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The Ubiquity of Lipomas: Seven cases illustrating pathology of subcutaneous tumors with a presumptive diagnosis of lipoma based on physical examination

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ABSTRACT

Lipomas are subcutaneous masses composed of adipocytes. They are benign neoplasias but may cause physical symptoms to a patient based on size or compression of adjacent tissues. They are commonly encountered by veterinary practitioners, especially in older canine patients. In general, lipomas are lenticular or ovoid in shape, soft to firm in consistency, have a smooth exterior, are encapsulated, and are freely movable. Usually, veterinary practitioners make a diagnosis of lipoma based on physical palpation or cytologic analysis of fine needle aspirates. However, many subcutaneous masses may mimic a lipoma in terms of physical appearance. Fine needle aspirates may lead to misidentification of lesions, especially if patient restraint is problematic, the tumor is small or difficult to localize, or cells of the targeted neoplasia do not exfoliate well. This paper examines seven cases whereby lipomas caused pathology themselves or were misidentified due to inaccurate diagnostic protocol. The author recommends small punch biopsy to obtain more definitive diagnosis.

Introduction

In veterinary medicine, patients often present for evaluation of cutaneous or subcutaneous masses. In the subcutaneous category, a frequent diagnosis is lipoma. Lipomas are tumors of the adipose tissue and are relatively common in older dogs. They are benign and do not metastasize to other tissues. Diagnosis of lipomas are generally made based on history and physical exam. Lipomas are usually subcutaneous, tend to be encapsulated, roughly lenticular to spherical in shape, soft and movable. They are rarely symptomatic, although can rarely occur in the thoracic cavity, abdominal cavity, spinal canal, or vagina of a dog where their presence may cause clinical abnormalities.[1,2] Lipomas are of mesenchymal origin. The cause is unknown but chromosomal abnormalities have been described.[3] Practitioners often diagnose subcutaneous masses on palpation alone. Unfortunately, this approach can lead to misdiagnosis, especially with other subcutaneous tumors that may be more malignant.

Lipomas can be problematic if they invade nearby organs or grow to large enough size that normal ambulation is impeded. Lipoma variations such as infiltrative lipomas and liposarcomas can cause pathologic problems to the patient based on more aggressive behavior exhibited by both forms. In addition, misidentification of more serious neoplasia based on palpation alone can lead to advanced disease behavior.

The following cases illustrate how misidentification of subcutaneous tumors can occur, and misidentification can allow a more progressive form of tumors to manifest themselves.

The cases presented here are ones that were personally managed by the author and demonstrate how lipomas may cause physiological problems, or malignant tumors can often be misidentified as benign lipomas without proper histopathologic examination of tissue samples. Each case is presented according to the pathological problems a tumor may exhibit and increase in the severity inherent to each.

Veterinary practitioners should perform at least minimal diagnostics to confirm the diagnosis of a lipoma, including cytological analysis of fine needle aspirates and/or histopathological analysis of biopsy samples. However, it should be remembered that even these diagnostic protocols are prone to error. Subcutaneous masses that continue to demonstrate abhorrent behavior, such as rapid growth and/or change in shape, should be re-evaluated.

CASE 1. LIPOMA

A 13-year-old, female spayed Golden retriever dog presented for evaluation of a large mass on the right thoracic flank. The mass had previously been identified via fine needle aspirate as a lipoma. The mass measured 10 cm x 14 cm. The mass had been growing slowly over the previous 5 years. Recently, the dog's owners had noted that the dog had recently been reluctant to sleep on its right side. Seemingly, unconnected the owners had noted a mild lameness on the right forelimb that was not responding to NSAID therapy. Radiographs showed no evidence of degenerative joint disease or osteoarthritis. On the physical exam, it was also noted that the dog had heavy dental calculus and tarter. A recommendation for a dental cleaning was made. Since dental cleanings for dogs and cats must be done under general anesthesia, the owners requested that the lipoma be removed during the procedure.

Pre-surgical bloodwork was clinically unremarkable, and the dog was cleared for surgery. Following a successful dental cleaning, the lipoma on the dog's right lateral thorax was surgically prepped. A curvilinear incision was made over the mass. The lipoma was sharply and bluntly dissected away from the surrounding connective tissue. The mass was encapsulated and well contained to the thoracic region. No part of the mass extended beyond the fascial plane, and did not appear to extend into the shoulder region. The lipoma weighed 2.1 kg after removal. A section of the mass was submitted to a commercial laboratory for pathological analysis. Histopathology confirmed that the mass was a lipoma.

The dog presented for suture removal two weeks post-surgery. The surgical wound had healed completely, and the skin sutures were removed. The owners noted that the dog had again started sleeping on her left side and that the right forelimb lameness had resolved.

While manipulation of the lipoma on previous examinations did not provoke a pain response in the dog, it is possible that sheer size of the mass caused compression to the thorax causing discomfort and/or made breathing more difficult when the dog laid on the affected side. Likewise, the size of the lipoma could have been such that her gait was affected, accounting for the apparent resolution of the right forelimb lameness appreciated on the previous physical exam.

Lipomas were ranked as the third most common nonlymphoid cutaneous tumor in dogs in a retrospective study of 6,282 dogs, representing 7.1% of the total[1]. It should be noted that this number may be an underestimate of the true prevalence of lipomas in that many are diagnosed during routine physical exams and not submitted to commercial laboratories for confirmation. The author has noted that while most lipomas do not grow to extreme sizes, those that originate on the flanks are usually the ones that achieve the larger sizes. An argument could be made that lipomas seen in these areas be removed pre-emptively while still at a more surgically manageable size.

