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What Is Your Neurologic Diagnosis?

In collaboration with the American College of Veterinary Internal Medicine

Acute onset of circling and altered mentation in an 8-year-old cat

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History

An 8-year-old 4.1-kg (9-lb) neutered male domestic shorthair cat was referred for evaluation of acute onset of circling to the right. The cat was

Neurologic Examination Form

Observation

Mental	Alert		Depressed	X	Disoriented		Stupor		Coma	
Posture	Normal		Head tilt		Tremor		Falling		Other	
Gait	Normal		Ataxia		Pelvic limbs		All 4		Circling	X
Paresis	Pelvic limb		Tetra		Hemi		Mono			
Other	The cat occasionally circled to the right side. No ataxia, paresis, or lameness detected during examination.									

Key: 4 = Exaggerated, clonus; 3 = Exaggerated; 2 = Normal; 1 = Diminished; 0 = None; NE = Not evaluated.

Postural reactions	Left forelimb	Right forelimb	Left hind limb	Right hind limb
Wheelbarrow	NE	NE		
Hopping	2	2	NE	NE
Extensor postural thrust			NE	NE
Proprioceptive positioning	2	2	2	2
Hemistand/walk	NE	NE	NE	NE
Placing–tactile	NE	NE		
Placing–visual	NE	NE		

Spinal reflexes	Left forelimb	Right forelimb	Left hind limb	Right hind limb
Quadriceps			NE	NE
Extensor carpi	NE	NE		
Flexion				
Crossed extensor	2	2	2	2
Perineal	2	2	2	2

Cranial nerves

	L	R
II, VII-Vision menace	NE	NE
II, III-Pupils resting	2	2
Stim L	2	2
Stim R	2	2
II-Fundus	NE	NE
III, IV, VI-Strabismus, resting	2	2
III, IV, VI, VIII-Strabismus, position	2	2

	L	R
VIII-Nystagmus, resting	2	2
VIII-Nystagmus, change	2	2
V-Sensation	2	2
VII-Facial mm	2	2
V, VII-Palpebral reflex	2	2
IX, X-Gag	2	2
XII-Tongue	2	2

Comments
Menace response was inconsistent.

Sensation (Locate and describe any abnormalities)

Hyperesthesia	0	
Superficial pain	NE	
Cutaneous reflex	2	
Deep pain	NE	

adopted 3 years earlier, and the current owner was not aware of any previous medical problems. Two nights before referral, the cat returned home from outside looking disorientated and consistently circling to the right side. The cat did not seem to recognize common surroundings and needed assistance with food and water. The owner brought the cat to a veterinary practice the following morning, where analgesic and antiemetic injections were administered. The cat improved the next day and could walk in a straight line, albeit with abnormal mentation. Performing physical and neurologic examinations was challenging, as the cat demonstrated aggressive behavior. The cat was mildly obtunded but still responded to the owner and environment. Mucopurulent discharge was observed on the left eye. A slight swelling was palpated on the right dorsal region of the skull. Other physical examination findings were normal.

Formulate your anatomic and etiologic diagnoses, then continue reading.

Assessment

Anatomic diagnosis

The presence of abnormal mentation and behavioral changes excluded spinal cord and neuromuscular disorders. Abnormal mentation including obtundation and disorientation was due to intracranial lesion either in the cerebrum or brainstem; however, the lack of other cranial nerve deficits concluded that a brainstem lesion was less likely. Circling to the right without presence of brainstem signs was most likely due to a right cerebral lesion. Normal gait, hopping, and intact spinal reflexes supported a lesion in the cerebrum.

Likely location of the lesion

Suspected location of the lesion was at the right cerebrum.

Etiologic diagnosis

Differential diagnoses considered for acute, progressive, lateralized right-sided cerebral lesion in this cat included traumatic injury, infection, or neoplasia. The initial diagnostic plan included a CBC, serum biochemical analysis, MRI, and CT of the head.

Diagnostic Test Findings

The CBC and serum biochemistry were unremarkable. On MRI **(Figure 1)**, there was an approximately 4 X 2.5 X 2-cm, irregularly shaped calvarial/extra-axial mass with heterogeneous intensity on T2-weighted (T2W) images on the right frontoparietal region of the skull, extending into the cranial cavity and resulting in midline shift of the right cerebral hemisphere to the left side. Subtentorial herniation was also observed on the sagittal MRI images, which raised suspicion of increased intracranial pressure. The mass appeared isointense relative

