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SHORT COMMUNICATION

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Epidemiologic study of tumors in dinosaurs

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Abstract Occasional reports in isolated fragments of dinosaur bones have suggested that tumors might represent a population phenomenon. Previous study of humans has demonstrated that vertebral radiology is a powerful diagnostic tool for population screening. The epidemiology of tumors in dinosaurs was here investigated by fluoroscopically screening dinosaur vertebrae for evidence of tumors. Computerized tomography (CT) and cross-sections were obtained where appropriate. Among more than 10,000 specimens x-rayed, tumors were only found in Cretaceous hadrosaurs (duck-billed dinosaurs). These included hemangiomas and metastatic cancer (previously identified in dinosaurs), desmoplastic fibroma, and osteoblastoma. The epidemiology of tumors in dinosaurs seems to reflect a familial pattern. A genetic propensity or environmental mutagens are suspected.

Introduction

Tumors are infrequently recognized in extreme antiquity. Limited to study of the skeleton (with the rare exception of mummies), the confident diagnosis of pre-Cenozoic tumors has been elusive. Exceptions include examples of osteoma (a benign slow growing mass of lamellar bone) in mosasaurs (Moodie 1917) and hemangioma (a benign proliferation of vascular endothelium) and metastatic cancer (a distant spread of malignant disease) in dinosaurs (Rothschild et al. 1998, 1999). The latter two were recognized only because chance sectioning of dinosaur bone revealed their presence.

The absence of any external evidence of tumor (Rothschild et al. 1998, 1999) has suggested that macroscopic examination is an insensitive technique for recognizing vertebral neoplasia (abnormal tissue growth or tumor). Systematic sectioning of vertebrae has been considered unacceptably destructive of valuable, non-renewable resources. Because the previously noted hemangioma and metastatic cancer were recognizable on x-rays (Rothschild et al. 1998, 1999), it seemed reasonable to conduct a radiologic survey to assess the occurrence of known dinosaurian vertebral tumors and the possible existence of any other varieties.

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Materials and methods

Given the logistical challenges of juxtaposing specimens, routine x-ray equipment and film development facilities, an alternative approach was considered. Fluoroscopy was chosen as the screening technique. Obviating the requirements for film and development facilities allows time-effective population screening. The use of a fluoroscope permits recognition of alterations in real time, in contrast to film radiography with its inherent film delays for each exposure. Real-time visualization also allows the overlying shadows from protuberant processes and taphonomic damage to be clearly distinguished from true pathology. Because the film technique requires problematic exposure times (with an associated risk of destruction of the expensive cathode ray tube), film–screen combinations are required. These are composed of phosphorescent sheets which magnify the effect of the x-ray photons. Therefore, shorter, more practical, exposures can be utilized, thus reducing the risk of damaging the x-ray cathode ray tube. Fluoroscopy overcomes these challenges. The fluoroscopic technique utilizes a cathode ray tube, as in routine x-rays. The image is visualized with an image intensifier and can be recorded digitally (Resnick 2002; Rothschild and Martin 1993), thereby eliminating the expense of x-ray film and development and providing immediately interpretable images. The shortcoming of the fluoroscopic technique utilized is the C-arm size (the space between the cathode ray tube and the image intensifier detection system). The latter can handle specimens up to 28 cm in diameter.

Given the common involvement of vertebrae in neoplastic processes (Resnick 2002; Rothschild and Martin 1993; Rothschild and Rothschild 1995) and size prohibition for other skeletal components in which neoplasia is commonly found in humans (Rothschild and Rothschild 1995), the study was limited to vertebrae less than 28 cm in diameter. The C-arm and portable nature of the fluoroscope allowed in situ radiography of mounted skeletons, as well as of separate elements. Size limitation, however, did preclude fluoroscopic examination of the largest adult sauropod cervical, thoraco-lumbar, and proximal caudal vertebrae.

Systematic x-ray survey screening of dinosaur vertebrae in the collections of the American Museum of Natural History, New York (AMNH); Black Hills Institute, Black Hills, South Dakota (BHI); Brigham Young University, Provo, Utah (BYU); Carnegie Museum of Natural History, Pittsburgh, Pennsylvania (CM); Denver Museum of Science and Nature, Denver, Colorado (DNMH); Field Museum of Natural History, Chicago, Illinois (FMNH); Los Angeles Museum of Natural History, Los Angeles, California (LACM); Museum of the Rockies, Bozeman, Montana (MOR); National Museum of Ancient Life, Lehi, Utah (NMAL); Canadian Museum of Nature, Ottawa, Ontario, Canada (CMN, aka NMC); National Museum of Natural History, Washington, D.C. (NMNH); Oklahoma Museum of Natural History, Norman, Oklahoma (OMNH); Royal Ontario Museum, Toronto, Ontario, Canada (ROM); Royal Tyrrell Museum, Drumheller, Alberta, Canada (RTM); Texas Tech Museum, Lubbock, Texas (TTM); University of Kansas Museum of Natural History, Lawrence, Kansas (KU); University of Texas Museum, Austin, Texas (TMM); University of Utah, Salt Lake City, Utah (UMNH); Wyoming Dinosaur Center, Thermopolis, Wyoming (WDC); Yale Peabody Museum, New Haven, Connecticut (YPM), and the private collection of Jack Henke, Danville, Kentucky was pursued utilizing the Xi-scan fluoroscopic unit. This included 10,312 vertebrae and 700+ individuals (minimum number based on associated/articulated skeletons). Vertebrae from incomplete specimens were identified to genus or family on the basis of the monospecific bone beds from which they were derived. Additionally, the bone of the previously suggested case of chondrosarcoma in an *Allosaurus*/*Torvosaurus* humerus (BYUVP 5009; Taylor 1992) was also examined macroscopically and radiologically.