CASE 2. INFILTRATIVE LIPOMA

An 11-year-old, 43 kg spayed female Labrador retriever dog presented for acute paraparesis. There was generalized weakness and lethargy. The dog was unable to stand on its rear legs without assistance. Neurological abnormalities included conscious proprioception deficits in the rear legs, hypereflexia of the patellar reflexes with the right hind leg more affected than the left. Pain was noted on the palpation of the thoracolumbar region of the spine. Exaggerated flexor withdrawal reflexes were present in both hindlimbs. Several lipoma-like masses were found, including a 5 x 8 cm diameter, lenticular mass suspected to be a lipoma on the dorsal aspect of the thorax, overlying the spine. A fine needle aspirate of this mass showed adipocytes confirming that the thoracic subcutaneous mass was a lipoma. Differential diagnosis for acute paraparesis at this time included intervertebral disk disease (IVDD), trauma, axonal degeneration, or neoplastic process. Biochemistry serum analysis, CBC, and urinalysis were all clinically unremarkable. Thoracic radiographs showed a normal size and shape cardiac silhouette. No metastatic lesions were noted in the lung fields. Spinal radiographs showed multiple areas of bridging spondylosis, however intervertebral disc space narrowing was not noted. Based on the most likely differential diagnosis of spinal cord compression due to intervertebral disc herniation, the dog was placed on a decreasing dose of prednisone at 1 mg/kg, however after no significant response, treatment was discontinued after 1 week. Advanced diagnostics such as magnetic resonance (MR) imaging was then pursued.

In T-2-weighted magnetic resonance images an extradural mass was visible on the right side at the fifth thoracic intervertebral space (T5). The mass had signal characteristics of fat and was causing severe spinal cord compression. In short *t* (need actual name here) recovery images, the signal was nulled, with a resultant signal again like that of subcutaneous fat. In T-1-weighted images acquired before contrast medium administration, signal from the abnormal mass was again nulled, yielding a signal to that of subcutaneous fat. Following contrast medium administration there was no enhancement of the mass. Based on the signal characteristics, primary consideration was given to an infiltrative extradural lipoma with spinal cord compression. The previously diagnosed lipoma overlying the thoracic spine was the suspected culprit.

A small 1 cm hemilaminectomy was performed just on the cranial lateral edge of the dorsal spinal process and lamina of T5. A mass was identified entering the vertebral canal and impinging on the spinal cord. The mass was similar to fat and was well circumscribed. The mass compressing the spinal cord was extracted

en toto. The mass was followed up to the previously described from subcutaneous lipoma overlying the T5 vertebral space and dissected away from surrounding tissue. The mass was submitted for histopathologic analysis. The dog recovered well and regained complete neurologic function within 2 weeks. Adjunctive therapy with chemotherapy or radiation therapy was not pursued. Twenty-four months after surgery, the dog remained fully ambulatory with no neurologic deficits. Histologic analysis of the extracted mass showed lobules of benign, well differentiated adipose tissue consistent with an infiltrative lipoma were found.

Infiltrative lipomas arise from adipocytes in the subcutaneous tissue and are identical histologically to lipomas.[4,5] They are composed of well-differentiated, unencapsulated, adipose cells without evidence of anaplasia. They are locally aggressive and may cause clinical signs due to invasion of adjacent tissue such as muscle, fascia, nerve, myocardium, joint capsule, and bone.[4,5,6,]. While surgery is the preferred method of therapy, because infiltrative lipomas are unencapsulated and diffuse in nature, it is difficult to completely remove the mass. Radiotherapy has been employed as a primary mode of therapy or in conjunction with surgery when complete resection cannot be achieved.[7]

In the dog described in this case, an infiltrative lipoma was identified impinging on the thoracic portion of the spinal cord causing upper motor neuron signs to the rear legs. It is rare that an infiltrative lipoma can cause spinal cord compression. To the author's knowledge, only a few other cases have been published.[8,9,10,11]

In one case, a four-year-old neutered male Maltese was presented after a two-month history of right hemiparesis. Radiographic analysis showed bone lysis and sclerotic changes in the right section of the fifth and sixth cervical vertebrae with mild radiolucent mass around the lesion. Magnetic resonance imaging revealed a hyperintense mass located in the region extending from the muscles to the vertebrae and compressing the spinal cord. The mass was surgically removed via a hemilaminectomy in the cervical area using a ventral and dorsal approach. Histologic analysis showed adipocytes confirming an infiltrative lipoma. The dog recovered fully and still had normal neurologic function 24 months post-surgery.[9] Another case described a 12-year-old male, fox terrier dog presented with an abnormal gait of the left pelvic limb. Similar MRI diagnostics showed a lipoma-like mass invading the spinal canal at the level of the L5-L6 lumbar vertebrae, resulting in the observed hind limb paraparesis. The mass was surgically resected and histopathology confirmed the mass to be an infiltrative lipoma.[10]

CASE 3. LIPOSARCOMA

An 8-year-old neutered male golden retriever/standard poodle cross dog was presented for evaluation of a rapidly growing mass that had been previous diagnosed as a lipoma on the basis of fine needle aspirate. The mass was located on the right side of the thoracic spine near the last rib and measured approximately 8 cm x 5 cm. The mass was soft, flocculent and firmly attached to the underlying soft tissue. The owners elected surgical removal of the mass. Pre-anesthetic bloodwork including T4 was unremarkable.

During surgery a curvilinear incision was made over the dorsal aspect of the mass. The mass was well encapsulated and on visual observation had the gross appearance of a lipoma. The initial skin incision was continued around the lateral edges of the mass with sharp and blunt dissection employed. Inadvertently, the capsule of the mass was punctured, allowing a soft, undifferentiated material with a semi-solid consistency to ooze out. This is atypical for lipomas in the author's experience in that lipomas will often shell out and are composed a firm solid material. The mass was removed, however due to the semi-solid nature of the mass, it was suspected that tumor-free margins were not achieved. A section of the mass was submitted for histopathology. The dog recovered well after surgery.

