Comparative Medicine
Copyright 2015
by the American Association for Laboratory Animal Science

Vol 65, No 2
April 2015
Pages 127–132

Case Report

Histiocytic Sarcoma and Bilateral Facial Vein Thrombosis in a Siberian Hamster (*Phodopus sungorus*)

Dondrae J Coble,[1,2,*] Margaret Shoemaker,[2] Bonnie Harrington,[2] Adrienne D Dardenne,[1,2] and Brad Bolon[2,3]

A 21-mo-old, male Siberian hamster (*Phodopus sungorus*) presented with left-sided facial swelling, proptosis of the left eye, and blepharospasm of the right eye. The hamster had been used only for breeding. Because of the poor prognosis, the hamster was euthanized without additional diagnostic assays or treatments. Routine gross pathologic evaluation demonstrated exophthalmos and presumptive hyphema of the left eye, bilateral facial edema, freely movable nodules within the mesentery, white foci within the liver, and a large mass effacing the cranial pole of the right kidney. On histologic evaluation, the mesenteric nodules and liver foci expressed histiocytic marker CD163 and thus were diagnosed as sites of histiocytic sarcoma, whereas the kidney mass was a well-differentiated renal cell carcinoma. The facial swelling resulted from bilateral, chronic, severe, branching thrombi in many facial veins. Additional age-related histopathologic findings were observed in other organs, including diffuse glomerulopathy, nesidioblastosis (pancreatic islet neoformation), and multiple foci of severe cartilage degeneration in the axial skeleton. To our knowledge, this report provides the first description of histiocytic sarcoma in a Siberian hamster.

Histiocytic sarcoma is a malignant proliferation of cells with morphologic and immunophenotypic features similar to those of mature histiocytes.[17,46] The disease is extremely rare in the human population and accounts for less than 1% of all hematolymphoid neoplasms.[45,46] Histiocytic sarcoma is diagnosed more frequently in men than women, with a median age at diagnosis of 46 y, although this neoplasm has been diagnosed in a 6-mo-old child.[17,46] Lymph nodes are the most commonly affected site, but the gastrointestinal tract, skin, and soft tissues can be involved.[3,20,39,46] The first reported human case of primary histiocytic sarcoma with primary esophageal involvement was described recently.[38] The disease course is very aggressive, with a limited response to chemotherapy and high mortality, in the human population.[31,38,46]

Histiocytic sarcoma lacks a definitive morphologic appearance,[38] which has complicated characterization and often has led to misdiagnosis.[17,20,31,38,39,45,46,48] This neoplasm must be distinguished from other histiocytic processes such as monocytic leukemia,[12,18,28,48] hemophagocytic syndrome,[12,18,24,25,43] and malignant histiocytosis.[9,10,18,24,25,43] In light of the absence of definitive morphologic traits, diagnosis is based on histologic and immunohistochemical evidence of histiocytic differentiation.[38,46] A hemoglobin scavenger receptor protein, CD163, is a recently identified immunohistochemical marker of monocytes and histiocytes that has shown high specificity when used to diagnose true histiocytic malignancies.[27,46,48,49] CD163 has considerable potential as a diagnostic tool because its expression is limited primarily to neoplasms of macrophage–histiocytic derivation, as well as nonneoplastic monocytes.[46] CD68 has also been used as a marker to highlight the macrophage–histiocytic derivation of tumors, but it is less specific than is CD163.[46]

Siberian dwarf (also called Djungarian) hamsters (*Phodopus sungorus*) are an animal model with unique biologic characteristics and numerous research applications. The use of Siberian hamsters as research models of cancer and cytogenetic studies began in the late 1960s and early 1970s.[40,41,47] This species has the most compressed reproductive cycle of any placental animal, and the reproductive biology in adult hamsters is completely dependent on environmental photoperiod.[14] Biologic data for this species, such as reference ranges for hematology and clinical chemistry as well as background pathology, have become more readily available recently.[6,11,26,34,40,41,44] Here we describe the concurrent presence of a histiocytic sarcoma, a renal cell carcinoma, severe thrombosis of craniofacial veins, and several marked age-related changes in an aged Siberian hamster. To our knowledge, this report is the first description of a histiocytic sarcoma in a Siberian hamster.

