An 11-year-old 5.84-kg (12.85-lb) castrated male Himalayan cat was referred to a veterinary teaching hospital because of sudden onset of dyspnea and ventral abdominal swelling that was noticed by the owner after the cat had a possible fall and had been cornered by the family dog.

**Clinical and Gross Findings**

On physical examination, the cat was lethargic, non-ambulatory, and profoundly dyspneic and had severe pitting edema of the ventral aspect of the abdomen and thorax as well as all 4 limbs. Thoracic radiography performed by the referring veterinarian revealed moderate pleural effusion and a diffuse bronchial pattern. A sample of the pleural fluid was collected by ultrasound-guided thoracocentesis. Results of fluid analysis of the pleural effusion sample indicated that it was serosanguineous fluid with a total protein concentration of 2.4 g/dL and a cell count of 0.472 × 10^3/μL (37% neutrophils, 32% monocytes, 29% lymphocytes, and 2% eosinophils). Atypical lymphocytes of intermediate to large size with deeply basophilic cytoplasm and cleaved to cloverleaf-shaped nuclei, coarse chromatin, and 1 or 2 nucleoli accounted for 12% of the cells. These cells were thought to be reactive, but lymphoid neoplasia could not be ruled out. Thoracocentesis was performed again the following day with the removal of an additional 170 mL of orange-tinged fluid; fluid analysis was not repeated. Results of a serum biochemical panel were unremarkable except for markedly high creatine kinase activity (2,365 U/L; reference range, 14 to 528 U/L), hyperlactatemia (4.1 mmol/L; reference range, 0.0 to 2.0 mmol/L), and slightly low total protein concentration (5.5 g/dL; reference range, 6.0 to 8.4 g/dL). Individually, albumin and globulin concentrations were within reference ranges. The high serum creatine kinase activity and hyperlactatemia were suspected to have been related to the reported fall and subsequent struggle after being cornered by the dog, but this was not further evaluated. Abdominal ultrasonographic findings were within normal limits except for the edematous subcutaneous tissues. Echocardiography revealed pleural effusion and a normal-sized left atrium. Subjective concentric hypertrophy of the left ventricle was evident, but the thicknesses of the interventricular septum in diastole and the left ventricular free wall in diastole were both < 0.6 cm (0.56 cm and 0.57 cm, respectively). The right heart structures appeared subjectively normal except for turbulence in the right ventricular outflow track with a right ventricular outflow track velocity of 2 m/s, consistent with dynamic right ventricular outflow tract obstruction. On the basis of the echocardiographic examination findings, the pleural effusion was judged to be noncardiac in origin.

The cat was hospitalized for 4 days, with progression of edema to the ventral cervical region and development of petechiae and erythema on the ventral aspect of the abdomen. The cat was suspected to have developed immune-mediated hemolytic anemia on the basis of a positive result of a saline agglutination test and detection of mild anemia (PCV, 30%). Results of examination of a biopsy specimen obtained from a swollen limb were inconclusive. Owing to progression of the edema and the need for additional thoracocentesis despite medical management, the owners elected to euthanize the cat and allow postmortem examination.

At postmortem examination, there was severe subcutaneous edema along the ventrum (Figure 1) and within all limbs. The thoracic cavity contained 200 mL of clear yellow watery fluid, and the lungs were diffusely atelectatic. The myocardium contained several irregular (maximum width, 2 mm), poorly demarcated, gray foci in the left ventricle and interventricular septum. The pericardium and cranial mediastinum were mildly thickened and edematous.

Formulate differential diagnoses from the history, clinical findings, and Figure 1—then turn the page→
Histopathologic Findings

Sections of skin from the ventral aspect of the abdomen, heart, pericardium, lungs, liver, kidneys, and popliteal lymph nodes were examined histologically. In sections of ventral abdominal skin, the dermis and subcutis were extensively infiltrated by a poorly demarcated neoplasm composed of round to spindle cells, which formed predominantly empty vascular channels by wrapping around adipocytes and bundles of dermal collagen (Figure 2). The neoplastic cells had oval, hyperchromatic nuclei with 1 or 2 small nucleoli and small to moderate amounts of eosinophilic cytoplasm. There was moderate anisocytosis and anisokaryosis with 3 mitotic figures/10 hpf (area examined, 2.37 mm²). Small numbers of perivascular lymphocytes and plasma cells and infiltrating foamy macrophages were also present. The myocardium, epicardium, pericardium, and mediastinum were multifocally and extensively infiltrated by similar neoplastic cells, with some areas forming solid aggregates or linear arrays and less frequent formation of discrete, vascular channels (Figure 3). There were no significant microscopic changes in the lungs, liver, kidneys, or popliteal lymph nodes apart from pleural mesothelial hypertrophy, mild hepatocellular lipid vacuolation, and mild chronic interstitial nephritis.

Immunohistochemical staining for factor VIII-related antigen revealed strong cytoplasmic expression in the neoplastic cells in the skin (Figure 2) and heart. With Jones methenamine silver–periodic acid–Schiff stain, there was discontinuous basement membrane staining underlying the neoplastic cells.

