**ABSTRACT**

A 4-year-old female neutered albino domestic ferret (*Mustela putorius furo*) was referred for acute progressive non-ambulatory paraparesis. Physical examination was unremarkable, whilst neurological examination revealed non-ambulatory paraparesis, decreased postural reactions on both pelvic limbs, upper-motor-neuron bladder and thoracolumbar pain. Pre-referral hematology and biochemistry were almost normal, whilst whole body computed tomography revealed a left-sided T13 cranial articular process fracture and material of uncertain nature inside the spinal canal with secondary compressive myelopathy. On magnetic resonance imaging the lesion was extradural. Decompressive surgery was performed and the surgically excised abnormal tissue was sent for histological investigations, which confirmed a plasma cell neoplasia clinically compatible with solitary osseous plasmacytoma. Prednisolone was started for a total of 5 months; at ten-month follow-up the ferret was comfortable and ambulatory with only residual left pelvic limb monoparesis. Surgical treatment should be considered in solitary vertebral plasmacytomas, as it seems to be successful giving a long survival time to the patient. This is the first report to describe the magnetic resonance imaging findings and successful surgical treatment for a vertebral solitary osseous plasmacytoma in a ferret with focal osteolysis in the absence of systemic disease and gammopathy.

**KEYWORDS**

ferret neurology; pediculectomy; plasma cell neoplasia; solitary osseous plasmacytoma

**ABBREVIATIONS**

CT Computed tomography

MM Multiple Myeloma

MRD Myeloma related disorder

MRI Magnetic resonance imaging

PCN Plasma cell neoplasia

SOP Solitary osseous plasmacytoma

**MANUSCRIPT**

A 4-year-old 0.6 kg female neutered albino domestic ferret (*Mustela putorius furo*) was referred for acute progressive painful asymmetric non-ambulatory paraparesis. A low-impact collision immediately prior to the onset of clinical signs was reported. One day later, pre-referral hematology and biochemistry revealed mild hypophosphatemia (2.45 mmol/l; reference range, 3.60 – 5.90 mmol/l) and moderate elevation of urea (20 mmol/l; reference range, 0.2 – 16.1 mmol/l). The ferret underwent a computed tomography (CT)[Siemens Somaton Scope, Erlangen, Germany] of the whole body that revealed a focal, minimally displaced fracture of the left cranial articular process of T13, accompanied by ragged focal lysis of the lateral aspect of the cranial third of the left pedicle of T13 **(Figure 1)**. An ill-defined, marginally hyperattenuating (compared to the cord) collection of material was also noted along the left lateral aspect of the spinal cord at T12-T13, resulting in moderate spinal cord compression. Due to the CT appearance, a fracture of the left articular T13 process associated with concurrent traumatic disc herniation and/or hemorrhage was suspected. However, the lytic appearance of the pedicle also raised the possibility of a pathological fracture. The thorax and abdomen were otherwise unremarkable on CT.

At referral, physical examination was unremarkable, whilst the neurologic examination revealed asymmetric non-ambulatory paraparesis (left more paretic), absent postural reactions on pelvic limbs, upper-motor-neuron bladder and thoracolumbar pain. To better characterize the extramedullary lesion seen on CT, the ferret was anesthetized to undergo an magnetic resonance imaging (MRI) of the thoracolumbar spine.

Sagittal and transverse Fast Spin Echo (FSE) T2-weighted sequences from caudal T12 to cranial L1 were performed using a low-field MRI(Hitachi Lucente 0.4 Tesla, Berkshire, UK), revealing increased T2-weighted signal intensity of the cranial articular process and cranial half of the left pedicle of T13, expanding into the epaxial musculature along the body of T13, and extradural material with similar signal characteristics extending into the left side of the spinal canal at the cranial aspect of the body of T13 **(Figure 2)**. This material resulted in an estimated cord compression of 40%; at this level the spinal cord was T2 hyperintense. All included intervertebral discs were normally hydrated and without evidence of associated disc extrusion. The included retroperitoneal and peritoneal structures were unremarkable. Given the compressive nature of the lesion, exploratory surgery with the attempt to decompress the spinal cord was performed.