Case Report

This 21-mo-old, male Siberian hamster (body weight, 32.2 g) was housed at The Ohio State University (Columbus, OH), an AAALAC -accredited institution. This animal was on an IACUC-approved protocol, and management was consistent with all applicable regulations as prescribed in the Animal Welfare Regulations[4] and in accordance with the *Guide for the Care and Use of Laboratory Animals*.[23] The hamster was housed as a member of a

Received: 21 Jul 2014. Revision requested: 04 Sep 2014. Accepted: 09 Nov 2014.
[1]Office of Research, [2]College of Veterinary Medicine, and [3]Comparative Pathology and Mouse Phenotyping Shared Resource, The Ohio State University, Columbus, Ohio.
**Corresponding author. Email: coble.27@osu.edu*

breeding pair, without undergoing any additional research manipulations, in static microisolation caging. Its diet consisted of pelleted rodent chow (Teklad 8640, Harlan Laboratories, Indianapolis, IN) with reverse-osmosis–purified water supplied in a hanging water bottle. Based on quarterly health surveillance of dirty-bedding–exposed hamster sentinels, the animals were free from pneumonia virus of mice, reovirus, Sendai virus, simian virus 5, lymphocytic choriomeningitis virus, *Encephalitozoon cuniculi*, and ecto- and endoparasites. The hamster was reported to the veterinary staff because of substantial left-sided facial swelling, proptosis of the left eye, and blepharospasm of the right eye (Figure 1). Ibuprofen-medicated (30 mg/kg) drinking water was initiated to manage clinical signs, but they did not resolve despite 24 h of treatment. In light of the poor prognosis, the hamster was euthanized via CO_2 asphyxiation without additional treatments or medical diagnostic procedures. The animal was submitted for pathologic evaluation.

Figure 1. Left-sided facial swelling, proptosis with reddening (presumptive hyphema) of the left eye, and blepharospasm of the right eye.

Gross Pathology

At necropsy, major organs were examined for gross abnormalities, and selected tissue specimens were collected and fixed by immersion in neutral buffered 10% formalin for 48 h Fixed samples were processed routinely to produce paraffin-embedded, hematoxylin- and eosin-stained sections. After the initial analysis, additional serial sections of liver were acquired for indirect immunohistochemistry to demonstrate selected cell-type–specific proteins: cytokeratin (an epithelial marker; monoclonal; dilution, 1:200 [clone AE1/AE3, Dako, Carpinteria, CA]); vimentin (a mesenchymal cell marker; monoclonal; dilution, 1:200 [clone 2707-1, Epitomics, Burlingame, CA]), and CD163 (a macrophage marker; monoclonal; dilution, 1:25 [clone AM-3K, TransGenic, Kobe, Japan]), as described previously.[37] A commercial immunofluorescence kit (MaxSAB, Maxvision Biosciences, Bothell, WA) was adapted for chromagen-based immunohistochemistry, with 3,3′-diaminobenzidine as the chromagen.

The primary gross findings at necropsy were exophthalmos and presumptive hyphema of the left eye, as suggested by reddening that extended 3 mm beyond the orbital rim, and diffuse and bilateral facial edema (Figure 1). Additional gross findings included multiple pale or white, soft, pedunculated or freely movable nodules within the abdomen, which were associated with the mesentery or serosae of major viscera (Figure 2), as well as a large, multilobulated, pale tan, firm mass located at the cranial pole of the right kidney (Figure 2). This renal mass did not involve the caudal vena cava or the adrenal gland. The right kidney weighed nearly 6 times more than did the normal-appearing left kidney (right, 0.953 g; left, 0.181 g), because of the presence of this mass (Figure 3). The spleen was diffusely enlarged and focally expanded in the center by a round, white, friable mass. The lungs were normal on gross evaluation.

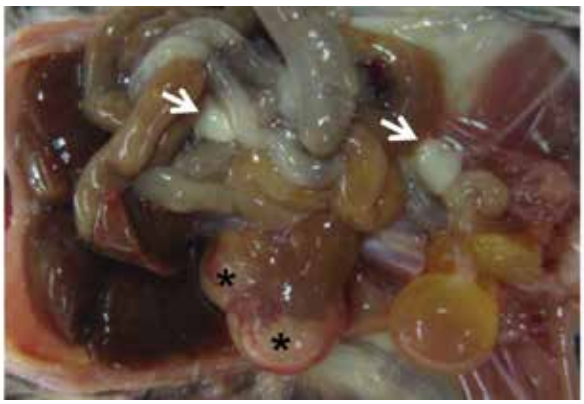

Figure 2. Additional gross findings included a large multilobulated, pale tan, firm mass at the cranial pole of the right kidney (*), and multiple soft, attached or free-floating, white nodules associated with the mesentery and visceral serosae (arrows).

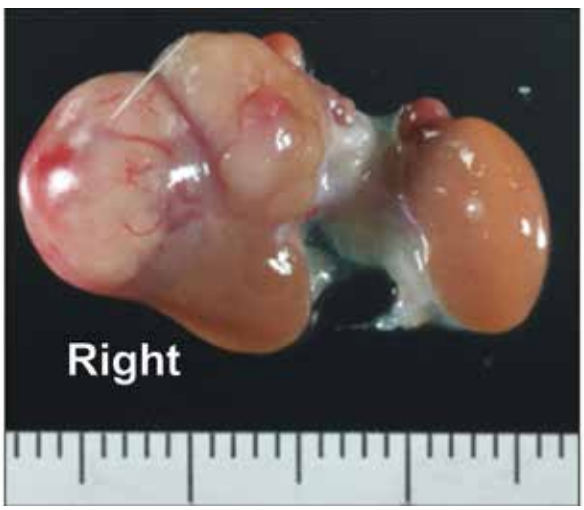

Figure 3. Gross depiction of the right kidney mass.

