Primary localized histiocytic sarcoma of the lumbar vertebrae in a four-toed hedgehog (Atelerix albiventris)

Iori KOIZUMI1), Naka OKUMURA2) and Hirotaka KONDO2)*

1) Koizumi Nest Animal Hospital, 3-24 Bettou, Yahata Nishi, Kitakyushu, Fukuoka 806-0062, Japan
2) Laboratory of Veterinary Pathology, College of Bioresource Sciences, Nihon University, 1866 Kameino, Fujisawa, Kanagawa 252-0880, Japan

ABSTRACT. We describe a case of primary localized histiocytic sarcoma of the lumbar vertebrae in a four-toed hedgehog. The case showed aggressive osteolysis of lumbar vertebrae on radiography, and a soft-tissue mass effacing this region was noted, suggesting a neoplastic lesion. No metastatic lesions were apparent. Antemortem diagnosis was challenging, and necropsy was performed. Histopathological and immunohistochemical findings were consistent with localized histiocytic sarcoma. This report provides documentation of the clinical and pathologic features of an unusual form of histiocytic sarcoma localizing to lumbar vertebrae in a four-toed hedgehog.

KEY WORDS: Atelerix albiventris, four-toed hedgehog, histiocytic sarcoma, neoplasia

Four-toed hedgehogs (Atelerix albiventris) are common pets in America, Europe and Asian countries, including Japan [12]. Neoplastic diseases are common in this species. A tumor incidence of 29–51.5% has been indicated from necropsy reports, with 85% of those neoplastic diseases being malignant [4, 17]. A recent study by two commercial laboratories in Japan revealed neoplastic lesions in 60% of samples from captive four-toed hedgehogs examined histopathologically, with 74.6% of those tumors classified as malignant [15]. Neoplastic diseases have been shown to account for 35.9% of all causes of death, representing the primary cause of death for four-toed hedgehogs kept in zoos [16]. As such, for adequate treatment planning and evaluation of prognosis, more precise knowledge is needed regarding the biological behaviors of those neoplastic diseases occurring in this species.

Histiocytic sarcoma (HS) is an interstitial dendritic cell- or macrophage-derived malignant tumor [11]. HS commonly develops in dogs, but is rare in cats [11]. Hematopoietic tumors are the second most frequently occurring group of tumors, accounting for 11% of all tumors in four-toed hedgehogs [4, 17]. Reports describing details of hematopoietic tumors in four-toed hedgehogs remain limited [2, 8]. Some case reports have described clinical courses and pathological features of HS in four-toed hedgehogs, occurring at the subcutis, brain, mesenteric lymph node and intraabdominal mass of unknown origin including dissemination form [7, 10, 13, 14]. One case series indicated that HS in four-toed hedgehogs presented an aggressive biological behavior with guarded prognosis similar to that in dogs [7]. Given the reported cases, the clinico/histopathological features of this neoplastic disease remain to be clarified more accurately.

This report describes a case of primary HS of the lumbar vertebrae in a four-toed hedgehog. This case showed very aggressive osteolysis of lumbar vertebrae and neoplastic invasion to surrounding tissue, but no metastatic lesions were identified.

