

## Calvaria and orbital metastases of pulmonary adenosquamous carcinoma in a cat: a diagnostic challenge

Diana BINANTI<sup>1</sup>\* and Davide Danilo ZANI<sup>2</sup>

<sup>1</sup>AbLab Veterinary Diagnostic Service, Via Privata Massa Neri, 19038 Sarzana (SP), Italy

<sup>2</sup>Department of Health, Animal Science and Food Safety, Veterinary University Hospital, Università degli studi di Milano, Lodi, Italy

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**ABSTRACT.** An 11-year-old cat with a 4-month history of lethargy, inappetence, dysphagia, partial mandibular paralysis and weight loss, was euthanized due to the rapid deterioration of his condition. Post-mortem radiographic examination revealed severe bone lysis of the left zygomatic arch, temporal and parietal bones. Magnetic resonance imaging of the head showed a large isointense mass of the left side of the skull associated with extensive lysis of the parietal and temporal bones and destruction of the adjacent tympanic bulla. Gross and histological examinations revealed a pulmonary adenosquamous carcinoma of the left lung, with metastases to the spleen, liver, mesenteric lymph nodes, mesentery, diaphragm, abdominal aorta, left orbit and calvaria. No limb or digit metastases were detected.

**KEY WORDS:** carcinoma, feline, lung, metastases, skull

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Primary lung tumors are rare in cats and occur as a sporadic disease in geriatric animals, with the average age at diagnosis ranging from 12 to 13 years and no breed or sex predilections [10]. An accurate and early diagnosis is often essential due to the poor prognosis in case of pulmonary neoplasm; however, cats affected by pulmonary tumors often have nonspecific clinical signs, and diagnosis can be difficult [4]. The present report describes an unusual metastatic pattern of primary pulmonary adenosquamous carcinoma in a cat presented for exophthalmos and swelling of the left side of the head, without premonitory respiratory signs.

An 11-year-old male, neutered, European shorthair cat was submitted for a full postmortem examination. The cat had a 4-month history of lethargy, inappetence, dysphagia, partial mandibular paralysis and weight loss. The referring veterinarians detected severe anorexia, moderate splenomegaly, left monolateral exophthalmos and swelling of the left side of the head. Due to the rapid deterioration of the cat's condition, the owner elected euthanasia, and a postmortem examination was conducted.

The body condition of the animal was extremely poor; external examination revealed massive swelling of the left region of the skull associated with moderate exophthalmos of the left globe and left deviation of the jaw associated to ankylosis of the temporomandibular joints.

Postmortem radiographic examination revealed severe permeative lysis characterized by coalescing regions of ill-defined bone destruction involving the left zygomatic arch,

temporal and parietal bones (Fig. 1). Postmortem magnetic resonance examination (MRI) of the head showed the presence of a large T1- and T2-weighted isointense mass on the left side of the skull, which was associated with mild right brain shift, severe lysis of the calvarium and destruction of the ipsilateral tympanic bulla and temporomandibular joint. On T2-weighted images, the tissue close to the outside of the mass showed marked hyperintensity (Fig. 1).

Gross examination of the thoracic cavity showed a severe deformation of the left lung that was completely compressed and effaced by a large multilobulated, poorly demarcated, whitish-tan, firm mass (Fig. 2A). The right lung was affected by severe diffuse atelectasis, resulting from the massive compression and severe congestion. Regional lymph nodes were severely enlarged. Moderate right ventricle hypertrophy was also detected.

In the abdominal cavity, multiple, small, whitish masses were detected in the spleen, mesenteric lymph nodes and on the abdominal side of the diaphragm.

Gross examination of the skull revealed that the left side of the brain was severely compressed by a firm, expansile, multilobulated mass attached to the calvarium (Fig. 2B). The mass involved the left parietal and temporal bones and the left temporomandibular joint (Fig. 2C). The mass was extremely firm, with gritty areas; the cut surface was white with whitish areas of mineralization. The brain was characterized by a severe asymmetry of the cerebral hemispheres due to compression by the mass. No abnormalities were noted in the limbs or digits.

Specimens from formalin-fixed tissues were embedded in paraffin wax, sectioned and stained with hematoxylin and eosin for histological examination.