Histopathologic Findings

Histologic evaluation revealed that the pale or white nodules in the abdominal mesentery and viscera and the renal mass were different neoplasms. Unexpectedly, the peritoneal polyps and accompanying visceral infiltration (mainly in the liver) were discovered to be foci of histiocytic sarcoma, with each lesion consisting of dense sheets of markedly pleomorphic, moderately proliferating histiocytes (Figure 4). Disorganized bundles and streams of these neoplastic cells also were found on the serosal surface of the gastrointestinal tract, on the vaginal tunic of the vas deferens, seminal vesicles, and epididymis, and effaced approximately 50% of the hepatic parenchyma. The

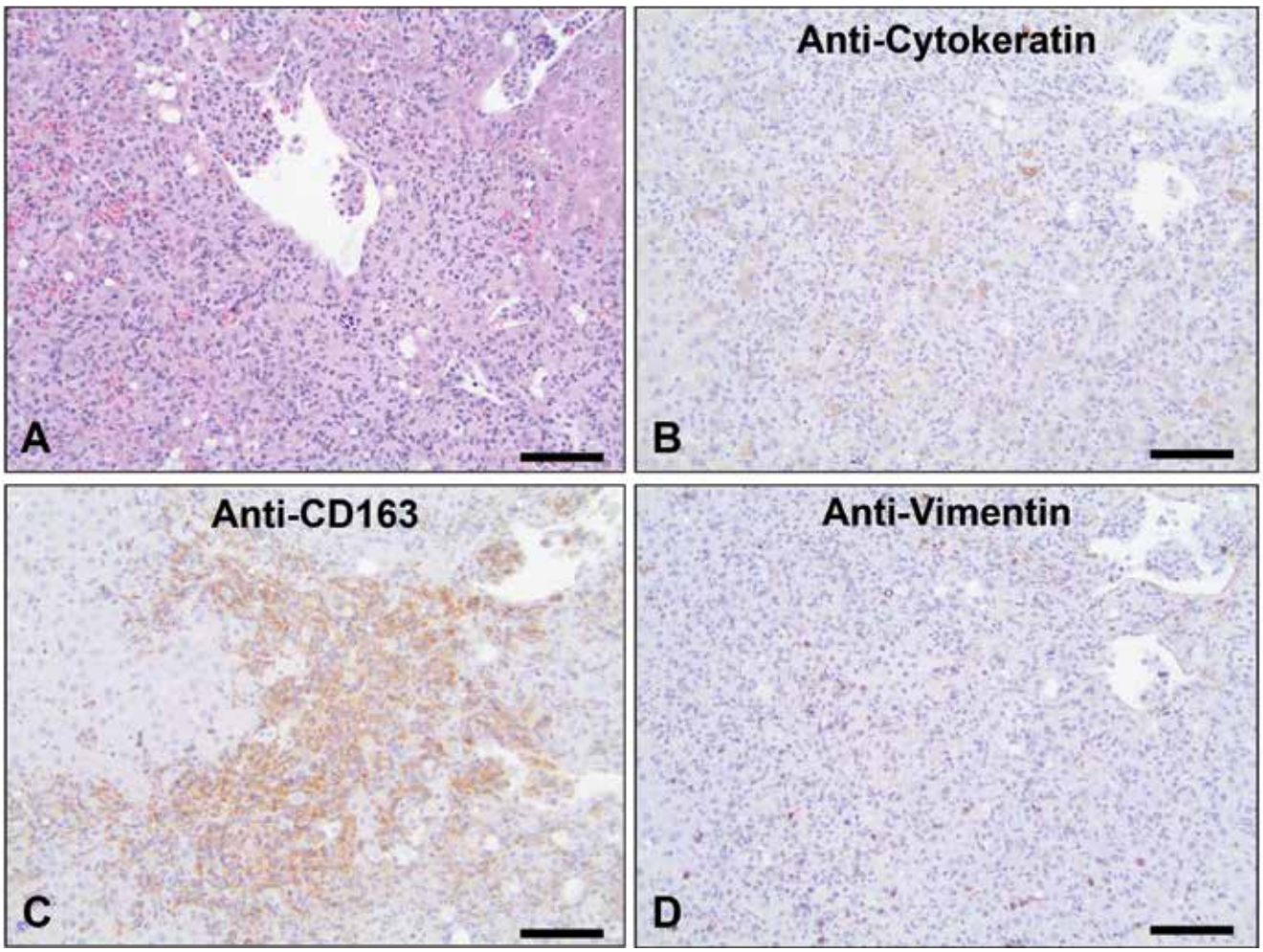

Figure 4. Coalescing foci of histiocytic sarcoma effaced the parenchyma in multiple viscera, especially the liver (shown here), and formed pedunculated and free-floating nodules within the abdominal cavity. Neoplastic cells were moderately to strongly labeled by antiCD163 but not by anticytokeratin or antivimentin, suggesting that the neoplasm was derived from macrophages instead of either epithelium or mesothelium. Note: The labeling in the anticytokeratin section was in residual hepatocytes, whereas that in the antivimentin section was in resident endothelium and fibroblasts. Stains used were hematoxylin and eosin (upper left) and single-antibody indirect immunohistochemistry using diaminobenzidine as the chromagen and hematoxylin as the counterstain. Bar,100 µm (and applies to all images).

cells varied from round to polygonal; had indistinct cytoplasmic borders; abundant, eosinophilic, vacuolated cytoplasm; and one to multiple round to elongate, central nuclei with as many as 2 prominent, basophilic nucleoli. Rare, randomly dispersed, multinucleated tumor giant cells containing, on average, 3 nuclei as well as moderate anisocytosis and anisokaryosis were present in this neoplastic cell population. Immunohistochemistry revealed that the neoplastic histiocytes were positive for CD163, whereas staining for cytokeratin and vimentin was negative (Figure 4); this expression pattern is indicative of a macrophage origin. The renal lesion was a well-differentiated renal cell carcinoma characterized by variably sized, tortuous tubules and islands composed of large, mildly pleomorphic tubular epithelial cells (not shown).

