, Quigley PJ, Krausz T, Sarraf CE, Alison MR (1994) Squamous cell carcinoma of the feline thymus with widespread apoptosis. *Research in Veterinary Science* **56**, 208–215.

Baer KE, Helton K (1993) Multicentric squamous cell carcinoma in situ resembling Bowen's disease in cats. *Veterinary Pathology* **6**, 535–543.

Bregazzi VS, LaRue SM, Powers BE, Fettman MJ, Ogilvie GK, Withrow SJ (2001) Response of feline oral squamous cell carcinoma to palliative radiation therapy. *Veterinary Radiology and Ultrasound* **42**, 77–79.

Carpenter JL, Valentine BA (1992) Squamous cell carcinoma arising in two feline thymomas. *Veterinary Pathology* **29**, 541–543.

Culine S, Lortholary A, Voigt JJ, Bugat R, Theodore C, Priou F, Kaminsky MC, Lesimple T, Pivot X, Coudert B, Douillard JY, Merrouche Y, Allouache J, Goupil A, Negrier S, Viala J, Petrow P, Bouzy J, Laplanche A, Fizazi K (2003) Cisplatin in combination with either gemcitabine or irinotecan in carcinomas of unknown primary site: results of a randomized phase II study − trial for the French Study Group on Carcinomas of Unknown Primary (GEFCAPI 01). *Journal of Clinical Oncology* **21**, 3479–3482.

Fidel JL, Egger E, Blattmann H, Oberhansli F, Kaser-Hotz B (2001) Proton irradiation of feline nasal planum squamous cell carcinomas using an accelerated protocol. *Veterinary Radiology and Ultrasound* **42**, 569–575.

Frimberger AE, Moore AS, Cincotta L, Cotter SM, Foley JW (1998) Photodynamic therapy of naturally occurring tumors in animals using a novel benzophenothiazine photosensitizer. *Clinical Cancer Research* **4**, 2207–2218.

Greene RT, Troy GC (1995) Coccidioidomycosis in 48 cats: a retrospective study (1984–1993). *Journal of Veterinary Internal Medicine* **9**, 86–91.

Gualtieri M, Monzeglio MG, Di Giancamillo M (1999) Oesophageal squamous cell carcinoma in two cats. *Journal of Small Animal Practice* **40**, 79–83.

Hahn KA, McEntee MF (1997) Primary lung tumors in cats: 86 cases (1979–1994). *Journal of American Veterinary Medical Association* **211**, 1257–1260.

Hamilton HB, Severin GA, Nold J (1984) Pulmonary squamous cell carcinoma with intraocular metastasis in a cat. *Journal of American Veterinary Medical Association* **185**, 307–309.

Hutson CA, Willauer CC, Walder EJ, Stone JL, Klein MK (1992) Treatment of mandibular squamous cell carcinoma in cats by use of mandibulectomy and radiotherapy: seven

cases (1987−1989). *Journal of American Veterinary Medical Association* **201**, 777−781.

Lana SE, Ogilvie GK, Withrow SJ, Straw RC, Rogers KS (1997) Feline cutaneous squamous cell carcinoma of the nasal planum and the pinnae: 61 cases. *Journal of American Animal Hospital Association* **33**, 329−332.

Lucroy MD, Edwards BF, Peavy GM, Krasieva TB, Griffey SM, Stiles JB, Madewell BR (1999) Preclinical study in cats of the pro-photosensitizer 5-aminolevulinic acid. *American Journal of Veterinary Research* **60**, 1364−1370.

Magne ML, Rodriguez CO, Autry SA, Edwards BF, Theon AP, Madewell BR (1997) Photodynamic therapy of facial squamous cell carcinoma in cats using a new photosensitizer. *Lasers in Surgery and Medicine* **20**, 202−209.

Mukaratirwa S, van der Linde-Sipman JS, Gruys E (2001) Feline nasal and paranasal sinus tumours: clinicopathological study, histomorphological description and diagnostic immunohistochemistry of 123 cases. *Journal of Feline Medicine and Surgery* **3**, 235−245.

Poirier VJ, Burgess KE, Adams WM, Vail DM (2004) Toxicity, dosage, and efficacy of vinorelbine (Navelbine) in dogs with spontaneous neoplasia. *Journal of Veterinary Internal Medicine* **18**, 536−539.

Rees CA, Goldschmidt MH (1998) Cutaneous horn and squamous cell carcinoma in situ (Bowen's disease) in a cat. *Journal of American Animal Hospital Association* **34**, 485−486.

Sironi G, Riccaboni P, Mertel L, Cammarata G, Brooks DE (1999) p53 protein expression in conjunctival squamous cell carcinomas of domestic animals. *Veterinary Ophthalmology* **2**, 227−231.

Stell AJ, Dobson JM, Langmack K (2001) Photodynamic therapy of feline superficial squamous cell carcinoma using topical 5-aminolaevulinic acid. *Journal of Small Animal Practice* **42**, 164−169.

Tannehill-Gregg S, Kergosien E, Rosol TJ (2001) Feline head and neck squamous cell carcinoma cell line: characterization, production of parathyroid hormone-related protein, and regulation by transforming growth factor-beta. *In Vitro Cellular and Developmental Biology − Animal* **37**, 676−683.

Theon AP, Madewell BR, Shearn VI, Moulton JE (1995) Prognostic factors associated with radiotherapy of squamous cell carcinoma of the nasal plane in cats. *Journal of American Veterinary Medical Association* **206**, 991−996.

Wolf AM (1987) Histoplasma capsulatum osteomyelitis in the cat. *Journal of Veterinary Internal Medicine* **1**, 158−162.