Histological examination revealed that the left pulmonary parenchyma was completely effaced and substituted by a densely cellular, unencapsulated, poorly demarcated, infiltrative neoplasm. The neoplasm was composed of polygonal

\*CORRESPONDENCE TO: BINANTI, D., AbLab Veterinary Diagnostic Service, Via Privata Massa Neri, 19038 Sarzana (SP), Italy. e-mail: diana.binanti@gmail.com

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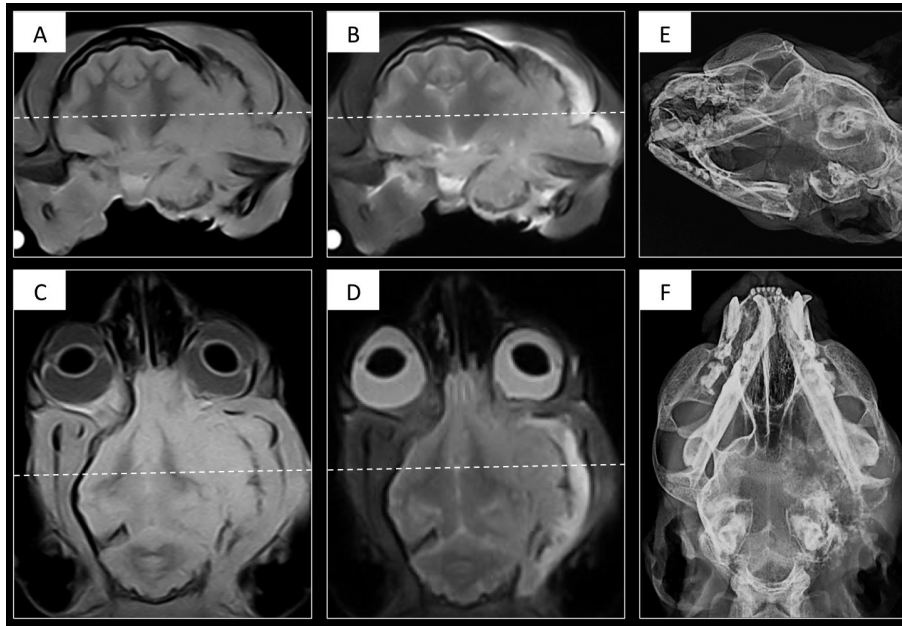


Fig. 1. T1- (A and C) and T2-weighted (B and D) transverse and dorsal images of the post-mortem MRI of the head showing a large isointense mass of the left side of skull associated with extensive lysis of the parietal and temporal bones and destruction of the adjacent tympanic bulla. There appears to be a slight mass effect with a right midline brain shift and diffuse hyperintensity of the tissue close to the outside of the mass. Radiographic examinations (E and F) revealed severe bone lysis of the left zygomatic arch, temporal and parietal bones.

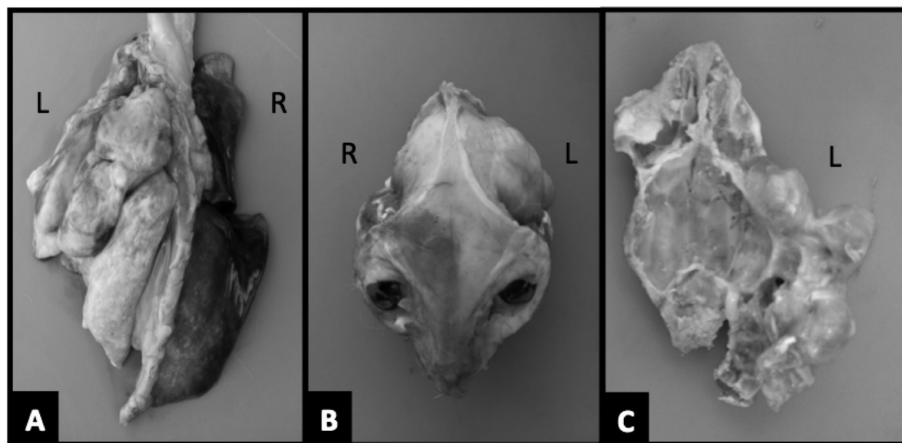


Fig. 2. (A) Note that on the left side, the left lung is completely effaced by a large multilobulated whitish-tan mass. On the right side, the right lung is characterized by severe edema, atelectasis and hyperemia. (B) The skull is characterized by massive swelling of the left region of the calvaria, with a large mass involved the left parietal and temporal bones and the left temporomandibular joint (C).