A transverse section of the cranium at the level of the caudal orbit demonstrated extensive facial swelling due to bilateral ophthalmic vein involvement and chronic thrombi that extended into the major draining veins (Figure 5). Large thrombi obstructed venous circulatory return bilaterally caudomedial to each eye, and the retrobulbar space was inundated with hemorrhage, which displaced the left globe laterally and dorsally. The thrombi contained alternating laminae of fibrin and intact RBC, indicating that they had been present for a considerable period but were still expanding. Degenerate neutrophils were associated with many of the fibrin-rich layers as well as the margin of the diffusely necrotic left Harderian gland. Surrounding structures, such as the adjacent lacrimal glands and skeletal muscle, also harbored a moderate amount of viable neutrophils and hemorrhage. The lungs were normal on histopathologic examination.

Several age-related, marked histopathologic findings were present in other organs. Chronic, mild, diffuse glomerulopathy affected most glomeruli of both kidneys. Multiple foci of epithelial transformation involved the conversion of preexisting exocrine pancreatic duct epithelium into new islets (that is, nesidioblastosis;[42,50] Figure 6). Other incidental findings included marked degeneration of multiple vertebral discs; focal vertebral disc herniation; marked, multifocal osteoarthritis of the intervertebral joints; and sternal disc fusion or degeneration

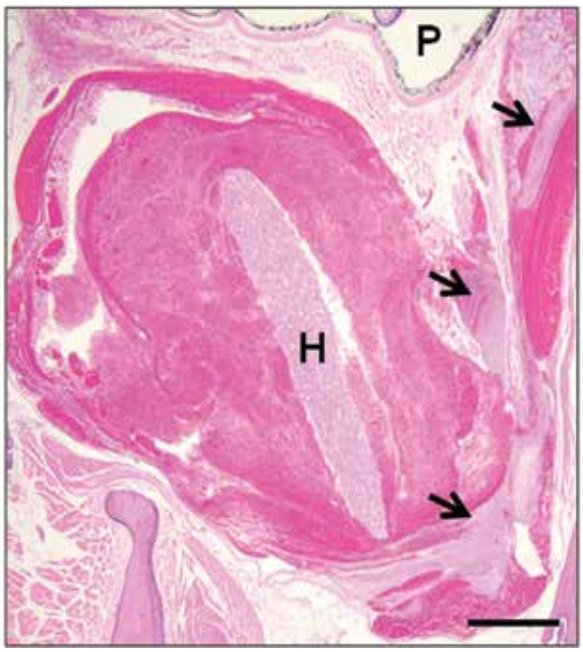

Figure 5. The bilateral facial swelling resulted from massive retroorbital hemorrhage (indicated by coalescing areas of red blood cell accumulation) intermingled with large, layered plaques of fibrin (arrows), where the layering indicates many small bleeding incidents followed by slow but continual building of the clot over time. These plaques were continuous with large intravascular thrombi that were partially occluding several deep facial veins (not shown). The Harderian gland (H) is greatly compressed by the most recent hemorrhagic episode. P, posterior chamber of the eye. Hematoxylin and eosin stain. Bar, 1 mm

