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EMBRYONAL RHABDOMYOSARCOMA IN A ROTHSCHILD'S GIRAFFE (*GIRAFFA CAMELOPARDALIS ROTHSCHILDI*)

Margarita Woc-Colburn, D.V.M., Suzan Murray, D.V.M., Dipl. A.C.Z.M., Nancy Boedeker, D.V.M., Tabitha Viner, D.V.M., Dipl. A.C.V.P., Michelle L. Fleetwood, D.V.M., Dipl. A.C.V.P., Tony C. Barthel, Kurt D. Newman, M.D., and Carlos R. Sanchez, D.V.M., MSc.

Abstract: A 3-yr-old male Rothschild's giraffe (*Giraffa camelopardalis rothschildi*) presented for acute swelling caudomedial to the left parietal horn. Following initial diagnostics and supportive treatment, the mass was surgically resected and intralesional chemotherapy was administered. Despite treatment, the giraffe's condition worsened and euthanasia was performed. Gross necropsy revealed neoplastic invasion and destruction of underlying parietal bone, adjacent horn base, and sinuses, and metastases in the tracheobronchial and mandibular lymph nodes and lung. Histologically, the tumor was composed of packets of anaplastic round cells. Immunohistochemical studies further characterized the tumor as an embryonal rhabdomyosarcoma. This is the first reported case of rhabdomyosarcoma in a giraffe.

Key words: Rothschild's giraffe, *Giraffa camelopardalis rothschildi*, embryonal rhabdomyosarcoma.

BRIEF COMMUNICATION

Rhabdomyosarcomas arise from either striated muscle or muscle progenitor cells.[11,16] These tumors are classified into three main types based on histopathologic features; namely embryonal, alveolar, and pleomorphic. The reported incidence of rhabdomyosarcomas in domestic animals is less than 1% of all neoplasias, most of which are reported in dogs.[2,3,6,10,11,15,16] No sex or age predisposition has been observed; however, botryoid embryonal subtypes are most commonly found in the urinary bladder of juvenile large-breed dogs.[10,15,16] In zoo animals, rhabdomyosarcomas have been reported in Baird's tapir (*Tapirus bairdii*), fallow deer (*Dama dama*) and white-tailed deer (*Odocoileus virginianus*).[1,5,9] The following is the first reported case of an embryonal rhabdomyosarcoma in a young Rothschild's giraffe (*Giraffa camelopardalis rothschildi*).

From the Smithsonian Institution's National Zoological Park, 3001 Connecticut Avenue NW, Washington, D.C. 20008-2598, USA (Woc-Colburn, Murray, Boedeker, Viner, Barthel, Sanchez); the Department of Veterinary Pathology, Armed Forces Institute of Pathology, 6825 16th Street NW, Washington, D.C. 20306, USA (Fleetwood); and the Children's National Medical Center, 111 Michigan Avenue NW, Washington, D.C. 20010-2970, USA (Newman). Present address (Sanchez): Chicago Zoological Society, Brookfield Zoo, 3300 Golf Road, Brookfield, Illinois 60513, USA. Correspondence should be directed to Dr. Woc-Colburn (margarita_woc@yahoo.com).

A 3-yr-old, male, 666-kg Rothschild's giraffe presented for an acute swelling around the left parietal horn. Examination revealed a 3-cm diameter, soft, fluctuant, subcutaneous mass caudomedial to the left parietal horn. A fine needle aspirate of the mass was obtained under chute-restraint. Cytologic analysis revealed peripheral blood and a presumptive diagnosis of hematoma was made.

One month after initial presentation, the giraffe had intermittent bouts of inappetence, lethargy, and abnormal neck posture. The mass remained unchanged. A repeat fine needle aspirate was obtained. Cytology revealed many clusters of round cells with a moderate amount of granular cytoplasm suggestive of poorly differentiated sarcoma. Using behavioral restraint, phlebotomy was performed for hematologic and serum biochemical evaluation. Complete blood count and serum chemistry abnormalities included mild hyperproteinemia (8.8 g/dl; reference range 5.9–7.9 mg/dl) and mild hyperfibrinogenemia (400 mg/dl; reference range 0–315 mg/dl).[7] Over the next 6 days, no improvement was seen. Biopsy of the mass was elected.

Standing sedation was performed using detomidine hydrochloride (Dormosedan, Pfizer Animal Health, New York, New York 10017, USA; 10 mg i.m.) delivered by hand injection. Sedation was antagonized with yohimbine (ZooPharm, Laramie, Wyoming 82070, USA; 66 mg i.m. [cumulative]). Analgesic treatment was achieved with ketoprofen (Ketofen, Fort Dodge Animal Health, Fort Dodge, Iowa 50501, USA; 300 mg i.m.).

