Clinical challenge

Käppeli, U; Eulenberger, U; Nitzl, D; Rohrer Bley, C; Steffen, F; Sydler, T; Schmid, N; Hatt, J M; Steinmetz, H W

Journal of Zoo and Wildlife Medicine 40(2): 398–401, 2009

CLINICAL CHALLENGE

Ursula Käppeli, cand. med. vet., Ulrike Eulenberger, med. vet., Dagmar Nitzl, Dr. med. vet., Dipl. E.C.V.D.I., Carla Rohrer Bley, Dr. Med. Vet., Dipl. A.C.V.R. (Radiation Oncology), Frank Steffen, Dr. med. vet., Dipl. E.C.V.N., Titus Sydler, Dr. med. vet., F.V.H., Nicole Schmid, Dr. med. vet., Jean-Michel Hatt, Prof. Dr. med. vet., Dipl. A.C.Z.M., Dipl. E.C.A.M.S., and Hanspeter W. Steinmetz, Dr. med. vet., M.Sc. W.A.H.

HISTORY

A 6-yr-old, 50-kg male snow leopard (*Uncia uncia*) with a current vaccination history presented with stumbling across thresholds with increasing frequency and severity over several weeks. Upon inspection, the snow leopard was bright and alert with a good general body condition, but was reluctant to move. Paresis and ataxia with lack of proprioception in both hind legs were recognized.

Anesthesia was induced (4.1 mg/kg ketamine, Narketan®, 10 ad us. vet., Vétoquinol, 3123 Belp, Switzerland, and 0.1 mg/kg medetomidine, Zalopine®, Orion Pharma, 02101 Espoo, Finland, i.m.) by blow pipe. The snow leopard was intubated and maintained with isoflurane (Attane™, Provet, 3421 Lyssach, Switzerland) in oxygen. Cardiopulmonary monitoring included electrocardiogram, noninvasive blood pressure, respiratory rate, capnography, and pulse oximetry (Datex Ohmeda, Cardiocap/5, Anandic Medical Systems AG, 8253 Diessenhofen, Switzerland). Blood was drawn for hematology and serum biochemistry.

Hematology results were normal against International Species Information System (ISIS) reference values[4] except for a mild leukocytosis (20.0×10^9/L), accompanied by neutrophilia (17.4×10^9/L). Serum protein electrophoresis did not reveal a monoclonal gammopathy. Serum biochemical data were normal against ISIS reference values[3] except for the presence of hyperglycemia (17.0 mmol/L or 306 mg/dl). Serologic assays for feline immunodeficiency virus (antibody capture enzyme-linked immunosorbent assay [ELISA], University of Zürich) and feline leukemia virus (antigen capture ELISA, University of Zürich) were negative. Cerebrospinal fluid (CSF) was obtained via an atlanto-occipital and lumbar puncture with a 20G spinal needle (Terumo® Spinal Needle, Terumo Europe N.V., 3001 Leuven, Belgium). High concentrations of protein (2.20 g/L), leukocytes (1 cell/μl), neutrophils (6%) and erythrocytes (40 cells/μl) were found in the lumbar CSF when compared to feline reference values.[8,9] Radiographs of the spine and myelography were performed via an atlanto-occipital and lumbar puncture (0.4 ml/kg iodine contrast media, Isovist®-240, Bayer AG, 8045 Zürich, Switzerland).

Examine obtained results and radiographs (Fig. 1) before continuing.

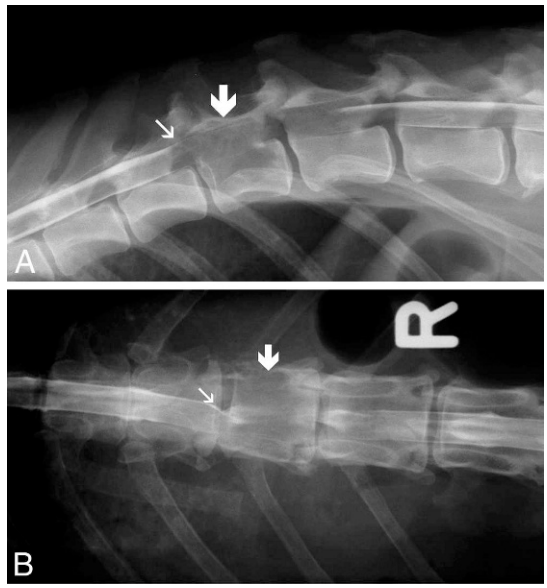

Figure 1. Right lateral (**A**) and ventrodorsal (**B**) myelographic radiographs of the thoracolumbar spinal column of a 6-yr-old snow leopard (*Uncia uncia*) presenting with hind leg paresis.