Histological examination of the mass confirmed a diagnosis of liposarcoma. Cytologic examination

showed a well differentiated adipocytes and poorly differentiated cells anaplastic cells arranged in coalescing clusters. These less differentiated cells were pleomorphic and had eosinophilic cytoplasm with indistinct cell borders and variable sized intracytoplasmic vacuoles. Moderate to marked anisokaryosis was evident and several cells contained multiple nucleoli. Observed mitotic figures were low (<1 per HPF). Giant cells with large hyperchromatic nuclei and multinucleated cells were scattered. Well-differentiated cells had the typical appearance of adipocytes consisting of large, single, clear vacuoles with missing or peripherally displaced nuclei. A histological subtype was not given.

Liposarcomas are uncommon malignant tumors originating from lipoblasts in older dogs. Liposarcomas do not appear to arise from malignant transformation of lipomas.[12,13] However, one case reported liposarcoma caused by a glass foreign body penetration into the subcutaneous has been reported in the dog.[15] Liposarcomas, like lipomas, are commonly reported in subcutaneous regions, particularly on the ventrum and extremities, but can also occur in other areas. Liposarcomas are differentiated from lipomas based on morphological appearance and cytologic characteristics. They are locally invasive, poorly circumscribed with a low metastatic potential, however metastasis to bone, lungs, spleen, and lungs has been reported.[16]

The dog in this case presented two weeks post-surgery for suture removal. The wound had healed well. Three-view radiographs obtained at this time did not reveal evidence of metastasis to the lungs. Routine rechecks conducted 3 months, 6 months, and 1 year post surgery failed to find evidence of regrowth of the tumor.

The prognosis of liposarcomas is good with appropriate surgical management. The median survival time after liposarcoma resection with clean margins is 1188 days.[1] In humans liposarcomas are classified as well differentiated, myxoid, poorly differentiated, pleomorphic, or dedifferentiated. This classification scheme has clinical and prognostic importance in humans. Pleomorphic liposarcomas have a high metastatic rate, myxoid liposarcomas are more likely to metastasize to extrapulmonary soft tissue structures. Well differentiated liposarcomas are unlikely to metastasize. However in a large retrospective study in dogs in which histological subtype was available, the authors found that histologic subtype was not prognostic indicator, however they did note that metastatic disease was more common in dogs with pleomorphic liposarcomas.[17]

CASE 4. ECTOPIC THYROID TUMOR

A spayed female, 26 kg Labrador retriever cross breed dog, aged 7 years 2 months presented for routine exam and vaccination. The owners reported that the dog had no history of major medical problems and no clinically significant findings were discovered on physical exam. The dog was current on vaccinations and heartworm prevention. Oral flea and tick prevention was given each month.

On the physical exam, the dog was in good body condition and had an appropriate weight for its' size. It was normothermic, heart rate of 96 bpm, respiratory rate of 30 bpm, and euhydrated. The dog had multiple subcutaneous masses which had been diagnosed as lipomas on previous exams via fine needle aspirate and cytology. A previously unconfirmed, approximately 5 cm diameter, subcutaneous mass was palpated on the right side of the dog's throat. The mass had been noticed by the owners approximately one month earlier and appeared to be getting larger. The mass was soft, flocculent, movable and had a lenticular shape similar to a lipoma in form and texture. The dog exhibited no pain when the mass was palpated. Communication between the mass and underlying structures could not be palpated. Based on physical exam findings and the similarity the mass had in relation to the previously confirmed lipomas, the presumptive diagnosis of a lipoma was made.

A fine needle aspirate was performed, and cellular material was recovered. The sample was submitted for histopathologic analysis by a commercial

laboratory. Serum biochemistry, serum thyroid level and complete blood count (CBC) were also performed. Urinalysis and radiography were performed.

Hematology parameters were within normal limits. The dog had a PCV of 50.1%. White blood cells were within normal limits at 10.5 K/µL. Platelet umbers were adequate at 146 K/µL. Serum biochemistry parameters were WNL, however SDMA was high normal at 14 µg/dL (0-14 µg/dL). Serum total T4 was normal at 1.9 µg/dL (1.0-4.0 µg/dL). Urinalysis showed a mild proteinuria (1+; 100-200 mg/dl). The urine specific gravity was 1.037. Three view thoracic radiographs were taken. Mild changes consistent with aging and/or chronic airway disease were noted. No evidence of metastatic disease was seen.

Histology of the mass revealed indistinct aggregates of epithelial cells with scattered individual cells. Centrally placed, round nuclei with finely stippled chromatin patterns were noted within the cells. Cytoplasmic junctions within aggregates were poorly defined. The cellular nuclei were arranged in acinar like structures. Cytoplasm appeared moderately abundant and individualized cells with a diffuse background were observed. In some cases, the cytoplasm of cells had a faintly eosinophilic, granulated background. Anisocytosis and anisokaryosis appeared mild.

Based on the cytologic results, a tentative diagnosis of epithelial neoplasia was made. While the definitive identity of these cells was difficult to assess, based on the location of the mass and the cellular morphology of the fine needle aspirates, it was felt that the cells were thyroid in origin. A decision was made to progress with surgery to obtain a biopsy sample for further histopathologic evaluation and if possible, remove the mass in its entirety.

The dog was transferred to a secondary care facility for the operation to be conducted by a board-certified surgeon. The surgery was conducted under sterile conditions. A curvilinear excision was made around the mass maintaining 2 cm margins in all directions. During surgical exploration, no obvious tissue connection or communication was noted between the mass and underlying structures including the thyroid gland. The mass measured 5.5 x 3 cm, was nodular in appearance, and was heavily vascularized.