The soft tissue mass contained a soft, fluctuant region cranially delimited by firm tissue. Two 4-

mm punch biopsies were obtained from the firm aspect of the mass. Cytology of a Wright's-stained impression revealed a monomorphic population of round cells with scant cytoplasm. The biopsy sample was fixed in 10% neutral buffered formalin and processed routinely for histology. Histopathology revealed packets of polygonal cells with indistinct cell borders, small amounts of fibrillar cytoplasm, and up to five irregularly round nuclei per cell with finely-stippled chromatin and variably distinct nucleoli. Packets of neoplastic cells were supported by a fibrovascular stroma. The cells often lined the boundaries of the packets, and cells at the center of the packets were vacuolated or had lost cell contact (Fig. 1). The mitotic activity was approximately 1 per ×400 field. In some areas, neoplastic cells were more anaplastic; with a loss of packeting arrangement, more abundant eosinophilic cytoplasm, anisokaryosis, anisocytosis, and large nucleoli. Immunohistochemical staining was performed on deparaffinized sections using the avidin-biotin-peroxidase complex technique for vimentin (mouse monoclonal antibody, clone V9, Ventana, Tucson, Arizona 85755, USA; premixed solution), neuron-specific enolase (mouse monoclonal antibody, clone E27, Ventana; premixed solution), glial fibrillary acidic protein (rabbit polyclonal antibody, Dako, Carpinteria, California 93013, USA; 1:16,000 dilution), Melan A (mouse monoclonal antibody, clone A103, Novocastra, Newcastle NE12 8EW, United Kingdom; 1:50 dilution), chromogranin (rabbit polyclonal antibody, Dako; 1:1,600 dilution), synaptophysin (rabbit polyclonal antibody, Ventana; premixed solution), muscle-specific actin (mouse monoclonal antibody, clone HUC1-1, Ventana; premixed solution), myogenin (mouse monoclonal antibody, clone F5D, Dako; 1:50 dilution), and myoD1 (mouse monoclonal antibody, clone 5.8A, Novocastra;1:50 dilution). Sections were also stained under identical conditions, with normal rabbit or normal mouse serum, to serve as negative controls. These immunohistochemical stains were incubated with diaminobenzidine chromogen (Ventana) and counterstained with Mayer hematoxylin.

Strong positivity for actin and desmin was found in the cytoplasm of approximately 50% of the neoplastic cells, and nuclei were positive for myogenin (100% of cells) and myoD1 (75% of cells). Nearly 100% of the neoplastic cells were also nonspecifically positive for vimentin in the cytoplasm, as well as for S-100 protein within nuclei. These immunohistochemical findings, coupled with the histomorphology of the mass, indicated embryonal rhabdomyosarcoma.[4,14,16]

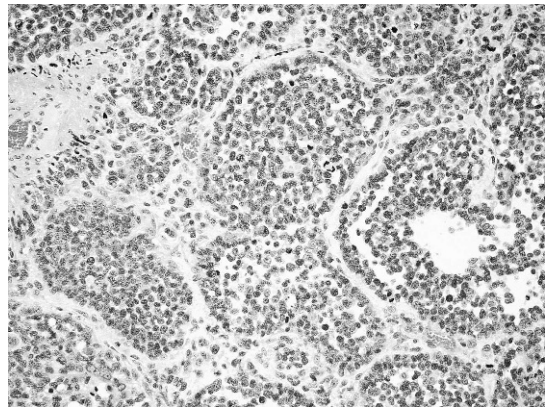

Figure 1. Embryonal rhabdomyosarcoma of a Rothschild's giraffe. Neoplastic polygonal cells are arranged in packets or sheets. Mitotic figures are present at a rate of approximately 1 per ×400 field. H&E, ×200.

Surgical excision of the mass, followed by intralesional chemotherapy under general anesthesia, was performed. The giraffe was immobilized with medetomidine hydrochloride (ZooPharm; 6 mg), ketamine hydrochloride (ZooPharm; 400 mg) and A3080 (ZooPharm; 3 mg) i.m. via hand injection. Muscle relaxation was maintained with guaifenesin (Vedco, St. Joseph, Missouri 64503, USA; 12,500 mg i.v. continuous drip). Anesthesia was antagonized with naltrexone (ZooPharm; 50 mg i.m.) and atipamezole (30 mg i.v. and 30 mg i.m.).

Right and left oblique skull radiographs revealed lytic changes of the parietal bone underlying the soft tissue mass. To control intracranial swelling, dexamethasone (VetOne, Meridian, Idaho 83680, USA; 500 mg i.v.) and prednisolone sodium succinate (Solu-delta-cortef, Pfizer Animal Health; 1,000 mg i.m.) were administered.

The soft tissue mass located caudal to the left parietal horn measured 10 × 10 × 6 cm. Wide lateral surgical margins were obtained. On the basilar aspect, the mass extended to the parietal bone and full surgical excision was not possible. Intralesional chemotherapy with 5-fluorouracil (Fluoroplex, Allergan Inc., Irvine, California 92612, USA; 300 mg) was given. Histopathology revealed that neoplastic cells extended to all cut borders of the tissue submitted.