A 5.9-year-old male four-toed hedgehog was brought into a clinic with a chief complaint of dragging hind legs. The animal had a 1-month history of lameness with progressive deterioration. The animal appeared alert with normal activity and appetite. Initial physical examination revealed paresis of bilateral hindlimbs, although detailed neurological examination was not performed due to roll-up behavior. Induction and maintenance of anesthesia with 2% isoflurane inhalant (ISOFLURANE Inhalation Solution; Pfizer, Tokyo, Japan) and oxygen (2 l/min) was performed for detailed examination. Biochemistry showed mild hypophosphatemia (2.9 mg/dl; reference range, 3.4–7.2 mg/dl), mild hyperproteinemia (7.0 mg/dl; reference range, 5.0–6.5 mg/dl), moderate hyperglobulinemia (4.3 g/dl; reference range, 2.2–3.2 g/dl) [6]. Radiographs showed severe osteolysis at the fifth lumbar vertebra. Decreased radiopacity was more apparent for the vertebral arch than for the vertebral body, with the vertebral arch difficult to identify on radiographs (Fig. 1). Ultrasound showed no abnormalities. The hedgehog was administered prednisolone (1 mg/kg, PO, q 24 hr, prednisolone tablets; Takeda Pharmaceuticals Co., Osaka, Japan), enrofloxacin (10 mg/kg, PO, q 24 hr, Reneval; Zoetis, Tokyo, Japan), famotidine (1 mg/kg, PO, q 24 hr, famotidine tablets; Takeda Pharmaceuticals Co.) for 1 week, although symptoms...
did not improve and the pharmacotherapies were subsequently discontinued by the owners. On Day 84, the animal was brought to the hospital with bilateral hindleg paralysis, anorexia and lethargy. An indurated, immobile subcutaneous mass was palpable on the dorsal aspect at the waist. Radiographs showed extensive, severe osteolysis affecting the third to sixth lumbar vertebrae. Vertebral arches around those lesions were not identifiable from radiography due to marked decreases in radiopacity, while vertebral bodies appeared ventrally bent with considerable osteolysis (Fig. 2). Ultrasonography from a ventral approach disclosed a 29.2 × 24.2-mm, round-to-ovoid, hypoechoic mass lesion including numerous hyperechoic components presenting with acoustic shadows dorsal to a severely distended urinary bladder. Ultrasound-guided fine-needle aspiration was performed under a dorsal approach. The resulting cytology was considered non-diagnostic due to the low cellularity of the sample. Although prednisolone (1.5 mg/kg, PO, q 24 hr), enrofloxacin (10 mg/kg, PO, q 24 hr), famotidine (1 mg/kg, PO, q 24 hr) was prescribed and instructions on performing gavage were provided, the animal died on Day 91.

On necropsy, the lumbar vertebrae appeared completely effaced by a 3.5 × 3.5 × 3-cm rubbery, gray mass. Both left and right kidneys and adrenal glands were adherent to the surface of the mass and appeared mildly compressed (Fig. 3). The cut surface of the mass was mottled gray to tan (Fig. 4). Other representative gross findings included: 1) multifocal to coalescing, variably sized nodules in the liver and spleen; 2) a nodular lesion in the right thyroid gland; and 3) hypertrophy of the seminal vesicles and prostatic glands. After fixation of the tissue samples in 10% neutral-buffered formalin, representative trimmed tissues were routinely processed, embedded in paraffin, sectioned at 5 µm, and stained with hematoxylin and eosin.

Histologically, the vertebral mass was a densely cellular neoplasm, comprising solid sheets and interlacing bundles of round to polygonal to short spindle-shaped cells (Fig. 5). Most neoplastic cells had indistinct cell borders and moderate amounts of eosinophilic homogeneous to granular cytoplasm. Nuclei were round to elongated, with coarsely stippled chromatin and one to three distinct nucleoli. Anisocytosis and anisokaryosis were moderate to prominent, and three mitoses per 10 high-powered fields (400×) were identified. Rare binucleated and multinucleated cells were observed. Within the neoplasm, pre-existent fragmented bony tissues were rarely present. At the margins between the neoplasm and adjacent residual vertebrae, the narrow spaces of the vertebral bodies were filled with neoplastic cells, with destruction and effacement of bony and associated tissues. In this region, the spinal cord appeared atrophic due to compression, with no invasion by neoplastic cells. There was no evidence of metastatic lesions or invasion of neoplastic cells in the kidney. In addition, neoplastic cells were immunolabelled with anti-ionized calcium-binding adapter molecule-1 (Iba-1) rabbit polyclonal antibody (1:500; Fujifilm Wako Pure Chemical Corp., Osaka, Japan) and anti-human leukocyte antigen-DR (HLA-DR) mouse monoclonal antibody (1:50; Dako Japan, Tokyo, Japan) (Fig. 6). Neoplastic cells appeared negative for other neurogenic (S-100, glial fibrillary acidic protein, neurofilament and synaptophysin) and myogenic (desmin and α-smooth muscle actin) antibodies used. These findings were consistent with HS localizing to the lumbar vertebrae. Other representative morphologic diagnoses included neuroendocrine tumor in the liver, spleen and cervical lymph node, thyroid carcinoma, and hyperplasia of accessory glands.