Histopathologic analysis confirmed a thyroid tumor and revealed proliferative epithelioid cells forming packets, cords, nests and small follicular structures, all supported by a fine fibrovascular stroma. The cells were cuboidal to polygonal with eosinophilic cytoplasm and round nuclei with small nucleoli. There was mild atypia with 11 mitotic figures per ten high-powered fields (HPF). The mass was partially disrupted by zones of necrosis and hemorrhage. Small nests of tumor cells partially infiltrated the outer capsule but were not observed to extend into adjacent tissue. Several foci of suspected vascular invasion were present. A thin rim of compressed thyroid tissue was identified at the periphery of the mass. No parathyroid tissue was observed. There were narrow tumor free surgical margins, with the lesion extending to less than 1 mm from the borders. Morphological diagnosis of an ectopic thyroid carcinoma was made in the ventral neck of a dog.

Thyroid tumors typically develop in older dogs and are considered relatively uncommon, representing 1-3% of all neoplasia in the dog.[18,19] While ectopic thyroid tissue is common in dogs, being identified in 50% of adult dogs on necropsy, tumors arising from ectopic thyroid tissue are rare.[18,19,20]. Ectopic thyroid carcinomas have been reported in the cranial mediastinum, sublingual area of the tongue, heart base and subcutaneously in the ventral neck region.[18,19,20,21] Most ectopic thyroid carcinomas occur in the heart base, cranial mediastinum or both[22,23,24] Generally, ectopic thyroid carcinomas are nonfunctional, thus dogs usually present with normal serum thyroxine (T4) concentrations.[18] Thyroid carcinomas arising from the thyroid gland are commonly malignant.[18,19] In contrast tumors arising from ectopic thyroid tissue often do not metastasize, however metastasis to the lungs has been reported.[25] Clinical symptoms include coughing, rapid breathing, dyspnea, dysphagia, change in bark tone or volume,

and facial edema.[18,19] These symptoms are usually due to mass effect of the tumor. Severe hemorrhage can occur if invasion of the thyroid carcinoma invades major vasculature.[26]

Although the report described a case whereby an ectopic thyroid carcinoma invaded thoracic vasculature, an ectopic thyroid tumor in the neck region may also cause severe hemorrhage if the mass infiltrated the cranial vena cava. In case presented here, the ectopic thyroid tumor was located near the vena cava but appeared encapsulated and non-invasive. In cases of ectopic thyroid tumors clinical signs may be a function of the tumor's location. For instance, a sublingual ectopic thyroid tumor was associated with hypersalivation.[22] Ectopic thyroid tumors occurring subcutaneously in the ventral neck region may be visible to the naked eye or palpable. Ectopic thyroid tumors not visible, such as those occurring at the heart base can be diagnosed with ^{99m}Tc-pertechotate imaging.[27]

Ectopic thyroid tumors can be treated with radiation therapy, chemotherapy, surgical excision, or a combination of the above.[28] In the case presented here, the dog was treated successfully with excisional surgery followed by systemic chemotherapy using carboplatin at a conservative dose of 250mg/m^2 IV. This dose was administered q 3 weeks for a total of 6 treatments.

Cytology confirms mass of thyroid origin in less than half of affected dogs, such as the case presented here.[22] However, fine needle aspiration and cytology is useful in that it may define the tumor as endocrine in origin, necessitating further diagnostic workup. Confirmatory diagnosis of ectopic thyroid carcinoma requires biopsy and histopathology.

The differential diagnosis for a freely movable, subcutaneous mass in the ventral neck region includes lipomas, salivary mucoceles, abscesses or granulomas, ectopic thyroid tumors and lymphomas. In the case presented here, the mass was initially suspected to be a lipoma based on palpation. Initially the mass was suspected to be a lipoma based on palpation, as the mass was soft, fluctuant, freely movable and well circumscribed. However, in this case cytology was able to rule out this differential and provide a tentative diagnosis of epithelial neoplasia.

CASE 5. SUBCUTANEOUS SOFT TISSUE TUMOR

A 12-year-old, FS Labrador Retriever presented for evaluation of a rapidly growing subcutaneous tumor located on the left ventral aspect of the neck. The mass had initially been diagnosed as a lipoma based on palpation. The owners noted that the mass had rapidly increased in size within the span of 2-3 months, and on a recheck visit, the mass measured 5cm x 5 cm. The mass palpated like a lipoma. It was lenticular in shape, soft, easily movable, and no communication to underlying structure could be felt. A fine needle aspiration was conducted.

Cellularity was low consisting of few scattered spindle shaped cells. The cells had moderate amounts of basophilic cytoplasm. The nuclei were oval with small nucleoli. A presumptive diagnosis of spindle cell proliferation was made; however the dearth of cellularity made more accurate diagnosis of spindle cell proliferation due to a benign process such as reactive fibroplasia or due to a more malignant process such as spindle cell tumor, difficult.

The dog was sent to surgery to remove as much as the mass as practicable and to obtain a biopsy to further define the mass. A curvilinear incision was made over the mass. The mass was then bluntly dissected away from ventral connecting tissue to avoid accidental incision into the underlying large blood vessels such as the carotid artery and the cervical vena cava. Unfortunately, this approach prevented achieving tumor free margins.