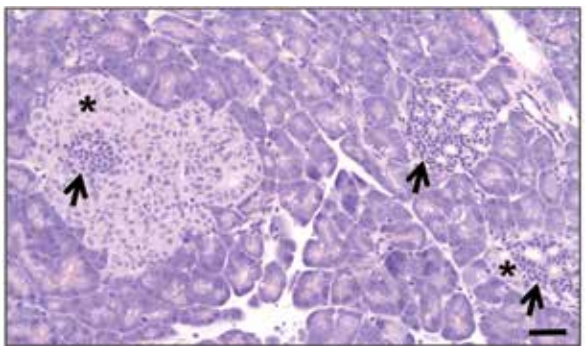

Figure 6. Multiple preexisting exocrine pancreatic ducts exhibited evidence that the simple cuboidal lining (arrows) of oval, dark basophilic nuclei and dark eosinophilic cytoplasm was reduplicating and transforming into new islet cells (asterisks) that appeared as oval, pale basophilic nuclei and very pale eosinophilic cytoplasm (that is, nesidioblastosis). Hematoxylin and eosin stain. Bar, 50 µm

(Figure 7). These findings are consistent with common incidental background findings in adult rodents, although they are more severe in this case than usual, given the advanced age of this hamster.

Discussion

Histiocytic sarcoma has been diagnosed in numerous anatomic locations in various animal species including mice,[19] rats,[7] cats,[15,16,22] dogs,[1,2,5,15,21,22,36] rabbits,[29] and camels.[35] To our knowledge, the current report represents the first case of this disease in a hamster. In addition, renal cell carcinoma and the various age-related findings are common occurrences in aged animals. Nesidioblastosis has been described previously in the Syrian hamster (*Mesocricetus auratus*), which is a recognized model of pancreatic ductal neoplasia,[42] although this lesion had not previously been reported to occur in Siberian dwarf hamsters.

The more interesting finding in this case was the bilateral, marked facial lesions that were the cause of the animal's initial presentation. The exophthalmos and hemorrhage that affected the left orbit were direct sequelae of the extensive facial venous thrombosis, which resulted in substantial extravasation of fluid and cells due to a chronic rise in local intravascular pressure within all facial tissues. This condition, in turn, likely was influenced by any or all of several factors that probably would have produced hypoproteinemia in this hamster. These speculations cannot be confirmed definitively because the animal was euthanized for humane reasons without additional diagnostic procedures, such as assessment of serum and urinary protein levels as well as clotting times. One obvious mechanism is cachexia of cancer, resulting from increased protein consumption by the massive renal cell carcinoma and widespread histiocytic sarcoma. A second possibility is increased protein loss resulting from bilateral, diffuse glomerulopathy; depletion of albumin and antithrombin III by this route has been associated with an increased risk of venous thromboembolism in humans.[13] A third option is diminished protein production by hepatocytes, given that the amount of structurally unaffected (that is, functional) hepatic parenchyma was markedly decreased by the invading neoplastic histiocytes. The neoplasms alone could have accounted for the hamster's moribund state, but substantial hypoproteinemia provides a compelling pathogenesis that ties together the entire spectrum of findings in this animal.

Thrombus formation, usually in the left atrium and auricle, are common findings that typically are associated with amyloidosis or changes in fibrinolytic parameters. The findings we describe in this case report have not been reported previously to occur in Siberian hamsters. However, Syrian hamsters are used routinely as models for investigating the pathogenesis of thromboembolism. These studies generally involve using the membranous cheek pouch, given its transilluminating capabilities, ease of harvest, and numerous small vessels, but the femoral and carotid arteries have also been used.[8,30,32,33] The Syrian hamster thromboembolism model has allowed researchers to investigate not only the pathogenesis of thromboembolism but also neointimal formation caused by cardiovascular procedures and the 'no reflow' phenomenon, in which tissues fail to perfuse again after the vascular obstruction has been alleviated. These studies have improved our understanding of endothelial damage and its sequelae and have highlighted areas of possible therapeutic intervention in thromboembolic states, such as the use of platelet glycoprotein IIb/IIIa antagonist in microthombi inhibition, combination therapy of angiotensin II antagonist and fibrinogen receptor antagonist after carotid angioplasty, and tissue plasminogen activator in ischemia–reperfusion injury.[8,32,33]

Acknowledgments

We thank Dr Randy J Nelson, ULAR laboratory animal health technicians and husbandry staff, and Julie Rectenwald and Florinda Jaynes (Comparative Pathology and Mouse Phenotyping Shared Resource [CPMPSR]) for performing the necropsy and indirect