From the Clinic for Zoo Animals, Exotic Pets and Wildlife (Käppeli, Eulenberger, Schmid, Hatt, Steinmetz), the Division of Diagnostic Imaging (Nitzl), the Division of Radio-Oncology (Rohrer Bley), the Division of Neurology (Steffen), and the Institute of Veterinary Pathology (Sydler), Vetsuisse Faculty, University of Zürich, 8057 Zürich, Switzerland. Correspondence should be directed to Dr. Steinmetz (hsteinmetz@vetclinics.uzh.ch).

DIAGNOSIS

Although the atlanto-occipital CSF was clear and of normal coloration with a cell count within normal limits similar to domestic cats,[9] the lumbar CSF was consistent with a mixed pleocytosis with an increased cellularity and protein content consisting of one nucleated cell/μL (reference range,[9] 0–0.5 cells/μL). The predominant cells were neutrophils comprising 84.6% of the total number of cells. No organisms or atypical cells were identified.

Radiographs of the spine showed a poorly defined radiolucent area within the 12th thoracic vertebral (Th 12) body (large arrow), with an interrupted vertebra base and the bilateral absence of the peduncles similar to the findings obtained with the myelogram (Fig. 1). Cisternal injection demonstrated an abrupt ending contrast medium column at the caudal end of the 11th thoracic vertebra (Th 11) and a lateral deviation of both columns to the left in the ventrodorsal view. Lumbar injection showed an apparent thinning of the dye column at the body of Th 12. Right lateral radiographs demonstrated a widening of the dye, whereas in ventrodorsal view a lateral deviation of both dye columns to the left were seen (small arrow). A poorly defined hypodense area within the body of Th 12 (large arrow), with an interrupted vertebra base and the bilateral absence of the peduncles, was noted (Fig. 1). Radiographic diagnosis of additional lesions was difficult in the current case. Only the aggressive bone lesion of Th 12 was detected, although various radiographs were taken. A pathologic examination and histology were able to detect the smaller lesions at the 13th thoracic vertebra (Th 13) and the second lumbar vertebra (L2).

Radiologic and laboratory findings were consistent with a severe extradural compressive lesion from right laterally and ventrally with aggressive bone lesion of Th 12. Neoplasia, similar to osteosarcoma, fibrosarcoma, or metastatic tumor, was suspected. Because of the poor prognosis of this diagnosis, the snow leopard was euthanized with pentobarbital (Vetanarcol®, ad us. vet., 0.8 ml/kg, i.v., Veterinaria AG, 8045 Zürich, Switzerland).

Postmortem examination revealed, in the longitudinal section of the vertebral column, that a white, soft, gelatinous mass, measuring approximately 2 × 2 × 2 cm, had displaced the bony structure of the craniodorsal region of the body of Th 12 (Fig. 2A, arrows). Additional blurred bordered white areas were found in the bone marrow of Th 13 and L 2.