Histopathology showed findings consistent with a Grade 1 soft tissue sarcoma (STS). Soft tissue sarcomas are a population of mesenchymal tumors that constitute 15% of all skin and subcutaneous tumors in the dog.[1] These neoplasia are grouped diagnostically due to similar histologic features and biologic behavior.[1,2] Common histologic subtypes in the dog include fibrosarcoma, myxosarcoma,

peripheral nerve sheath tumor and perivascular wall cell tumor.[1,29] Canine cutaneous STS are generally characterized by a low to moderate risk of post-surgical local recurrence after complete resection and low metastatic potential. Reported median survival times after complete surgical resection range from 1013-1416 days.[1]

Clinically STSs demonstrate highly invasive behavior, infiltrating between fascial planes, and sometimes have a false pseudo-capsule.[1,2,30]Complete surgical excision is characteristically difficult.[31]

Histologic grading is prognostically significant for both risk of recurrence and risk of metastasis.[1] The grading scheme is based on degree of differentiation, mitotic count and degree of necrosis, assigning a grade of I (low), Grade II (intermediate, or Grade III (high).[1,29,31] The dog described in this case had a low grade of I, with a differentiation score of 1, a mitotic count of 1 per HPF, and a necrosis score of 0. Vascular invasion was not observed, however complete surgical margins were not achieved, with tumor cell extending to the edge of the cut incision. However, on re-examination 283 days post-surgery, no evidence of tumor regrowth was noted.

CASE 6. FIBROSARCOMA

A 15-year-old, 5.5 kg, neutered female domestic cat presented for lameness on the left hind limb. The cat had first exhibited lameness one week prior to the present exam. On physical exam, the cat had lost approximately 1 kg since its last physical exam 1 year prior, but was still in good body condition, well hydrated, and mentally alert. The cat displayed a III/IV lameness on the left rear leg. Crepitus was palpated in the stifle joint. An approximately 3 cm diameter, soft tissue mass distal and caudal to the left stifle was noted during the physical exam. The mass was edematous, soft, lenticular to ovoid in shape and freely movable.

Radiographs of the left stifle showed the presence of three intraarticular osteophytes. A soft tissue opacity was noted distal to the stifle and assumed to be the mass found on examination. Radiographs showed the soft tissue mass was discreet and well organized. It did not impinge on the tibial bone, nor did it appear to extend to the underlying soft tissues. A fine needle aspirate was obtained from the mass and submitted to a consulting laboratory for cytologic analysis. A board-certified veterinary pathologist reported the presence of mature adipocytes, red blood cells, and moderate numbers of keratin scrolls and concurred that the submitted sample was consistent with a lipoma. However, it was noted that the sample contained low cellularity and that the aspirate may have penetrated the primary mass into the subcutaneous fat adjacent to the lesion of interest. The cat was placed on an anti-inflammatory medication for lameness.

The owners returned with the cat two months later because they felt the mass had grown. At this presentation the mass measured 3.5 cm x 3 cm. Another fine needle aspirate was taken and again submitted to a commercial laboratory. Histopathology was done by a board-certified pathologist who noted the submitted slide contained adipocytes, red blood cells, and keratin scrolls. The pathology report agreed with the previous report that the most likely diagnosis was a lipoma but also felt that the analyzed sample was of low cellularity and the diagnosis should be interpreted with caution.

The cat presented again 3 weeks later. The mass had an irregular texture and had increased in size to 4.0 cm x 3.2 cm and was starting to encompass the tarsus. The cat was sedated with a ketamine/butorphanol/dexmedetomidine solution IM. Local anesthesia in the form of lidocaine was injected in the area above the mass. The area was clipped and surgically prepped. A 4 mm punch biopsy was collected and submitted to a commercial laboratory. Results of the biopsy analysis demonstrated the presence of well vascularized, dense collagenous tissue. The tissue was edematous with regions of increased numbers of fibroblasts. No neoplastic cells were noted. A diagnosis of soft tissue edema and fibrosis was made. The cat was placed on an oral antibiotic. After seven days of therapy, the size of

the mass had not reduced. The cat was then referred to a referral center for a second opinion.

A second biopsy performed at the referral center showed that the mass was consistent with a fibrosarcoma. The mass was composed of spindle to polygonal cells forming tightly packed and intersecting streams and bundles supported by fine fibrovascular stroma. The cells were small to medium and had indistinct cell borders. They contained small to moderate amounts of eosinophilic fibrillar cytoplasm. The nuclei were oval to fusiform and contained 1-2 small to large nucleoli. The mitotic count was <5 in 10 HPF. The degree of anisocytosis and anisokaryosis was moderate. Several cells were multi-nucleated.

In addition, the mass increased to 6 cm x 3.5cm and extended from the tarsus to mid-femur. The area proximal to the mass appeared normal. Three view thoracic radiographs showed no evidence of metastasis. Serum biochemistry profile and CBC were unremarkable. Abdominal ultrasound examination showed no progression of the cancer to internal organs.

Because it was not possible to surgically remove the fibrosarcoma while still maintaining acceptable tumor-free margins, a total leg amputation was performed. No further therapy for the fibrosarcoma was conducted. The cat adapted well after the surgery.

During routine physical examination a year later, the cat was in good health. The owners reported that the cat was ambulatory and had a good quality of life. On the physical exam, the cat was in good body condition, having gained 1.5 kg since the surgery 1 year prior. The area proximal to the amputation site was palpated and no evidence of fibrosarcoma re-occurrence was noted. The abdomen palpated normally with no obvious masses felt. Three-view thoracic radiographs showed no signs of metastases to the lungs. Abdominal radiographs did not reveal any obvious masses or organomegaly. Serum biochemistry profile, CBC, and urinalysis were clinically normal.