cells often arranged in pluristratified islands, with multifocal progressive central keratinization, or arranged in small tubules supported by a moderate amount of fibrous stroma (Fig. 3A). Neoplastic cells were cuboidal to columnar, often ciliated, with indistinct cell borders, a moderate amount of eosinophilic cytoplasm, a round to oval central nucleus, a margined chromatin and one evident magenta nucleolus

(Fig. 3B). Anisocytosis and anisokaryosis were severe, and mitoses ranged between 2 and 3 per HPF. Multifocal areas of necrosis and mineralization were present. The apical lobe of the left lung was characterized by diffuse hemorrhages, necrosis and numerous macrophages filled with brown pigment (hemosiderin). The right lung was characterized by diffuse and severe edema, hyperemia and atelectasis, due to

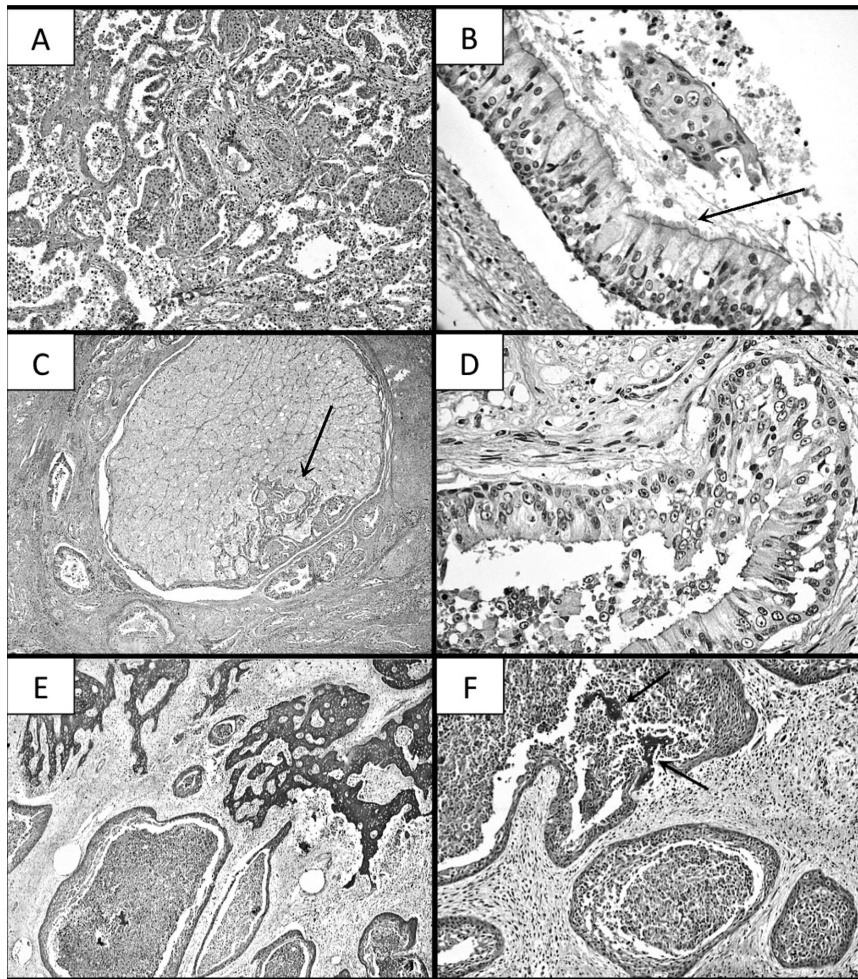


Fig. 3. Histological findings of the left lung (A, B), optic nerve (C, D) and calvarium (E, F). **A:** Histological examination of the left lung compressed by an epithelial neoplasm composed of polygonal cells arranged in pluristratified islands, with multifocal keratinization, or arranged in small tubules. **B:** Details of the neoplastic epithelium; tubules were lined with pseudostratified cuboidal to columnar, often ciliated, cells (arrow). **C:** Histological examination of the left retrobulbar and orbital soft tissues. The optic nerve is infiltrated by columnar epithelial cells arranged in tubular structures (arrow). Other tubular structures are present at the periphery of the optic nerve. **D:** Details of the neoplastic epithelium; a portion of the optic nerve is visible in the upper-left corner. Tubules were lined with pseudostratified cuboidal to columnar, often ciliated, cells. **E:** Histological examination of the calvarium; a multifocal epithelial neoplasm composed of islands and tubules expanded and effaced the normal bone architecture. **F:** Details of the neoplastic epithelium; irregular osteolytic bone trabeculae (arrows) are surrounded by islands of neoplastic cells, often characterized by progressive keratinization.

the compressive effect of the contralateral mass.