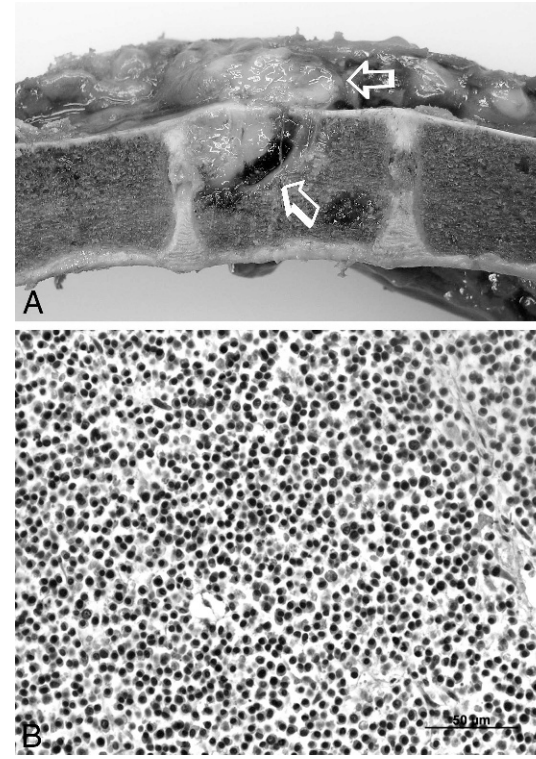

Figure 2. A. Gross longitudinal section of the vertebral column of a 6-yr-old snow leopard (*Uncia uncia*). A white, gelatinous soft mass of 2 × 2 × 2 cm with displacement of the bony structure of the craniodorsal region of the body of the 12th vertebra. **B.** The histologic section from the infiltrative growing white mass. H&E, original magnification ×1,000.

The white mass in Th 12 protruded into the vertebral canal, compressing the spinal cord. Histologic sections confirmed compression of the spinal cord at the level of Th 12, characterized by mild Wallerian degeneration in the white matter of the spinal cord. The thoracic vertebral masses consisted of infiltrative, densely packed sheets of round cells that replaced the architecture of the vertebrae and bone marrow. The round cells had abundant centric to eccentric nuclei and mostly homogenous eosinophilic cytoplasm with distinct cell borders consistent with plasma cells with occasional irregular perinuclear pallor (Fig. 2B). Final diagnosis of multiple myeloma was confirmed by histopathology and immunology of the mass in Th 12 according to the International Myeloma Working Group.[11]

DISCUSSION

Clinically, the animal presented with progressive ataxia and paresis of his hind legs. Spinal radiographs, including myelography, revealed an extreme extradural compression with an aggressive bone lesion within Th 12. Histopathology and immunohistologic investigations identified the mass in Th 12, as well as the other masses in Th 13 and L2, as a plasma cell neoplasia, and the diagnosis of multiple myeloma was formulated according to the International Myeloma Working Group.[11]

Multiple myelomas have been classified together with monoclonal gammopathies and plasmacytomas as myeloma-related disorders (MRDs).[11] Myeloma-related disorders are less common in domestic cats than in dogs and humans,[4] and epidemiologic details for large felids have not been documented previously. The current case describes an MRD in a relatively young animal, contrary to studies in domestic cats, in which MRD occurred in older cats.[12] The main characteristics of this case are the isolated bone lesions in the vertebral bodies. Plasma cell neoplasias are more often seen in bones responsible for active hematopoiesis.[13] Nevertheless, MRDs in domestic cats present less frequently with radiographic bone lesions than in humans, and extramedullary presentation is more frequent.[4] Common findings in feline multiple myeloma normally include bone lesions and multi-organ involvement.[7] In this case, characteristic bone lesions with atypical plasma cell morphology were found, though visceral organ infiltration was lacking.

It is assumed that most cases of solitary plasmacytoma eventually progress to systemic multiple myelomas similar to the present case.[12] Prognosis depends on the time of presentation, the localization of the neoplasm, and the potential of developing metastases. Although extramedullary plasmacytoma treatment can often be curative, plasmacytoma of bone carries a poor prognosis, for it typically progresses to systemic multiple myeloma.[11] Therefore, early detection of developing metastases is crucial for treatment consideration and prognosis. Further evaluation of the patient by computer tomography is strongly recommended before treatment is attempted to detect metastasis.

Differing opinions exist concerning treatment options in domestic animals, and they are limited to nonexistent experiences in exotic felids. In general, plasmacytomas as well as multiple myelomas are thought to be chemosensitive and radiosensitive.[6,10,12,13] The therapy of disseminated lesions is affected via melphalan, a chemotherapy drug that can be given orally as a continual therapy. Melphalan combined with methylprednisolone after surgical excision has shown promising results in cats with solitary plasmacytoma of bone,[5] and in one study, the treatment of multiple myelomas with melphalan and prednisolone showed complete remission in four out of eight cats.[1] Only one single case report of a chemotherapeutic treated big cat was found in the research literature.[2] However, surgery in combination with chemotherapy on the basis of companion animal and human medicine experiences could be useful in the treatment of genetically valuable zoo animals.