Over the next 11 days, the giraffe was treated supportively. Five days postoperatively, a new

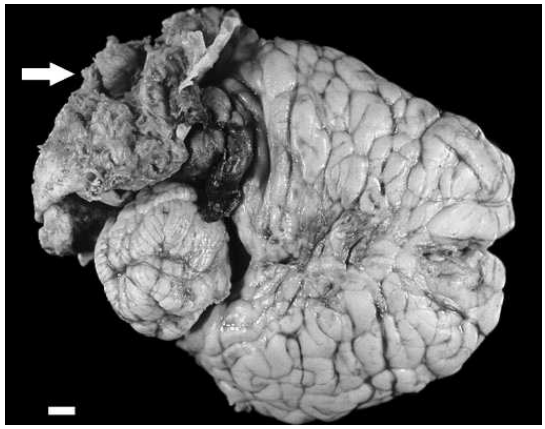

Figure 2. Brain from a 3-yr-old Rothschild's giraffe. The embryonal rhabdomyosarcoma that extended through lysed calvarial bone and sinus distorts and displaces the cerebellum and adjacent cerebrum. Bar = 1 cm.

mass 2 × 4 cm developed at the incision site. Eleven days after surgery, the giraffe became ataxic, obtunded, and developed bilateral horizontal nystagmus. Brief improvement of vestibular signs was seen with diphenhydramine (Benadryl, Baxter Healthcare, Deerfield, Illinois 60015, USA; 500 mg i.m.) administration. Euthanasia was elected due to a grave prognosis.

On gross necropsy, a poorly healed incision site with an 8 × 8 × 4 cm hematoma subadjacent to the incision was noted between the left parietal horn and pinna. Below the hematoma, there was a 10 × 10 × 4 cm irregular, soft, pale tan mass infiltrating the adjacent skeletal muscle, salivary gland, and bone. There was a 4 × 4 cm area of complete bone loss in the base of the parietal horn and the adjacent parietal bone covering the parietal sinus. The bone between the parietal sinus and the brain, at the level of the left cerebral cortex and cerebellar hemisphere, was completely lost. The tumor filled the sinus between the areas of bone loss, compressed the left side of the cerebellum, and was attached to the meninges of the caudal left cerebral hemisphere (Fig. 2). The caudal left cerebral cortex was malacic. There were multifocal, large hemorrhages in the caudal left cerebral cortex, the dorsal surface of the brainstem, and between the left side of the brainstem and the ventral aspect of the cerebellum. Enlargement of the left mandibular lymph node, due to tumor metastasis, was present. There were numerous firm, tan nodules that were up to 2 cm in diameter throughout the lung. Tissues were fixed in 10% neutral buffered formalin, processed routinely, and stained with hematoxylin and eosin (H&E). Histopathology revealed that the neoplasm previously described had eroded the skull and caused extensive malacia and gliosis of the adjacent gray and white matter. Neoplastic cells focally infiltrated the meninges. Tumor cells had also embolized to the spinal cord vasculature in the area of C1–2. Based on the histopathology and immunohistochemistry, a diagnosis of embryonal rhabdomyosarcoma with metastasis to the lung, mandibular, and tracheobronchial lymph nodes was made.

In humans, embryonal rhabdomyosarcomas are the second most-common malignant head and neck tumor (18%) in the pediatric population.[14] Those found along the parameningeal sites have a poor prognosis, as 35% of the patients develop metastases into the meninges and the central nervous system.[6] In contrast, very few embryonal rhabdomyosarcomas have been reported along the head and neck of animals.[1–3,5,6] Several of these have been reported to affect parameningeal sites such as the paranasal sinus, nasal cavity, and infratemporal fossae, with metastases to the meninges.[1,2,6,10] This giraffe's tumor may have originated in the parameningeal region. Similar to other parameningeal rhabdomyosarcomas, it could have spread to the meninges and surrounding skeletal muscle.

In both humans and domestic animals, treatment of choice is wide surgical excision of tumor followed by radiation or chemotherapy.[12,14] A five-fluorouracil, a pyrimidine antagonist, has been used in some protocols with varying success.[12] However, survival rates of patients with embryonal rhabdomyosarcoma, even with chemotherapy, rapidly decrease with the presence of metastasis.[14] Areas of necrosis that involved large swaths of neoplastic cells with enmeshed blood vessels were observed on histopathology of the tumor. This could indicate that intralesional chemotherapy had a limited effect on tumor control.

Few spontaneous tumors have been reported in giraffes. These include a pelvic chondrosarcoma and a teratoma of the umbilical cord.[8,13] At the National Zoological Park, a thyroid adenoma and uterine leiomyoma have also been observed (unpubl. data). None of these have been reported to cause neurologic signs.

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