Fibrosarcomas arise from the skin, subcutaneous tissue or oral cavity.[32,33] They represent malignant fibroblasts. Tumors are usually well differentiated with spindle shaped tumor cells with scant cytoplasm.[1,29,32] Tumors tend to occur in older dogs and cats with no breed or sex predilection. They are usually locally invasive and can be painful especially if they invade or compress normal tissue. Metastasis is rare but tumors can reoccur at surgical removal sites because microscopic tumor cells may remain along fascial planes.[33]

Cytologically, fibrosarcomas can be well differentiated, exhibiting spindle-shaped tumor cells with scant cytoplasm.[29] The more anaplastic tumors are very cellular and have marked pleomorphism often associated with a pink collagenous material.[29,32] They may consist of abundant numbers of large, plump spindle cells, which occur individually or in aggregates and are associated with many mitotic figures. Anaplastic fibrosarcoma cells have a higher nuclear-to-cytoplasm ratio than their more differentiated counterparts.[29]Multi-nucleated giant cells may be present.[29]

Treatment involves wide surgical excision or amputation.[33] Radiotherapy, immunotherapy, chemotherapy alone or in combination may also be employed during post operative treatment (as described in the case here).[1,32] In cases treated with surgery alone, recurrence rates in dogs have been reported to be 30%.[29] Prognosis is good to poor depending on the degree of anaplasia.[1,29]

The case described above is interesting in the fact that the fibrosarcoma tumor had been mis-identified as a lipoma on three separate occasions previously, with two fine needle aspirate samples and a core biopsy sample reviewed by a board-certified pathologist.

CASE 7. MAST CELL TUMOR

An eight-year-old, neutered male 9.0 kg mixed breed dog presented for a second opinion of a subcutaneous mass in the left groin region. The mass had been previously diagnosed as a lipoma

at another clinic, although the dog's history did not indicate whether the initial diagnosis was made on physical palpation itself or had been confirmed with fine needle aspirate and histopathology. The owners reported that another mass, similar in size, shape and texture and in the same general area as the aforementioned mass had also been diagnosed as a lipoma. Within the last 2-3 months prior to presentation, the mass in the inguinal area had grown rapidly and changed color with respect to the second mass, which had remained unchanged since the initial diagnosis.

The left groin mass measured 3.5 cm x 3.0 cm and had the skin overlying it had turned red. The second mass measured 1cm x 1 cm. No skin discoloration was associated with this second mass was observed. A 4 mm punch biopsy was taken of both masses. Histopathologic analysis of the second mass confirmed the mass as a lipoma. However, histopathological analysis of the mass in the dog's left inguinal area was shown to be a high-grade mast cell tumor (MCT). The cytopathological description noted that the submitted sample was highly cellular with undifferentiated cytoplasmic boundaries. A moderately bloody background with many free, metachromatic granules was also noted. Nucleated cells were comprised mostly of mast cells and were distributed individually or in crowded aggregates. The mast cells had a moderate volume of cytoplasm that contained sparse cytoplasmic granules. Nuclei were irregular in size and shape. Nucleoli were inapparent. Anisocytosis and anisokariosis were moderate. Large numbers of eosinophils and fibroblasts were also noted in the sample. A diagnosis of a high grade MCT was made.

The fine needle aspirates of the inguinal lymph node and of the popliteal lymph node were both negative for mast cells. Thoracic radiographs did not show the presence of pulmonary metastasis. A CBC was unremarkable with normal PCV (44%) and normal WBC of 6.8 K/uL (N=4-15.5 k/uL). Serum biochemistry profile showed an increase in ALT of 192 IU/L (N=12-118 IU/L), ALKP of 330 IU/L (N=5-131 IU/L). There was a slightly low creatinine of 0.4 mg/dl (N=0.5-1.6 mg/dl). Urinalysis showed low specific gravity of 1.011 (N=1.015-1.050), an alkaline pH of 8.0 (N=5.5-7.0), and trace urine protein.

Because the tumor was too large to remove surgically, on the advice of a veterinary oncologist, the dog was started on a chemotherapy protocol consisting of vinblastine 2.25mg/m2 IV q 1x weekly for 4 weeks and oral prednisone at 2mg/kg. At recheck two weeks later, it was found that the mast cell tumor had spread to the inguinal lymph node, and the chemotherapy protocol was changed to palladia 15mg PO every other day and the prednisone dose decreased to 5mg in the a.m. and 2.5 mg in the p.m.

At recheck 6 weeks after starting the palladia/ prednisone therapy, the tumor had shrunk to 3cm x 3 cm. According to the owners, the dog appeared to have a good quality of life.

Mast cell tumors account for about 16-21% of skin tumors.[1] Cutaneous and subcutaneous mast cell tumors are usually solitary, non-encapsulated and highly infiltrative into the dermis and subcutis.[29] They are thought to arise from tissue mast cells in the dermis and subcutaneous tissue, although the mechanism for malignant transformation is incompletely understood. Earlier studies showed that MCT could be induced in young dogs through the transmission of tissues and cell-free extracts, suggesting a viral etiology, but ultrastructural evaluation of affected tissue so far has failed to consistently identify viral particles.[34,35,36] More recent studies suggest that mutations of c-kit receptor tyrosine kinase can cause malignant mast cell transformation. Normal c-kit signaling is important in the signaling, differentiation, migration and survival time of connective tissue mast cells.[36,37,38]

Mast cell tumors are classified according to the degree of differentiation histologic grade. Previously, MCT were divided into three grades: Grade I were considered low-grade and the least aggressive in terms of potential pathology to the patient, Grade II MCT were of intermediate grade, and Grade III MCT

were high grade and displayed the most aggressive behavior in terms of regional spread and distant metastasis.[39] Because of the wide variation in the histologic pattern of canine MCTs, and the overlap of certain grading parameters, the three-tiered system has largely been discarded, and MCT divided into either low grade (highly differentiated cells) or high grade (poorly differentiated cells).[35] High grade MCT are more aggressive, and carry a poorer prognosis for the patient that low grade MCT.