This report describes a case of primary HS affecting lumbar vertebrae in a four-toed hedgehog. This case showed very aggressive osteolysis of the lumbar vertebrae and neoplastic invasion into surrounding tissue, while necropsy identified no metastatic lesions. This feature has not been reported in previous descriptions of HS in this species and represents a unique finding in the present case. Some case reports have described clinical courses and pathological features of HS in four-toed hedgehogs. The age of affected animals ranges from 1.5 to 3.7 years, with primary sites reported were the subcutis, brain, mesenteric lymph node and intraabdominal mass of unknown origin [7, 10, 13, 14]. Disseminated HS (DHS), a subcategory with lesions forming in multiple organs, also have been reported [7, 13]. Case series indicated that HS in four-toed hedgehogs presented an aggressive biological behavior similar to the feature of DHS in dogs, suggesting guarded prognosis [7]. Immunohistochemistry is warranted for definitive diagnosis of HS in four-toed hedgehogs due to a wide variety of cell morphologies [7, 13, 14]. To the best of our knowledge, no previous studies have described HS occurring primarily in the bone tissue in four-toed hedgehogs, and only the single case arising in the subcutis showed a metastatic lesion to the humerus [7]. In a case report of primary HS in the brain of a four-toed hedgehog, necropsy confirmed no metastatic lesions in any other organs [14]. A similar case of primary HS in the brain was reported in a cat [5]. In dogs, HS commonly show a disseminated form involving various organs, including lymph nodes, skin and subcutaneous tissues, oral mucosa, lungs, liver, spleen, kidney, bone and joints, vertebra, and central nervous system [1, 9, 19, 20]. Even in the early stages of localized HS, widespread metastasis occurs and the prognosis of canine HS is thus poor [1, 20, 21]. In a retrospective study of 19 canine HS cases with skeletal lesions, 6 cases (32%) showed the lesions in vertebrae, including 5 cases considered to be DHS [19]. In contrast, the lesion of HS in the present case was localized to the lumbar vertebrae and surrounding tissue without dissemination. To clarify more precise biological behaviors and clinicopathological features of this neoplastic disease in four-toed hedgehogs, elucidation of whether the primary site is associated with the rapidity of disease progression, tendency for metastasis or prognosis seems useful.

This case presented with paresis and paralysis of both hindlegs and severe distortion of the urinary bladder. In clinical practice, neurological disease (e.g., wobbly hedgehog syndrome, intervertebral disc disease, or neoplasia of the central nervous system) should be considered among the differential diagnoses [3, 12, 18]. Findings from radiography or ultrasonography were characterized by aggressive osteolysis and a soft-tissue mass lesion, facilitating consideration of a neoplastic process. Similar lesions have been seen for HS affecting the vertebrae in dogs [19]. Radiography on Day 1 showed more aggressive osteolysis of the vertebral arch than of the vertebral body for the fifth lumbar vertebra. Given these features identified from precise radiological and pathological assessments, the primary site of HS in this case was concluded to be the fifth lumbar vertebral arch.

Differential diagnoses for the vertebral mass included HS and soft-tissue sarcoma. Previous reports have noted that HS in four-toed hedgehogs presents with various morphologies, with definitive diagnosis of HS requiring immunohistochemistry [7, 13, 14].
Fig. 1. Radiograph on Day 1 shows severe osteolysis at the fifth lumbar vertebra with the vertebral arch difficult to identify (arrow).

Fig. 2. Radiograph on Day 84 shows extensive, severe osteolysis affecting the third to sixth lumbar vertebrae (arrows).

Fig. 3. Gross findings at necropsy. The lumbar vertebrae are completely effaced by a 3.5 × 3.5 × 3-cm rubbery, gray mass.

Fig. 4. Gross findings at necropsy. The cut surface of the mass at the level of the kidneys appears mottled gray to tan. Both left and right kidneys are adherent to the surface of the mass.

Fig. 5. Histological findings of the mass. The mass (asterisk) is formed at the lumbar vertebrae, effacing pre-existing bone tissue. Arrow, spinal cord; arrowhead, vertebral body. Hematoxylin and eosin. Bar=500 µm. Inset: The mass comprises a solid sheet and interlacing bundles of round to polygonal to short spindle-shaped cells, with marked pleomorphism. Hematoxylin and eosin. Bar=20 µm.

Fig. 6. Immunohistochemical findings of the mass. Neoplastic cells show positive membranous or cytoplasmic staining for anti-Iba-1 (A) and positive cytoplasmic staining for anti-HLA-DR (B). Counterstain with Mayer’s hematoxylin. Bar=20 µm.
Our case supports the recommendations of previous reports. Further study is required to expand the body of knowledge regarding the wide diversity of histopathological images of HS in a greater number of four-toed hedgehogs.

We have described herein a case of primary HS localized to the lumbar vertebrae in a four-toed hedgehog. In this case, the aggressive osteolysis of the lumbar vertebrae due to neoplastic mass without metastases or invasion to the adjacent organs was impressive.

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