In summary, a spinal tumor, such as solitary plasmacytoma of bone or multiple myeloma, should be considered as a differential diagnosis for any big cat that presents with progressive hind leg paresis. Myelography via atlanto-occipital and lumbar puncture was very useful in visualizing the aggressive lesion with its compression of the spinal cord. In the future, further investigations, such as computer tomography, biopsy, or fine-needle aspiration should be considered in similar cases when treatment options and prognosis are evaluated. Computer tomography should be part of the diagnostic plan in cases suspected to have this neoplasm for better evaluation, and to differentiate between solitary plasmacytoma and multiple myeloma.

Acknowledgment: The authors gratefully acknowledge the work and support of Ms. G. Hürlimann.

LITERATURE CITED

1. Hanna, F. 2005. Multiple myelomas in cats. J. Feline Med. Surg. 7: 275–287.

2. Harrison, T. M., J. Sikarskie, B. Kitchell, D. S. Rosenstein, H. Flaherty, S. D. Fitzgerald, and M. Kiupel. 2007. Treatment of malignant lymphoma in an African lion (*Panthera leo*). J. Zoo Wildl. Med. 38: 333–336.

3. ISIS. 2002. Physiological Data Reference Values. International Species Information System, Eagan, Minnesota.

4. Mellor, P. J., S. Haugland, S. Murphy, K. C. Smith, A. Holloway, J. Archer, R. M. Powell, G. A. Polton, S. Tasker, D. McCormick, M. E. Tempest, P. E. McNeil, T. J. Scase, C. D. Knott, U. Bonfanti, E. J. Villiers, D. J. Argyle, M. E. Herrtage, and M. J. Day. 2006. Myeloma-related disorders in cats commonly present as extramedullary neoplasms in contrast to myeloma in human patients: 24 cases with clinical follow-up. J. Vet. Intern. Med. 20: 1376–1383.

5. Mellor, P. J., G. A. Polton, M. Brearley, S. Haugland, K. C. Smith, T. J. Scase, P. E. McNeil, A. Holloway, J. Archer, R. M. Powell, E. J. Villiers, M. E. Herrtage, D. J. Argyle, and M. J. Day. 2007. Solitary plasmacytoma of bone in two successfully treated cats. J. Feline Med. Surg. 9: 72–77.

6. Munshi, N. C., and K. C. Anderson. 2005. Plasma cell neoplasms. *In:* DeVita, V. T., S. Hellmann and S. T. Rosenberg (eds.). Cancer Principles and Practice of Oncology, 7th ed. Lippincott Williams & Wilkins, Philadelphia, Pennsylvania. Pp. 2155–2188.

7. Patel, R. T., A. Caceres, A. F. French, and P. M. McManus. 2005. Multiple myeloma in 16 cats: a retrospective study. Vet. Clin. Pathol. 34: 341–352.

8. Rand, J. S., J. Parent, R. Jacobs, and R. Johnson. 1990. Reference intervals for feline cerebrospinal fluid: biochemical and serologic variables, IgG concentration, and electrophoretic fractionation. Am. J. Vet. Res. 51: 1049–1054.

9. Rand, J. S., J. Parent, R. Jacobs, and D. Percy. 1990. Reference intervals for feline cerebrospinal fluid: cell counts and cytologic features. Am. J. Vet. Res. 51: 1044–1048.

10. Rusbridge, C., S. J. Wheeler, C. R. Lamb, R. L. Page, S. Carmichael, M. J. Brearley, and A. P. Bjornson. 1999. Vertebral plasma cell tumors in 8 dogs. J. Vet. Intern. Med. 13: 126–133.

11. The International Myeloma Working Group. Criteria for the classification of monoclonal gammopathies, multiple myeloma and related disorders: a report of the International Myeloma Working Group. 2003. Br. J. Haematol. 121: 749–757.

12. Vail, D. M. 2001. Plasma cell neoplasms. *In:* Withrow, S. J., and E. G. MacEwan (eds.). Small Animal Clinical Oncology. W. B. Saunders Co., Philadelphia, Pennsylvania. Pp. 626–637.

13. Wassermann, T. H., 1997. Myeloma and plasmacytomas. *In:* Perez, C. A., and L. W. Brady (eds.). Principles and Practice of Radiation Oncology, 3rd ed. Lippincott-Raven Publishers, Philadelphia, Pennsylvania. Pp. 2013–2023.

Received for publication 17 July 2008