Low grade, well differentiated MCT tend to be small (1-4 cm diameter), solitary, soft, and slow growing. Usually they are not ulcerated, but hair loss over the mass is sometimes noted. In contrast, high grade, poorly differentiated MCT are rapidly growing, can attain a larger size, and may have ulceration present. Low-grade MCT are the most common form of the tumor and surgical excision with surgical margins of at least 2 cm is often curative.[40] High-grade tumors can metastasize and are usually treated with surgical debulking of the mass, radiotherapy, chemotherapy, or a combination of these protocols.[41,42,43] More recent therapies involving the use of tyrosine kinase inhibitors has shown much promise.[44,45,46]

Mast cell tumors are initially diagnosed via fine needle aspirate and cytologic analysis. However, fine needle aspirates do not contain a histologic grade. In addition, aqueous based Wright stains, such as Diff-Quik™ (employed by many small animal practitioners including this author), often show a lack of granulation, especially in high grade MCT because the granular contents are water soluble.[29] For this reason, suspected MCT aspirates should be submitted to a laboratory that can employ Giemsa or toluidine blue stains. This author prefers to diagnose suspected MCT utilizing a 4mm punch biopsy. A biopsy sample allows for histologic grading and is less likely to result in accidentally sampling non-tumor tissue. Using a 4mm punch biopsy is advantageous in that it can usually be done on a non-sedated patient by using a local anesthetic such as lidocaine. Patients usually tolerate the procedure well and it leaves only a small surgical wound whereby hemostasis can be achieved with a single suture, silver nitrate application, or surgical glue. This author routinely performs this procedure within the confines of a scheduled visit.

Discussion

The cases presented here demonstrate the importance of confirming the diagnosis of lipoma. They begin with relatively benign conditions and increase roughly in pathological severity through each case presented. Although subcutaneous lipomas tend to have distinctive appearance, shape, and texture, other more aggressive neoplastic processes can mimic these traits. Practitioners should confirm suspected lipomas through empirical means including cytological analysis of a fine needle aspirate or histopathological analysis of biopsy samples.

The first case illustrates that lipomas can lead to pathological issues due to their mass effect on nearby organs or secondary effects from their size. The dog described was generally healthy but experienced discomfort due to the position and size of a lipoma, which caused compression in the thoracic cavity, particularly when lying on the affected side. The lipoma, which had incrementally increased in size over the dog's lifetime, eventually led to breathing difficulties and discomfort, especially when the dog lay on the side with the tumor. Because the mass had been confirmed as a lipoma, surgical removal of the mass could be conducted. The surgery returned the dog to its former quality of life and further treatment protocols were not needed.

In Case 2, an infiltrative lipoma had caused compression of the spinal cord in the lumbar region of the dog described, resulting in paraparesis. Although most subcutaneous tumors are encapsulated and are not locally invasive, infiltrative lipomas tend to be less discrete in organization. They are composed of well differentiated adipose tissue without evidence of anaplasia.[1]Often, they are unencapsulated, diffuse and can grow into adjacent areas, such as nearby muscle tissue. When infiltrative lipomas affect adjacent structures, they can interrupt the normal

function of affected tissue structures or organs. Infiltrative lipomas have been reported to cause pathological issues when they invade adjacent muscle, fascia, nerve, joint capsule, and the spinal canal (as demonstrated in this case).[47]

Computed tomography (CT) is used to better distinguish these tumors; however CT does not contrast enhance and differentiating infiltrative lipomas from normal adipose tissue is difficult.[1,48] Thus contrast MRI scan is often employed to better differentiate from surrounding adipose tissue. T-2-weighted MRI was used to confirm the mass was an infiltrative lipoma and to trace its pathway into the spinal column. Surgery was performed with the knowledge that the targeted tissue was not malignant, and thus wide surgical margins did not have to be maintained. Surgery can be considered alone or in combination with radiation therapy for treatment.[47]

In Case 3, a dog was presented for surgical removal of a large lipoma. Previous fine needle aspirates confirmed the mass as a lipoma, however aspects of the mass noted during surgery did not correlate with the diagnosis. Histopathologic analysis of a biopsy sample showed the mass to be a liposarcoma. Liposarcomas are rare malignant histologic variants of lipomas. They are difficult to distinguish cytologically from lipomas, as both arise from adipocytes and malignant transformation is often not observed in sample submitted for histopathologic analysis. Liposarcomas are not thought to arise from malignant transformation of existing lipoma tissue.[13]

Case 4 describes the occurrence and treatment of an ectopic thyroid tumor. In necropsy studies, 30-50% of thyroid tumors were found to be benign adenemoas.[48] Thyroid tumors are typically non-functional, and the in the dog presented here, the thyroid hormone, measured by both total T_4 and free T_4 was within normal limits.[1,48] Surgical resection of the tumor proved curative in this case.

Case 5 and Case 6 demonstrate soft tissue sarcomas (STS) occurrence. STS include a variety of neoplasias that develop from mesenchymal tissue. These include peripheral nerve sheath tumors, fibrosarcomas, leiomyomas, rhabdomyosarcoma, hemangiomas and other subcutaneous neoplasms arising from mesenchymal tissue. Although STS do not undergo distant metastasis, they are capable of aggressive local invasion. Although the STS described in Case 5 could not be identified to a particular subtype, the behavior of it showed that it was causing significant pathology to the surrounding tissues. Surgical resection proved to be adequate in the treatment of this case, however some cases are treated with a combination of surgery, chemotherapy, and radiosurgery. The cat described in Case 6 had a fibrosarcoma. Fibrosarcomas are extremely fast growing and invasive forms of STS. Some fibrosarcomas in cats have been associated with vaccine administration.[50] The cat presented in this case had a fibrosarcoma that developed far away from typical vaccine injection sites and therefore was not felt to be a vaccine site fibrosarcoma. Surgical removal of fibrosarcoma mandates that surgical margins must be clear of microscopic remnants of the tumor to ensure that it does not re-occur. In the case presented here, total leg amputation was considered the only viable method to treating the cancer. The cat remains active and tumor free at the writing of this article.