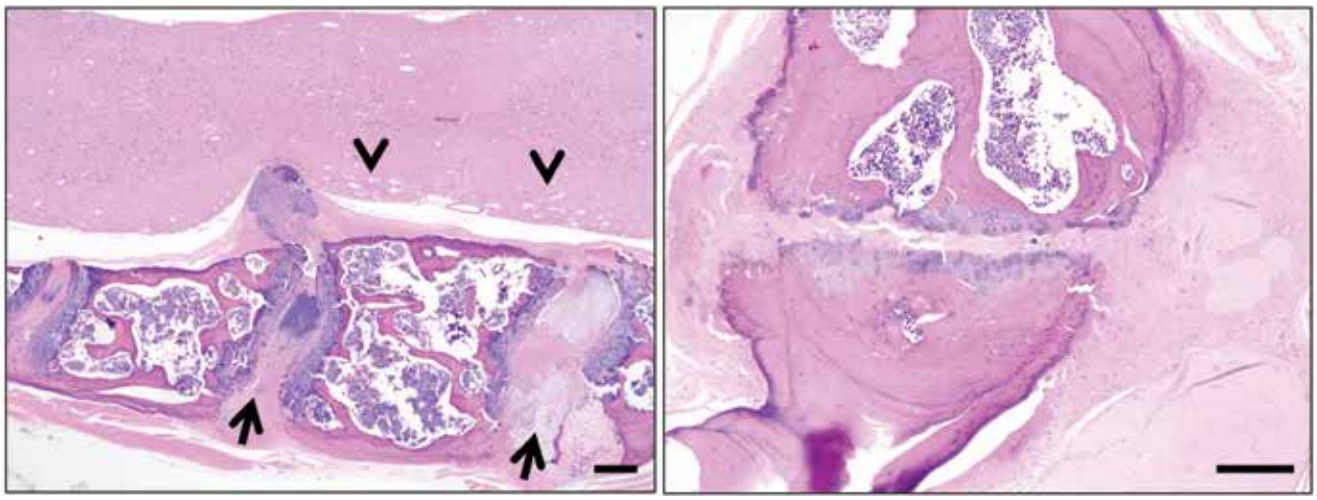

Figure 7. The left panel shows that multiple intervertebral discs were degraded (arrows), and one that had herniated resulted in spinal cord compression and axonal degeneration (clear vacuoles in the ventral white matter tracts [arrowheads]). The panel on the right demonstrates that some intervertebral joints had facets in which the joint space was filled with fragments of disintegrating articular cartilage, with extrusion of debris into the fibrotic periarticular soft tissues. Hematoxylin and eosin stain. Bars, 200 µm (left panel) and 100 µm (right panel)

immunohistochemistry, respectively. The Comparative Pathology and Mouse Phenotyping Shared Resource of the OSU Comprehensive Cancer Center and the Department of Veterinary Biosciences is supported in part by grant P30 CA016058 from the National Cancer Institute (Bethesda, MD).

