Invasive cutaneous angiomatosis and thrombocytopenia in a cat

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Clinical Findings—Physical examination findings were unremarkable except for a 2-mm-diameter erosion of the right metacarpal pad. A CBC revealed marked thrombocytopenia. Serum biochemical analyses, retroviral screening, thoracic radiography, and abdominal ultrasonography revealed no abnormalities. Via ultrasonographic examination, the vasculature in the right metacarpal pad appeared increased, compared with that of the left pad; an aberrant arterial plexus that was confined to the metacarpal pad was identified via arterial angiography.

Treatment and Outcome—Surgical resection of the metacarpal pad (without digital pad transposition) with primary closure was performed. Histologic evaluation of the pad tissue revealed invasive cutaneous angiomatosis. The incision healed without complications, and limb function was considered normal. Administration of prednisone (2 mg/kg [0.91 mg/lb], PO, q 24 h) was initiated 4 weeks prior to surgery to treat suspected immune-mediated thrombocytopenia and continued afterwards with a tapering dosage. Platelet count was within reference limits 4 months after surgery; at 12 months, there was no evidence of recurrence of abnormal vasculature in the right metacarpal pad region.

Clinical Relevance—Complete resection of the metacarpal pad (without pad transposition) resulted in successful and well-tolerated treatment of cutaneous angiomatosis of the metacarpal pad of a cat. Recurrence of abnormal vasculature was not evident at a 12-month follow-up examination. Thrombocytopenia is commonly associated with vascular anomalies in humans and may have been a contributing factor in this cat. (J Am Vet Med Assoc 2009;234:381–384)

D uring a 3-year period, a 9-year-old 6.9-kg (15.18-lb) castrated male Siamese cat was examined by a referring veterinarian several times for investigation of repeated episodes of hemorrhage from the right metacarpal pad. The cat had been neutered and declawed at an early age and was otherwise in good health. The first episode of hemorrhage occurred shortly after a suspected cat fight. Exploration of the metacarpal pad at that time resulted in profuse bleeding; however, no anomaly was identified. Over time, hematomas began to develop and, subsequently, rupture, in the right metacarpal pad. Initially, these episodes resolved with bandaging at home, but with increasing severity and frequency (episodes occurring every 2 to 3 weeks), further veterinary attention was sought. No bleeding was reported from any other body location. The referring veterinarian performed a CBC and serum biochemical profile. The serum biochemical analyses revealed no abnormalities; however, the CBC revealed marked thrombocytopenia (23 × 10^9 platelets/L; reference range, 120 to 600 × 10^9 platelets/L). The cat was referred to the Veterinary Teaching Hospital of the Ontario Veterinary College in Guelph, ON, for further evaluation.

At the initial examination, the cat was overweight (body condition score, 8/9) and had a 2-mm-diameter erosion that was surrounded by bruising on the medial aspect of the right metacarpal pad. Physical examination revealed no other abnormalities. Blood samples were submitted for a CBC, serum biochemical analyses, and assessment of serum thyroxine concentration. The only notable abnormality was severe thrombocytopenia (12 × 10^9 platelets/L; reference range, 93 to 514 × 10^9 platelets/L). Results of a coagulation profile, retroviral screening, and anti-nuclear antibody tests were unremarkable. Abdominal and thoracic radiography and abdominal ultrasonography revealed no clinically important abnormalities. The cat was housed strictly indoors, had been last vaccinated 9 months earlier, and was not receiving any medications. A tentative diagnosis of primary immune-mediated thrombocytopenia was made. The cat was discharged from the hospital, and the owner was instructed to administer prednisone (2 mg/kg [0.91 mg/lb]) orally once a day. The referring veterinarian was to perform a CBC or platelet count weekly to assess response to treatment.

Serial CBCs revealed a gradual increase in the number of platelets, and 3 weeks after the initial examination, the cat was returned to the hospital for further evaluation of the footpad lesion. Despite improvement in the platelet count, the owner reported an increase in
the amount and frequency of bleeding from the pad, which necessitated almost continuous bandage application to the affected area. Physical examination findings remained unremarkable, except for the bruised and eroded region on the right metacarpal pad. The cat's platelet count was $69 \times 10^9$ platelets/L, and clumped platelets were evident on examination of a blood smear; however, the total platelet count was assessed as being within the reference range.

Given the history of thrombocytopenia, minimally invasive diagnostic tests were pursued to evaluate underlying causes of the footpad hemorrhage. An ultrasonographic examination of the metacarpal pad revealed that the vasculature within the footpad was increased, compared with that of the left pad. Several small cavernous areas of static fluid were detected within the pad; these were considered hematomas. The entire pad was affected, and many tortuous vessels ran in a disorganized fashion throughout (Figure 1). The presence of an arteriovenous fistula was not supported because venous distention or pulsation was not detected. No abnormal tissues or foreign bodies were evident within the pad.