In particular, a left T13 pediculectomy was performed to decompress the spinal cord and a suspected neoplastic tissue arising from the left pedicle was excised and sent for histopathology. The spinal cord appeared swollen but macroscopically did not seem to be affected by the pathological process. The tiny fractured articular process of T13 vertebra was removed, whilst the stability of the vertebral column was not affected as only pediculectomy was performed. Systemic dexamethasone(Dexamethasone, Hameln, Gloucester, UK) 1 mg/kg, IV, once and topical methylprednisolone(Depo-medron, Pfizer, NY, USA) 0.1 mg/kg, epidural, once were used during surgery as round cell tumour was suspected. After six days of hospitalisation, the ferret was discharged on dexamethasone 1.5 mg/kg, PO, q 24 h and clindamycin(Antirobe, Zoetis, NJ, USA)14 mg/kg, PO, q 12 h. The latter was elected due to its broad-spectrum effect against to aerobic and anaerobic bacteria, and protozoa, and its indications for wounds, abscesses and/or osteomyelitis. At discharge, the ferret was non-ambulatory paraparetic and comfortable. One week later, enrichment culture from the wound revealed infection by Bacillus cereus, sensitive to fluoroquinolones; thus clindamycin was discontinued and was replaced by enrofloxacin (Baytril, Bayer, Leverkusen, Germany) 15 mg/kg, PO, q 24h, for a two-week course.

Formalin-fixed tissue from the pediculectomy site was embedded in paraffin, and 4µm sections were stained with hematoxylin and eosin (H&E). Histologically, neoplastic cells were in close association with bone but did not appear to invade the skeletal muscle. The neoplastic cells were arranged in sheets, packets with central accumulations of blood or eosinophilic amorphous material and scant stroma (**Figure 3**). The cells had distinct cell boundaries, scant to moderate amount of eosinophilic cytoplasm and exhibit plasmacytoid features with eccentric nuclei and a perinuclear clear halo (Golgi zone). Nuclei were irregularly round to oval, with dense hyperchromatic, granular chromatin and indistinct nucleoli. Anisokaryosis was moderate and anisocytosis was mild. The mitotic count was two mitoses per 10 high-power fields (400x). On the basis of the morphological findings the differentials were multiple myeloma (MM), solitary osseous plasmacytoma (SOP) and plasmocytoid lymphoma. Immunohistochemistry was performed using a panel of antibodies against MM oncogene 1 mouse monoclonal (MUM-1)[MUM-1, DakoCytomation Ltd , Ely, UK], rabbit polyclonal CD20 (Rabbit polyclonal CD20, Thermo Fisher Scientific Ltd, UK) and mouse monoclonal CD3 (Mouse monoclonal CD3, Dako Cytomation Ltd DC, Ely, UK). Negative controls consisted of substitution of omission of primary antibody. Normal ferret lymph node served as a positive control. The tumour cells within the biopsy material consistently expressed CD20 and MUM-1 and were negative for CD3 supporting the diagnosis of plasma cell neoplasia. In this present case, due to the presence of a singly involved vertebra, absence of hyperglobulinemia and gammopathy, and lack of involvement of other organs, a final diagnosis of SOP was made. Consequently, immunoregulatory dose of prednisolone was administered 1 mg/kg, PO, q 12 h for five months. At ten-month follow-up, the ferret was comfortable and ambulatory with mild monoparesis of the left pelvic limb.