Case 7 describes a case of a dog with a Mast cell tumors (MCT). MCT can imitate lipomas in texture and shape. Like lipomas, they can arise in subcutaneous tissue. MCT are based on histopathologic grading system, the most common being a two-tiered system with low-grade MCT considered less aggressive and high-grade MCT considered more aggressive. Low-grade MCT are characterized by well-defined cells, low or zero mitotic count, and absent nucleoli. Low grade MCT do not metastasize to distant organs, but they can be locally aggressive. Surgery is usually the mainstay of therapy, however chemotherapeutic and/or radiotherapeutic protocols can be used in addition. High grade MCT are characterized with pleomorphic cell structure, larger numbers of mitotic cells, and prominent nucleoli. High grade

MCT are capable of distance metastasis and are treated with surgery, chemotherapy, radiotherapy and/or a combination of these. The dog presented in Case 7 demonstrates how quickly a high-grade MCT can advance.

The cases reviewed here demonstrate the importance of early diagnosis and confirming that a mass suspected of being a subcutaneous lipoma is in-fact a subcutaneous lipoma. Usually, a lipoma can be substantiated via a bed side test such as a fine needle aspirate. This procedure is quick, relatively non-invasive and inexpensive. A sterile needle is inserted transdermally through the skin and into the mass. This author finds that using 1 inch, 20 – 22 gauge needles yields good samples. Several quick retractions of the syringe plunger are performed, causing cells to exfoliate from the mass. The aspirated sample is ejected onto a microscope slide. Lipomas will often show up as oily smears on a microscope slide and wash off with alcohol fixatives. Intact adipocytes can sometimes be observed using a commercially available triple stain such as Diff Quik. If cytologic or other material is observed remaining on the slide, it can be submitted to a commercial laboratory for histopathologic analysis. A fine needle aspirate and microscopic review of collected material of any new or growing subcutaneous tumors is recommended.

A fine needle aspirate and microscopic analysis in a clinic setting is a quick and usually reliable method of confirming a lipoma. However, it should be remembered that this method is not infallible. Since the adipocytes found in lipomas are cytologically the same or very similar to other areas of adipose reserves, such as the subcutis, it is possible to miss the target mass or pierce the mass completely resulting in a sample of the surrounding fat and not of the mass. This can happen if the patient is moving or is difficult to restrain during collection attempts. Also, lipomas can be movable and if they are not isolated properly during collection attempts, it is possible to miss the intended target tumor, inadvertently sampling surrounding soft tissue.

Cytological assessment of fine needle aspirates is typically inadequate for the definitive diagnosis of soft tissue sarcomas, including liposarcomas. Aspirate samples that yield cellular material other than adipocytes should be biopsied to confirm diagnosis. This may be especially important for masses that change shape, size or texture or if the patient exhibits pain on palpation of the mass. This author prefers to biopsy suspect tumors with a 4mm punch biopsy. The procedure can be performed on a non-sedated patient with the use of a local anesthetic. Patients usually tolerate the procedure well. The process leaves only a small surgical wound, and hemostasis can be achieved with the application of surgical glue, silver nitrate or a suture. Visual examination of the recovered tissue can give the practitioner confidence that the recovered material is representative of the indented target tumor.

To perform the procedure, a small area of skin overlying the targeted mass is clipped and aseptically cleansed. A local anesthetic, such as lidocaine or procaine, is infused into and around the area to be sampled. A punch biopsy is placed on the skin above the mass and rotated until initial dermal penetration is achieved. The underlying mass can then be manually directed toward the punch biopsy tool. The tool is rotated again until the practitioner is confident that the sample chamber contains tissue from the intended target. The tissue is placed into formalin and submitted to a commercial laboratory for histopathologic analysis. Hemostasis from the surgical wound is achieved via placing a silver nitrate stick into the collection site. If this approach is insufficient to control bleeding, then a surgical stable or monofilament suture can be placed. This author finds that using one throw of a 3-0 monofilament suture in a cruciate pattern is sufficient. It is usually unnecessary to send the patient home on pain medications or antibiotic coverage, unless an infected source is suspected (such as a walled-off abscess).

Lipomas and lipoma variants such as infiltrative lipomas, can cause pathology to surrounding

structures, either through direct infiltration of tissue, or compression of adjacent organs. In the first two cases presented here, confirmation that the masses were in fact lipomas became vital knowledge to the surgeon in preparing a surgical strategy.

As the cases demonstrated in this paper reflect, some cancer variants can mimic the appearance of a benign lipoma. As newer and better treatment options appear on the market for cancer treatment, it is becoming more imperative to make an early diagnosis of a potentially malignant mass.

Conclusion

Dogs and cats are often presented to veterinarians for evaluation of subcutaneous masses. As in human patients, there exists a wide variety of subcutaneous neoplasias in canine and feline patients. A frequent diagnosis is lipoma, a benign tumor composed of adipocytes. Veterinary practitioners often diagnose lipomas based on palpation alone. Lipomas usually yield only adipocytes on microscopic exam, and often the aspirated material will completely wash off during staining.

However, more malignant tumors can mimic lipomas on palpation. Even fine needle aspirates and biopsy of subcutaneous masses can give erroneous results. Suspect subcutaneous tumors should be monitored. Those that show rapid growth should be re-evaluated.

As demonstrated here, early diagnosis and therapy can yield favorable outcomes.

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