Prior to arterial angiography, the cat was premedicated with hydromorphone (0.05 mg/kg [0.023 mg/lb], IV) and acepromazine (0.02 mg/kg [0.01 mg/lb], IV). Anesthesia was induced by use of propofol (2 mg/kg, IV) and midazolam (0.2 mg/kg [0.09 mg/lb], IV) and maintained with isoflurane (1.5%). A 22-g over-the-needle catheter was placed into a small artery along the right antebrachium via surgical dissection. Iohexol contrast medium was injected via the catheter, and fluoroscopy was performed to view the aberrant vasculature. The angiogram confirmed the presence of an anomalous vascular plexus that was confined to the metacarpal pad (Figure 2). A single artery appeared to feed into the pad and branched into many irregular, convoluted vessels; those vessels subsequently coalesced to exit the pad as a single vein. No other vascular anomalies within the limb were detected.

Complete pad resection with possible digital pad transposition was elected. Surgical concerns included hemorrhage and excessive tension leading to inability to close the wound or wound dehiscence. The preoperative platelet count was within reference limits ($201 \times 10^9$ platelets/L). The cat was anesthetized by use of the same protocol as that used for angiography. A soft rubber tourniquet was placed proximal to the right elbow joint for hemostasis. Sharp dissection at the junction of the skin and right metacarpal pad followed by blunt dissection was used to remove both the pad and underlying subcutaneous tissue en bloc. The subcutaneous tissue and skin were closed horizontally with 3-0 polydioxanone suture and 3-0 polypropylene suture, respectively, in simple interrupted patterns. The closure had minimal tension when the right foot was held in neutral or flexed position and moderate tension when the foot was held in full extension. No bleeding was observed upon release of the tourniquet. Transposition of a digital pad was not performed. The limb was placed in a padded palmar splint with the foot slightly flexed to decrease tension. The cat recovered well from anesthesia.

The cat was returned for examination every 3 to 5 days during the 2-week period following surgery, and the splint was maintained during that interval. The cat was bright and alert and had no signs of pain; the owner reported that the cat had good use of the limb at home. Sutures were removed at 14 days after surgery, at which time the incision had healed.
Histologic examination of the footpad tissue revealed invasive cutaneous angiomatosis that extended throughout the pad and to the surgical margins (Figure 3). The deep dermis, superficial dermis, adnexa, and adipose tissue of the pad contained multiple coalescing nodules of vascular channels that were lined with well-differentiated endothelium. These channels were surrounded with layers of spindle cells of variable thickness, and several vascular spaces were present. The surrounding dermis was obliterated and compressed in areas by the mass. The mass center contained a large vascular channel (3 mm in diameter) with a large thrombus (2 mm in diameter) and neutrophils.

The cat was reevaluated biweekly for the first 2 months after the initial examination. No evidence of recurrence of the metacarpal lesion was detected, and the cat had apparently normal use of the limb. Platelet count remained low, and clumps of platelets were often observed during microscopic examination of blood smears. Manual platelet count estimates were consistent with mild to moderate thrombocytopenia. The cat continued to be treated with prednisone (2 mg/kg, PO, q 24 h) and was assessed monthly. Four months after the initial examination, the platelet count was within reference limits (102 × 10^9 platelets/L). Two subsequent counts were also within reference limits, and a gradual reduction of the dosage of prednisone was initiated. The prednisone dose was tapered by 50% every 4 weeks if no abnormality in platelet count developed. As the dosage of prednisone was decreased, there was no recurrence of thrombocytopenia; after 4 months, treatment with prednisone was discontinued. The site of surgical resection was examined ultrasonographically at 3, 6, and 12 months after surgery to assess for recurrence, and abnormal vasculature was not observed.

**Discussion**

Angiomatosis is a benign vascular anomaly in which a tumor forms blood vessels. Angiomatosis has been rarely reported in the veterinary medical literature, but the condition develops relatively commonly in people as a diffuse form of hemangioma. Many proliferative vascular diseases have similar clinical features, and differentiation among hemangiomas, well-differentiated hemangiosarcomas, angiolipomas, and reactive angiogenesis can be difficult. Histologically, angiomatosis can be differentiated from neoplasms by the formation of mature vessels that are comprised of multiple cell types—tumors are typically growths that are derived from the uncontrolled proliferation of 1 cell type. Cutaneous angiomatosis is typically characterized by dermal and subcutaneous blood-filled vascular structures of variable size that are separated by apparently normal or myxomatous mesenchymal tissue. Vascular channels vary with regard to lumen size and are lined by mature or slightly large endothelial cells and are often interconnected. Thrombi may also develop.