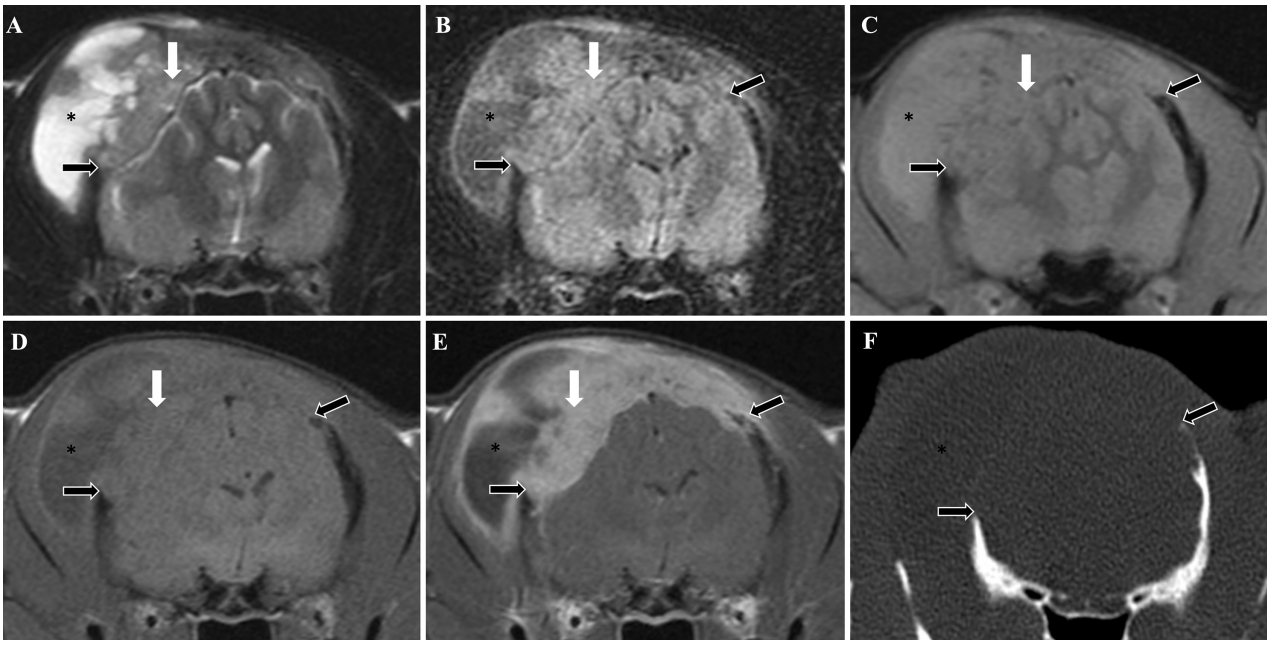

Figure 1—Transverse MRI and CT images of the calvarium of a cat with a skull mass. T2-weighted (T2W) image (A), FLAIR (B), T2* (C), T1-weighted (T1W) image precontrast (D), T1W image postcontrast (E), and CT bone window (F). Imaging demonstrated a large, irregular calvarial/extra-axial mass (marked by a white arrow) compressing the cerebrum. The mass extended into the cranial cavity, resulting in a midline shift of the right cerebral hemisphere to the left side. A large cystic component (marked by an asterisk) was observed in the right temporal muscle region. Notice the evidence of osteolysis on the calvarium confirmed by CT (F; marked by black arrows). The mass was located in the right frontoparietal region of the skull, had heterogeneous intensity signal on T2W imaging (A), was isointense relative to brain tissue on T1W imaging (D), and exhibited diffuse hyperintensity on FLAIR (B). Postcontrast images showed marked and homogenous contrast enhancement with hypointense signal in the cyst center (E). No signal void was observed on T2* (C).

to the gray matter on T1-weighted (T1W) images. Furthermore, there was also a large cystic component in the region of the right temporal muscle that appeared hyperintense on T2W but hypointense on T1W images and hyperintense on FLAIR. The mass also affected the right frontal sinus, leading to compression and lysis of the left frontal bone of the skull. Postcontrast T1W images were obtained after IV injection of gadobutrol (Gadovist) at 60.5 mg/kg (1.0 mmol/mL) and demonstrated marked and homogenous contrast enhancement with hypointense signal in the cystic center. Additionally, meningeal enhancement could be seen on the right cerebral hemisphere in postcontrast images.

A CT scan of the skull revealed osteolytic lesions at the right frontal sinus, dorsal cribriform plate, and frontoparietal bone (Figure 1). No osteoproliferation or evidence of calcification was seen. No significant abnormalities were observed in the thorax. The changes were most suggestive of neoplasia, such as intraosseous/intracranial meningioma, lymphoma, osteosarcoma, or fibrosarcoma. Other differential diagnoses included an inflammatory process most likely of infectious origin, although overall it was considered less likely.

Treatment and Outcome

Cerebrospinal fluid collection was not performed due to the high risk of herniation given the suspicion of increased intracranial pressure. A slow IV bolus of mannitol at 0.25 g/kg and SC injections of buprenorphine at 0.02 mg/kg and dexamethasone at 0.01 mg/kg were administered during recovery. Cytological evaluation from aspirates of the cystic fluid and mass showed malignant spindle cells, including several large giant cells and mitotic figures. Due to the guarded prognosis, the owner elected euthanasia and opted for postmortem examination.