Morphologic Diagnosis and Case Summary

Morphologic diagnosis and case summary: ventral abdominal lymphangiosarcoma with cardiac, pericardial, and mediastinal metastasis in a Himalayan cat.

Figure 2—Photomicrographs of sections of the ventral abdominal skin from the cat in Figure 1. A—The deep dermis and subcutis is expanded by a neoplasm forming infiltrative vascular channels (asterisk). H&E stain; bar = 500 µm. B—Higher magnification view of the area in panel A. Notice the empty vascular spaces lined by plump spindle cells with hyperchromatic nuclei. H&E stain; bar = 50 µm. C—The neoplastic cells have strong cytoplasmic expression of factor VIII–related antigen. Factor VIII–related antigen-specific immunohistochemical stain with 3,3′-diaminobenzidine chromogen and hematoxylin counterstain; bar = 50 µm.
Lymphangiosarcoma is an aggressive neoplasm originating from the endothelial cells of lymphatic vessels. Development of lymphangiosarcoma is rare and has mainly been described in humans, dogs, and cats; a few horses, a cow, an Asian small-clawed otter, and a Fischer-344 rat have also reportedly been affected. In humans, chronic lymphedema is a predisposing factor. No predisposing factors for the malignant transformation have been definitively identified in other animals.

Published cases of feline lymphangiosarcoma report an age range of 3 to 15 years with no breed or sex predilection among affected cats. The disease most commonly develops in the skin and subcutis of the ventral aspect of the abdomen; other possible locations include the ventral aspect of the thorax or neck, axillary or inguinal area, interdigital area, mediastinum, or mesentery. The most common clinical sign is a constant or recurrent serous discharge from the neoplastic site. Other clinical signs may or may not be present, including signs of depression, lethargy, anorexia, weight loss, pyrexia, vomiting, or dyspnea or tachypnea associated with hydro- or chylothorax. Clinicopathologic findings are usually unremarkable or nonspecific. The cat of the present report had suspected immune-mediated hemolytic anemia, similar to findings of a previously published case.

Grossly, the classic appearance of lymphangiosarcoma is a poorly defined, fluctuant mass; extensive pitting edema in the subcutis; or both. Differential diagnoses for the effusion and edema caused with lymphangiosarcoma in the case described in the present report included cardiac failure (ruled out by echocardiographic findings), hypoproteinemia (ruled out by results of a serum biochemical panel), and vasculitis (ruled out by histologic examination findings). Other common gross abnormalities associated with lymphangiosarcoma include petechiae and ecchymoses, ulceration, alopecia, or erythematous plaques or macules. On cut surface, the masses appear gelatinous and ooze clear or serosanguineous fluid; small yellow or dark pink nodules may be intermixed. Metastases are uncommon but may occur in regional lymph nodes, liver, lungs, spleen, or serous membranes. If lymphangiosarcoma is present in the mediastinum or mesentery, as in the cat of the present report, effusion may develop.

Histologically, lymphangiosarcomas are characterized by irregular vascular channels lined by plump, spindle-shaped neoplastic cells that wrap around collagen bundles or preexisting cellular or stromal components. The spaces typically contain little blood, helping to differentiate lymphangiosarcoma from hemangiosarcoma. Lymphangiosarcomas are differentiated from lymphangiomas by greater cellular atypia, greater mitotic activity, and the potential for metastasis, as in the case described in the present report.

The endothelial origin of lymphangiosarcomas is typically confirmed by immunohistochemical staining directed against CD31 or factor VIII–related antigen; however, these markers do not differentiate between lymphatic origin and blood vessel origin. In recent years, lymphatic-specific markers have been validated in cats, including prospero-related homeobox gene-1 (PROX-1), podoplanin, and lymphatic vessel endothelial receptor-1 (LYVE-1). In addition, periodic acid-Schiff staining (or Jones methenamine silver–periodic acid–Schiff staining) or ultrastructural examination of neoplastic tissue may reveal a discontinuous basal lamina, supporting a lymphatic vessel origin, in contrast to the continuous basal lamina expected in neoplastic tissue of blood vessel origin.

Figure 3—Photomicrographs of sections of pericardial adipose tissue (A) and myocardium (B) from the cat in Figure 1. The neoplastic cells in these tissues have greater pleomorphism and form less discrete vascular channels than those in Figure 1. H&E stain; bar in both panels = 50 μm.
Treatment for lymphangiosarcoma is often unrewarding and typically involves wide resection with or without radiation or chemotherapy. Recurrence is common because of the difficulty in achieving clean surgical margins. There are 2 reports of successful treatment involving surgical excision followed by chemotherapy in dogs. Limbal lymphangiosarcoma in a cow was successfully treated by exenteration alone. Overall, however, the prognosis for small animals with lymphangiosarcoma is poor. Most cats with lymphangiosarcoma die or are euthanized within 2 weeks to 10 months after diagnosis.

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References