Other nodules, composed of the same neoplastic cells, were detected on the abdominal side of the diaphragm and on the liver, spleen, mesenteric lymph nodes, mesentery and abdominal aorta. The tumors in all these organs were histologically similar to the primary tumor, but showed a more extensive scirrhous reaction and multifocal necrotic foci. Neoplastic emboli were also detected on small vessels of the brain (mainly meningeal vessels). No metastases were present in the limbs and digits.

Metastases of the pulmonary adenosquamous carcinoma were also observed on the left retrobulbar and orbital soft tissues (muscles and adipose tissues), surrounding and infiltrat-

ing the optic nerve (Fig. 3C and 3D). Most of the choroidal vessels were filled with neoplastic emboli.

The normal architecture of the calvarium was completely effaced by an infiltrative epithelial neoplasm with aspects similar to a pulmonary mass. Bone was characterized by extensive remodeling, bone lysis and new bone and cartilage formation. The epithelial neoplasm was composed of islands, nests and tubules with direct contact to irregular bone trabeculae (Fig. 3E and 3F) with scalloped borders and large multinucleated osteoclasts in resorption pits on the bone surface (bone resorption). Abundant fibrous reactions and areas of immature cartilage were present surrounding islands and tubules (desmoplasia). Areas of necrosis and mineralization



were also detected.

A diagnosis of primary pulmonary adenosquamous carcinoma of the left lung, with metastases to the spleen, liver, mesenteric lymph nodes, mesentery, diaphragm, abdominal aorta, left orbit and calvaria, was made.

Compared with the case in humans, primary pulmonary neoplasms are an infrequent finding in domestic animals, and most lung tumors are metastatic [1, 2, 10]. The most commonly reported primary lung neoplasms are of epithelial origin, and most of them are malignant [10]. The most common type of pulmonary neoplasm in cats is adenocarcinoma, while squamous cell carcinoma, adenosquamous cell carcinoma, sarcoma and benign tumors are less common [2, 10]. Non-respiratory clinical signs, such as weight loss, weakness, lethargy, vomiting and lameness, are, in many cases, the first complaint of the owner and may precede dyspnea, tachypnea or cough [8, 9]. This late appearance of respiratory signs, in the course of the disease makes early diagnosis difficult, and the diagnosis is often made at necropsy.

The association between lameness and pulmonary carcinoma, or “lung-digit syndrome”, is well known, and it may be related to the angioinvasive properties of pulmonary carcinomas and high digital blood flow [4, 8]. Occasionally, feline pulmonary carcinoma can metastasize to other sites, such as the skin [3, 7], eye [9], skeletal muscle [6] and long bone [8], as well as more common sites of metastases, such as the liver and spleen [4]. Few reports of bone metastasis in cats aside from that in the digits are described in the literature [8]. Recent studies have reported cases of pulmonary carcinoma with uncommon metastasis to the bone, such as metastatic spread to the ulna [8] and to the ribs [5].

The present case showed an unusual metastatic pattern, with widespread metastases without digit involvement. Often lung carcinomas are diagnosed after an animal has been presented for lameness, and this is often the only complaint [4]. Single or multiple digits (especially the weight-bearing ones) of 1 or more limbs may be affected, with classical osteolysis of the third phalanx, sometimes with invasion of the intra-articular space [4]. In the present case, no lameness was reported in the cat history, and no metastases were observed in the limbs or digits. Despite the frequency of metastases and widespread involvement in feline pulmonary carcinoma, calvarium and orbital metastasis are uncommon. Intraocular metastasis has been described in a cat with pulmonary carcinoma [9], but in the present case, in addition to numerous neoplastic emboli in the choroidal vessels, metastases of the pulmonary adenosquamous carcinoma were also observed in the retrobulbar and orbital soft tissues, surrounding and infiltrating the optic nerve, extremely uncommon features in cats.

Metastasis of primary pulmonary carcinoma should be included among differential diagnoses in cases of swelling of the skull or exophthalmos in aged cats. To the best of our knowledge, this is the first report of primary pulmonary adenosquamous carcinoma with calvaria, orbital and widespread metastasis in a cat. Moreover, in the present case, no metastasis was present in the limbs and digits, although the association between lameness and pulmonary carcinoma is the best known metastatic pattern in cats.

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