On gross examination, the mass was firm to very firm, approximately 3 cm in diameter and up to approximately 1.5 cm in thickness, poorly delineated and irregular in shape, extending from rostral to midcalvarium, and replacing the bony cranium. The cystic region was located toward the dorsal periphery of the lesion and contained pale-pink, translucent, and mildly viscous material. The intracranial component of the mass compressed the underlying frontal and parietal regions of the dorsolateral right cerebral hemisphere.

On histopathology examination, the skull mass was characterized as a nonencapsulated and infiltrative neoplastic process within the bone, composed of pleomorphic plump and spindly to polygonal neoplastic cells forming interlacing streams, bundles, and sheet-like arrangements, commonly interspersed by amorphous, palely eosinophilic material (osteoid) and in multiple regions also by numerous multinucleated giant cells with up to 18 nuclei, which typically were smaller when compared to the nuclei of the mononuclear population. The nuclei of the mononuclear cells were irregularly round or oval with ropey and marginated chromatin and up to 2 large, magenta-colored nucleoli; a high number of mitotic figures (up to 8/hpf), including multiple bizarre forms, were also observed in the mononuclear population. The cystic region of the mass, lined by neoplastic cells, contained palely eosinophilic (proteinaceous) material, while the compressed cerebral cortex exhibited mild to moderate gliosis.

Thus, the histopathologic diagnosis of the grossly osteolytic, cavernous skull mass characterized by the vast predominance and atypia of the mononuclear population, the substantial intralesional production of osteoid, and the differing nuclei in mono- and multinuclear population, represented an osteosarcoma of the osteoblastic, productive subtype, multifocally also exhibiting features of a giant cell–rich osteosarcoma (GCRO).

Comments

Acute/peracute onset of clinical signs in this cat did not match a neoplastic process; however, it could have been attributed to increased intracranial pressure and subsequent brain herniation. Traumatic injury may have fit the sudden-onset mild swelling on the skull and temporary improvement seen in this cat; however, MRI findings did not support the diagnosis. Magnetic resonance imaging and CT features may share similarities with inflammatory processes caused by an infectious agent, although overall were deemed unlikely in this case. Histopathological examination of the skull and intracranial mass revealed the presence of an osteosarcoma of osteoblastic and productive subtype, however, also exhibiting multiple foci containing moderate to large numbers of multinucleated giant cells, in turn consistent with a GCRO in these regions.

Osteosarcoma is the most common primary bone tumor in cats, accounting for 70% to 80% of primary feline malignant bone tumors.[1] Several case studies have reported lesions affecting the orbit, mandible, and maxilla; however, the skull is only documented in around 5% of feline cases.[1] Advanced imaging modalities are valuable in obtaining clinical diagnosis. Computed tomography characteristics of osteosarcoma are space-occupying lesions with well-defined margins and aggressive osteolysis on the calvarium.[2] Reports on MRI characteristics of calvarial osteosarcoma in dogs and cats are scarce yet document axial/extramedullary lesions with signal heterogeneity on T2W images, isointensity to normal gray matter on T1W images, heterogenous contrast enhancement, osteolysis, osteosclerosis, and a long zone of transition.[2] Periosteal proliferation and meningeal enhancement also are prominent in 50% of axial osteosarcoma cases.[3] The atypical finding in this case was the cystic lesion present toward the periphery of the mass and in histological investigations lined by the neoplastic cells. Osteosarcomas typically appear as solid masses, and a cystic change has not previously been reported in dogs and cats. In contrast, large cystic components, however, have been observed and described in several human extraskeletal osteosarcomas.[4]

The final diagnosis of osteosarcoma is typically achieved through biopsy or postmortem examination. Osteoblastic subtypes are the most common histological variant of osteosarcoma, while the GCRO subtype is reported only rarely in both the veterinary[1] and human literature.[5] Typically, the sites most affected with GCRO in humans are the extremities, although a few cases have been reported affecting the maxilla and mandible.[5] The origin of multinucleated giant cells in osteosarcoma is poorly understood but may arise by fusion of osteoclasts.

Osteosarcomas in cats affecting the skull or vertebrae are generally associated with a less favorable prognosis and survival rate than appendicular osteosarcoma, as complete resection is not always possible.[1] Histologically, a high mitotic index is the only variable that affects survival rate.[1] The average survival time in cats with axial osteosarcoma with or without resection or radiation therapy is reported to be around 6 months compared to 64 months in cases with appendicular osteosarcoma.[1] Osteosarcoma must be included as a differential diagnosis in cats with masses arising from or affecting the calvarium.

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