References

1. **Abadie J, Hédan B, Cadieu E, De Brito C, Devauchelle P, Bourgain C, Parker HG, Vaysse A, Margaritte-Jeannin P, Galibert F, Ostrander EA, André C**. 2009. Epidemiology, pathology, and genetics of histiocytic sarcoma in the Bernese mountain dog breed. J Hered **100 Suppl 1:**S19–S27.
2. **Affolter VK, Moore P.** 2002. Localized and disseminated histiocytic sarcoma of dendritic cell origin in dogs. Vet Pathol **39:**74–83.
3. **Akishima Y, Akasaka Y, Yih-Chang G, Ito K, Ishikawa Y, Lijun Z, Kiquchi H, Lipscomb G, Strong JP, Ishii T.** 2004. Histiocytic sarcoma with fatal duodenal ulcers. Pathol Res Pract **200:**473–478.
4. **Animal Welfare Act.** 2008. 9 CFR §3.129.
5. **Arnold EJ.** 2012. What is your diagnosis? J Am Vet Med Assoc **240:**821–823.
6. **Baba Y, Takahashi K, Nakamura S.** 2003. Androgen-dependent atypical fibromas spontaneously arising in the skin of Djungarian hamsters (*Phodopus sungorus*). Comp Med **53:**527–531.
7. **Bauchet AL, Fouque MC, Belluco S, Château-Joubert S, Elies L, Maliver P, Schorsch F, Fontaine JJ.** 2008. An atypical case of histiocytic sarcoma in a Wistar rat (*Rattus norvegicus*). Exp Toxicol Pathol **59:**385–390.
8. **Bertuglia S, Colantuoni A.** 2000. Protective effects of leukopenia and tissue plasminogen activator in microvascular ischemia–reperfusion injury. Am J Physiol Heart Circ Physiol **278:H**755–761.
9. **Cattoretti G, Villa A, Vezzoni P, Giardini R, Lombardi L, Rilke F.** 1990. Malignant histiocytosis—a phenotypic and genotypic investigation. Am J Pathol **136:**1009–1019.
10. **Egeler RM, Schmitz L, Sonneveld P, Mannival C, Nesbit ME.** 1995. Malignant histiocytosis: a reassessment of cases formerly classified as histiocytic neoplasms and review of the literature. Med Pediatr Oncol **25:**1–7.
11. **Endo Y, Sato T, Shirai W, Matsuo K.** 2000. Malignant fibrous histiocytoma in a Djungarian hamster. J Vet Med Sci **62:**539–541.
12. **Favara BE, Feller AC, Pauli M, Jaffe ES, Weiss LM, Arico M, Bucsky P, Egeler RM, Elinder G, Gadner H, Greasik M, Henter JI, Imashuku S.** 1997. Contemporary classification of histiocytic disorders. Med Pediatr Oncol **29:**157–166.
13. **Folsom AR, Lutsey PL, Heckbert SR, Cushman M.** 2010. Serum albumin and risk of venous thromboembolism. Thromb Haemost **104:**100–104.
14. **Fox JG, Anderson LC, Loew FM, Quimby FW.** 2002. San Diego, CA, Academic Press.
15. **Friedrichs KR, Young KM.** 2008. Histiocytic sarcoma of macrophage origin in a cat: case report with a literature review of feline histiocytic malignancies and comparison with canine hemophagocytic histiocytic sarcoma. Vet Clin Pathol **37:**121–128.
16. **Fulmer AK, Mauldin GE.** 2007. Canine histiocytic neoplasia: an overview. Can Vet J **48:**1041–1043.
17. **Gergis U, Dax H, Ritchie E, Marcus R, Wissa U, Orazi A.** 2011. Autologous hematopoietic stem-cell transplantation in combination with thalidomide as treatment for histiocytic sarcoma: a case report and review of the literature. J Clin Oncol **29:e**251–253.
18. **Gonzalez CL, Jaffe ES.** 1990. The histiocytoses: clinical presentation and differential diagnosis. Oncology 4:47–60; discussion 60, 62.
19. **Hao X, Fredrickson TN, Chattopadhyay SK, Han W, Qi CF, Wang Z, Ward JM,Harley JW, Morse HC 3rd.** 2010. The histopathologic and molecular basis for the diagnosis of histiocytic sarcoma and histiocyte-associated lymphoma of mice. Vet Pathol **47:**434–445.
20. **Hornick JL, Jaffe ES, Fletcher CD.** 2004. Extranodal histiocytic sarcoma: clinicopathologic analysis of 14 cases of a rare epithelioid malignancy. Am J Surg Pathol **28:**1133–1144.
21. **Ide T, Uchida K, Kagawa Y, Suzuki K, Nakayama H.** 2011. Pathological and immunohistochemical features of subdural histiocytic sarcomas in 15 dogs.. J Vet Diagn Invest. **23:**127–132.
22. **Ide T, Uchida K, Tamura S, Nakayama H.** 2010. Histiocytic sarcoma in the brain of a cat. J Vet Med Sci **72:**99–102.
23. **Institute for Laboratory Animal Research.** 2011. Guide for the care and use of laboratory animals, 8th ed. Washington (DC). Washington (DC): National Academies Press.
24. **Jaffe ES.** 2001. Pathology and genetics of tumours of haematopoietic and lymphoid tissues, vol 3. Lyon (France): International Agency for Research on Cancer.
25. **Jaffe, ES, editor.** 1985. Surgical pathology of the lymph nodes and related organs. Philadelphia (PA): WB Saunders.
26. **Kondo H, Onuma M, Shibuya H, Sato T.** 2008. Spontaneous tumors in domestic hamsters. Vet Pathol **45:**674–680.
27. **Kristiansen M, Graversen JH, Jacobsen C, Sonne O, Hoffman H, Law SA, Moestrup SK.** 2001. Identification of the haemoglobin scavenger receptor. Nature **409:**198–201.
28. **Lauritzen AF, Delsol G, Hansen NE, Horn T, Ersboll J, Hou-Jensen K, Ralfkiaer E.** 1994. Histiocytic sarcomas and monoblastic leukemias.

A clinical, histologic, and immunophenotypical study. Am J Clin Pathol **102:**45–54.