Whether the development of these lesions represents a hamartomatous process is the subject of debate because some lesions contain immature endothelium, whereas others do not. The young age at which angiomatosis is typically detected in humans supports a developmental origin, and there are several reports of angiomatosis in young animals of other species. Angiomatosis of the thoracic vertebrae in 4 cats < 2 years old and extensive forelimb cutaneous angiomatosis in a 1-year-old dog have been reported. Bovine juvenile angiomatosis is a recognized disease entity. However, older animals may also be affected; cutaneous angiomatosis in particular has been identified in an adult dog and 2 cats in addition to the cat of this report. The cases of angiomatosis among older animals suggest an acquired rather congenital disease process. It has been proposed that juvenile bovine angiomatosis is the result of either an aberrant repair mechanism in response to trauma or a hamartomatous process. In humans, the differential list must be expanded to include reactive angioendotheliomatosis, which develops in response to severe systemic disease; diffuse dermal angiomatosis, which develops in association with severe atherosclerosis; pseudo-Kaposi sarcoma; and several other syndromes that have not been reported in veterinary medicine. Angiomatosis is known to develop more commonly in individuals with HIV infection or severe systemic illness and in children, suggesting both acquired and developmental causes may exist. Rongioletti and Rebora proposed the unifying term cutaneous reactive angiomatosis and have suggested a common underlying etiology of occlusion of normal vasculature. They proposed that developmental, infectious, traumatic, and neoplastic causes all act through the same pathogenetic mechanism. Cutaneous angiomatosis among cats and dogs is so infrequently reported that no causal pattern has been identified.

In a report of 3 cases of cutaneous angiomatosis in an adult dog and 2 adult cats, 2 animals were affected on the face and 1 was affected on the forelimb. To our knowledge, that report was the first description of cutaneous angiomatosis in domestic cats and dogs. In each case, the diagnosis was made on the basis of results of histologic examination of full-thickness biopsy specimens of the lesions; those findings were consistent with cutaneous angiomatosis and were similar to the histopathologic changes identified in the metacarpal pad of the cat of this report. The dog and 2 cats were each treated successfully with laser photocoagulation. The laser treatments caused thermal necrosis and skin
sloughing, and the resulting lesion was then allowed to heal via secondary intention. In both animals with facial lesions, recurrence of cutaneous angiomatosis was evident within 6 months of treatment; the remaining cat died of unrelated causes 6 months after treatment. Laser therapy was not considered a viable option for the cat of this report because the lesion was limited to the metacarpal pad; at that location, necrosis and secondary intention healing would not be tolerated well. Embolization of the abnormal vascular plexus by either catheter placement of a metallic coil or cyanoacrylate occlusion was considered, but posed similar risks. Incisional biopsy was not performed on the footpad lesion because of the concerns for pain, poor healing, and especially hemorrhage, given the cat's history of thrombocytopenia. As such, lack of definitive diagnosis also imposed restrictions on treatment planning.

Excisional biopsy was performed with both diagnostic and curative intent. The location of the lesion negated any attempt to obtain wide surgical margins; however, removal of the pad was deemed the best option to both resolve the episodic hemorrhage and obtain a histologic diagnosis. It has been suggested that complete pad resection could be tolerated in cats; however, complete surgical resection of the metacarpal pad without pad transposition in cats has not been described to the authors' knowledge. Postoperative recovery and healing were uneventful, and long-term limb use appeared normal in the cat of this report.

Initially, a diagnosis of immune-mediated thrombocytopenia was made for the cat of this report. In cats, immune-mediated thrombocytopenia is a rare disease; it is assumed that 2 separate disorders exist. Among cats with thrombocytopenia, 1% to 2% have primary immune-mediated thrombocytopenia. Secondary immune-mediated destruction of platelets appears to be a far more common cause of thrombocytopenia in cats, and infectious diseases or neoplasms are the most common inciting causes. Thoracic radiography, abdominal ultrasonography, serum biochemical analyses, urinalysis, retroviral screening, and investigation of recent medical history did not reveal an inciting cause in the cat of this report. Immune-mediated destruction of platelets associated with the vascular anomaly or a consumptive coagulopathy, which has been associated with certain vascular abnormalities in humans, cannot be ruled out.

To the authors' knowledge, cutaneous angiomatosis with concurrent thrombocytopenia in a nonhuman animal has not been reported previously. Following complete metacarpal pad resection in the cat of this report, forelimb function was considered good. No further episodes of hemorrhage were reported. Ultrasonographic evaluation at 12 months after surgery revealed no evidence of aberrant vasculature. In a report of other animals with cutaneous angiomatosis that were treated with laser therapy, lesions recurred within this time frame; this suggests that excision, where possible, may be the treatment of choice. Histologic examination of excised tissues and long-term follow-up should be performed in all cases.

References