**DISCUSSION**

Tumours with plasma cell morphology include plasmacytoma, lymphoplasmacytic lymphoma, plasmablastic lymphoma, MM, and myelomoa-related disorder (MRD). Myeloma is a clonal proliferation of malignant plasma cells that originates in bone marrow and is associated with monoclonal gammopathy, multiple osteolytic bone lesions and hypercalcemia.1 The disease category called MRD is used for similar tumours and disease entities in cats.2 Plasmacytoma is a proliferation of monoclonal differentiated B- lymphocytes that originate primarily in soft tissues, oral and subcutaneous locations and rarely in nodes, organs, or bone without paraproteinemia. Most feline and canine patients with PCN have generalized disease at diagnosis (extramedullary plasmacytoma). In contrast, SOP in humans is nearly always localized and has a high cure rate with local treatment.3 In ferrets, PCN has been reported to cause two clinical syndromes: MM4-6 and solitary osseous plasmacytoma6 both resulting in neurological signs. To date, there are no known established criteria for the diagnosis and classification of neoplastic plasma cell proliferation in ferrets, making the diagnosis of plasma cell neoplasia and treatment protocols challenging. This is the first report to describe the MRI findings and surgical treatment (pediculectomy) for a vertebral SOP in a ferret with focal osteolysis in the absence of systemic disease and gammopathy.

Plasma cell neoplasia in ferrets can cause myelopathy4-7 that is generally a result of vertebral column infiltration, pathologic fracture or compressive extradural mass.8 Multiple myeloma is a systemic disease that in dogs and cats usually involves multiple bone marrow sites;8 diagnosis is based on the presence of bone marrow derived clonal proliferation of malignant plasma cells, multiple osteolytic lesions and monoclonal gammopathy.1 The ferret described in this report did not meet the above-mentioned criteria for MM. In fact the only abnormalities on the blood works were hypophosphatemia and moderate elevation of urea, most likely due to dehydration secondary to pain stress or ambulation-related restriction to regular water access. There were neither hyperglobulinemia nor gammopathy to suggest systemic disease and therefore a myeloma was fully excluded. The presence of a single mass was suggestive of either an extramedullary plasmacytoma localized to the soft tissue close to the vertebral column or a vertebral SOP. Solitary osseous plasmacytomas are lytic and locally destructive neoplasms.1 In this particular case, the presence of minimally displaced fracture of the left cranial articular process of T13, accompanied by focal lysis were most consistent with an osseous plasmacytoma. In the literature, nine cases of PCN have been reported in ferrets; eight of them diagnosed with suspected MM and only one with SOP. Although PCN is most commonly seen in ferrets over 5 years old,5-6 it has also been reported in younger animals.4 Pelvic limb ataxia and/or paraparesis appear to be the most common clinical manifestations of PCN in ferrets.4-6 There are no established treatment protocols for ferrets with PCN. Based on the literature, four ferrets were euthanized after diagnosis, two received prednisone with or without chemotherapy (vincristine), one received radiotherapy with chemotherapy (unknown), one received no treatment and lost to follow-up, and one died.4-7 In the singly published SOP the ferret was euthanized without treatment. Chemotherapy using vincristine with prednisone has been reported to give a survival time of 107 days in PCN of ferrets, whilst survival time with only prednisolone was 2 days.6 Combination of radiotherapy and chemotherapy has been reported to be the most successful treatment in PCN of ferrets with a median survival time of 10 months.7 In this case, based on the absence of any other organs involvement, lack of hematological abnormalities, normoglobulinemia (and presumed lack of gammopathy) and normal macroscopic appearance of the spinal cord, SOP was presumed, and surgical treatment followed by immunoregulatory dose of steroids were initiated.

Surgical treatment for intervertebral disc disease has been previously described in ferrets and has been associated with successful outcome.9-10 The combination of surgical and medical treatment for SOP has never been reported in ferrets. This is the second suspected SOP reported in ferrets; in the first report SOP affected the lumbar vertebral column.6 In this case, the long term outcome was good and the ferret was still alive at the time of writing (10 months from the diagnosis). In the present case, limited imaging studies (two MRI sequences without contrast), absence of serum protein electrophoresis to confirm the gammopathy and lack of bone marrow sampling (outside of the lesional surgical site) are the major limitations of this study.