29. **Leissinger M, Brandão J, Wakamatsu N, Roux A, Rich G, Gaunt S.** 2013. Pulmonary histiocytic sarcoma in a rabbit. Vet Clin Pathol **42:**364–367.
30. **Lutz BR, Fulton GP.** 1954. The use of the hamster cheek pouch for the study of vascular changes at the microscopic level. Anat Rec **120:**293–307.
31. **Mainardi C, D'Amore ES, Pillon M, Toffolutti T, Rosolen A.** 2011. A case of resistant pediatric histiocytic sarcoma successfully treated with chemo–radiotherapy and autologous peripheral blood stem cell transplant. Leuk Lymphoma **52:**1367–1371.
32. **Matsuno H, Kozawa O, Nagashima S, Kanamaru M, Uematsu T.** 1999. Comparative antiplatelet effects of aspirin, vapiprost, and GR144053, a GPIIb/IIIa antagonist, with a special reference to the role of platelet microaggregates. Br J Pharmacol **127:**1129–1134.
33. **Matsuno H, Kozawa O, Niwa M, Kaida T, Hayashi H, Uematsu T.** 1997. GR144053, a fibrinogen receptor antagonist, enhances the suppression of neointima formation by losartan, an angiotensin II receptor antagonist, in the injured carotid artery of hamster. Br J Pharmacol **122:**1099–1104.
34. **McKeon GP, Nagamine CM, Ruby NF, Luong RH.** 2011. Hematologic, serologic, and histologic profile of aged Siberian hamsters (*Phodopus sungorus*). J Am Assoc Lab Anim Sci **50:**308–316.
35. **Molenaar FM, Breed AC, Flach EJ, McCandlish IA, Pocknell AM, Strike T, Routh A,Taema M, Summers BA.** 2009. Brain tumours in 2 bactrian camels: a histiocytic sarcoma and a meningioma. Vet Rec **164:**684–688.
36. **Naranjo C, Dubielzig RR, Friedrichs KR.** 2007. Canine ocular histiocytic sarcoma. Vet Ophthalmol **10:**179–185.
37. **Ohnishi K, Tanaka S, Oghiso Y, Takeya M.** 2012. Immunohistochemical detection of possible cellular origin of hepatic histiocytic sarcoma in mice. J Clin Exp Hematop **52:**171–177.
38. **Pakravan A, Bhatia R, Oshima K, Chen G, Fesler M, Prather C, Taylor JR.** 2014. Histiocytic sarcoma: the first reported case of primary esophageal involvement. Am J Gastroenterol **109:**291–292.
39. **Pileri SA, Grogan T, Harris N, Banks P, Campo E, Chan J, Favera RD, Delsol G, De Wolf-Peeters C, Falini B, Gascoyne RD, Gaulard P, Gatter KC, Isaacson PG, Jaffe ES, Kluin P, Knowles DM, Mason DY, Mori S, Müller-Hermelink HK, Piris MA, Ralfkiaer E, Stein H, Su IJ, Warnke RA, Weiss LM.** 2002. Tumours of histiocytes and accessory dendritic cells: an immunohistochemical approach to classification from the international lymphoma study group based on 61 cases. Histopathology **41:**1–29.
40. **Pogosianz HE.** 1975. Djungarian hamster—a suitable tool for cancer research and cytogenetic studies. J Natl Cancer Inst **54:**659–664.
41. **Pogosianz HE, Sokova OI.** 1982. Tumours of the Djungarian hamster. IARC Sci Publ **34:**451–455.
42. **Pour PM, Kazakoff K.** 1996. Stimulation of islet cell proliferation enhances pancreatic ductal carcinogenesis in the hamster model. Am J Pathol **149:**1017–1025.
43. **Risdall RJ, McKenna RW, Nesbit ME, Krivit W, Balfour HH, Simmons RL, Brunning RD.** 1979. Virus-associated hemophagocytic syndrome—a benign histiocytic proliferation distinct from malignant histiocytosis. Cancer **44:**993–1002.
44. **Sato T, Takada M, Shibuya H, Shirai W, Matsuo K.** 2004. A malar granular cell tumor in a Djungarian hamster. J Vet Med A Physiol Pathol Clin Med **51:**23–26.
45. **Sun W, Nordberg ML, Fowler MR.** 2003. Histiocytic sarcoma involving the central nervous system: Clinical, immunohistochemical, and molecular genetic studies of a case with review of the literature. Am J Surg Pathol **27:**258–265.
46. **Takahashi E, Nakamura S.** 2013. Histiocytic sarcoma: an updated literature review based on the 2008 WHO classification. J Clin Exp Hematop **53:**1–8.
47. **Turusov VS.** 1976. Pathology of tumours in laboratory animals, vol I. Tumours of the rat, part 2. Lyon (France): International Agency for Research on Cancer.
48. **Vos JA, Abbondanzo SL, Barekman CL, Andriko JW, Miettinen M, Aguilera NS.** 2005. Histiocytic sarcoma: A study of five cases including the histiocyte marker CD163. Mod Pathol **18:**693–704.
49. **Walter RB, Bachli EB, Schaer DJ, Ruegg R, Schoedon G.** 2003. Expression of the hemoglobin scavenger receptor (CD163/HbSR) as immunophenotypic marker of monocytic lineage in acute myeloid leukemia. Blood **101:**3755–3756.
50. **Zumkeller W.** 1999. Nesidioblastosis. Endocr Relat Cancer **6:**421–428.