In conclusion, combination of surgical and medical treatment should be considered for spinal PCN in ferrets, especially when SOP with secondary spinal cord compression is suspected. Prognosis seems to be favourable in this single report, with a survival time of at least eight months. This is the first report describing the MRI findings and surgical treatment for a vertebral osseous plasmacytoma in a ferret.

**ACKNOWLEDGMENTS**

Authors declare no any source of funding or conflict of interest for this study.

**REFERENCES**

1. Meuten D: Tumors of the hemolymphatic system, in Meuten D (ed): Tumors in Domestic Animals. Ames, IA, Iowa State Press, pp 218-225, 2017
2. Mellor PJ, Haugland S, Murphy S, et al: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, 2006.
3. Soutar R, Lucraft H, Jackson G, et al: Guidelines on the diagnosis and management of solitary plasmacytoma of bone and solitary extramedullary plasmacytoma. Clin Oncol (R Coll Radiol) 16:405-413, 2004
4. Methiyapun S, Myers R, Pohlenz J: Spontaneous plasma cell myeloma in a ferret (*Mustela putorius furo*). Vet Pathol 22:517-519, 1985
5. Marks A, Gaschen L, Tully T, et al: What is your diagnosis? J Am Vet Med Assoc 237:1033-1034, 2010
6. Clagett D, Johnston M, Han S: Malignant plasma cell neoplasia in ferrets: a review of 6 cases. J Exot Pet Med 26:36-46, 2017
7. Mauldin G, Shiomitsu K: Principles and practice of radiation therapy in exotic and avian species. Sem Av Exot Pet Med 14:168-174, 2005
8. Vail D: Myeloma-related disorders, in Withrow S, Vail D and Page R (eds): Withrow & MacEwen’s Small Animal Clinical Oncology. (edn 5). St. Louis, MO, Elsevier Saunders, pp 665-678, 2013
9. Lu D, Lamb C, Patterson-Kane J, et al: Treatment of a prolapsed lumbar intervertebral disc in a ferret. J Small Anim Pract 45:501-503, 2004
10. Morena N, Xavier V, Mascort J: Intervertebral disc prolapse in a ferret. Vet North Am Clin Exot Anim 9:667-671, 2006

**FIGURE LEGENDS**

**Figure 1.** Computed tomography images of the thoracolumbar spine of a 4-year-old female ferret with acute onset non-ambulatory paraparesis, that was referred to a veterinary hospital for surgery. Sagittal (A), dorsal (B) and transverse (C) bone reconstruction. There is a minimally displaced, oblique pathological fracture of the left cranial articular process of the T13 vertebra (arrows). Thinning and ragged lysis of the left side of the cranial half of the left pedicle of the same vertebra is present (arrowheads).

**Figure 2.** Magnetic resonance images of the thoracolumbar spine of a 4-year-old female ferret with acute onset non-ambulatory paraparesis, that was referred to a veterinary hospital for surgery. (A) T2-weighted sagittal sequence, revealing epaxial musculature hyperintensity along the body of T13 (arrowhead). (B) T2-weighted transverse sequence revealed increased hyperintensity of the cranial articular process and cranial half of the left pedicle of T13, expanding into the epaxial musculature along the body of T13 (arrowhead). (C) T2-weighted transverse sequence revealing the spinal cord compression due to the extradural material with similar signal characteristics extending into the left side of the spinal canal at the cranial aspect of the body of T13 (arrowhead).

**Figure 3**. Photomicrographs of a portion of an extradural mass (ferret osseous plasmacytoma) excised from the left pedicle of T13 vertebra of a 4-year-old female ferret presented with acute progressive non-ambulatory paraparesis. These histologic images of the left pedicle of T13 bone present (A) the densely cellular plasmacytoma which is invading the bone (H&E stain; bar = 200 μm), (B) the densely cellular plasmacytoma which is invading the bone and adjacent musculature (H&E stain; bar = 200 μm), (C) the plasma cells being well -differentiated and containing moderate amounts of eosinophilic cytoplasm and occasionally intracytoplasmic Russell bodies ((H&E stain; bar = 400 μm).