Further radiologic examination of identified abnormal vertebrae was performed with a triple-phase generator at 30 kV and 190 milliamp-seconds (mAs) utilizing the high resolution Kodak-2000 system. Computerized tomographic (CT) x-rays (General Electric, Sytec-i 3000) were obtained using both 1 and 3 mm thick slices. The images were photographed digitally (Mavica, Sony and GRj-DVM90, JVC) and analyzed for disruption of trabecular patterns.

Results

Epidemiology of tumors

Radiologic evidence of neoplasia was limited to one family, Hadrosauridae (Table 1). Within that family, only *Brachylophosaurus*, *Gilmoreosaurus*, *Bactrosaurus*, and *Edmontosaurus* were affected and only caudal vertebrae were attacked. Hemangiomas were found in all of these taxa. Desmoplastic fibroma (benign tumor of fibroblast cells), osteoblastoma (benign tumor of bone cells), and metastatic cancer were found in *Edmontosaurus*.

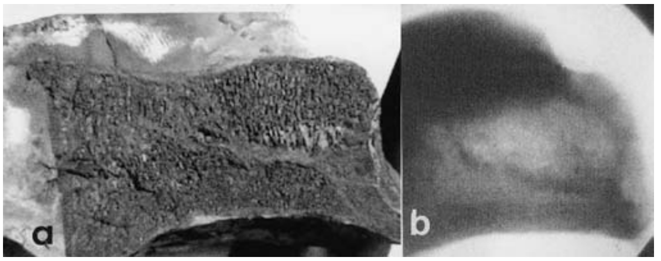

Fig. 1 Cross-section (**a**) and x-ray (**b**) views of *Edmontosaurus* (CM 12100) vertebra. **a** Trabeculae in right upper portion clearly different from surrounding trabecular pattern. **b** Radiologically lucent, very circumscribed lesion with sclerotic margin and fine trabeculation at anterior superior aspect. Posterior superior density is matrix artifact

Metastatic cancer was extremely rare, found in only 1 out of 548 (0.2%) *Edmontosaurus* vertebrae. Absence in other genera may simply reflect an inadequate sample, rather than species specificity. However hemangiomas present in 669 *Edmontosaurus* at a frequency of 3% were absent in 286 *Corythosaurus* (χ^2=7.307, P<0.004). The absence of hemangiomas in vertebrae of 7,475 sauropods, ceratopsians, stegosaurs, theropoda, ornithomimids, and ankylosaurs was statistically significant (χ^2=, 4.14, P<0.05). Osteoblastoma and desmoplastic fibroma were only found in hadrosaurs and were extremely rare; only one example of each was found.

Radiologic examination of hemangioma revealed a sharply defined, abnormal area completely enclosed by normal bone. The abnormal bone consisted of unidirectionally thickened bone trabeculae, separated by wide zones of matrix. There was no evidence of bone expansion. Desmoplastic fibroma was recognized on the basis of the characteristic trabeculated radiolucent defect.

Occurrence of osteoblastoma

Specimen Carnegie Museum (CM 12100) was collected by J. Leroy Kay in 1937 from Location 2488: Fred Townsend's Ranch, Carter County, Montana (Late Cretaceous). Currently classified as *Edmontosaurus*, the specimen consists of caudal vertebrae, 6 ribs, 3 chevrons, pubes, left ischium, and skin impressions. Osteoblastoma in this individual was recognized in one vertebra on the basis of a radiologically lytic, very circumscribed, lesion with sclerotic margin and very fine trabeculae (see Fig. 1).

Comments on specimen BYUVP 5009 *Allosaurus*/*Torvosaurus*

Examination of an *Allosaurus*/*Torvosaurus* humerus (BYUVP 5009) with a cauliflower-like growth (Taylor 1992) revealed no evidence of cancer. The shape of the humerus had been altered, with acute angulation midshaft. The area of angulation was surrounded by reactive (not

Table 1 Evaluation of dinosaur vertebrae for presence of neoplasia

	Minimum no. of individuals	No. of vertebrae	No. of individuals with tumors
Hadrosauran dinosaurs			
Lambeosaurine			
Bactrosaurus	2	94	3H[a]
Corythosaurus	13	286	
Eolambia	9	16	
Hypacrosaurus	2	117	
Lambeosaurus	5+	518	
Parasaurolophus	3	86	
Lambeosaurid	3	21	
Hadrosaurine			
Brachylophosaurus	2+	175	6H[a]
Cheneosaurus	1	2	
Edmontosaurus	16+	669	15H[a] 1M[a] 1D[a] 1B[a]
Gryposaurus	1	9	
Hadrosaurus	6	67	
Kritosaurus	10	90	
Maiasaura	5	317	
Prosaurolophus	5	172	
Saurolophus	4	81	
Edmontosaurid	6	36	
Non-lambeosaurine/hadrosaurine			
Gilmoreosaurus	1	49	2H[a]
Non-specific	3	32	
TOTAL HADROSAURS	97	2,837	29[a]
Non-hadrosauran dinosaurs			
Order Saurischia			
Suborder Sauropodomorpha	3	38	
Titanosauridae			
Alamosaurus	2	20	
Titanosaurus	3	59	
Diplodocidae			
Apatosaurus	21+	254	
Barosaurus	8	30	
Diplodocus	30+	327	
Camarasauridae			
Camarasaurus	60+	434	
Anchisauridae			
Plateosaurus	3	94	
Cetiosauridae			
Haplocanthosaurus	32	45	
Brachiosauridae			
Astrodon	57	58	
Marshosaurus/Stokesaurus	?	234	
Non-speciated sauropods	13	48	
Suborder Theropoda			
Podokesauridae			
Coelophysis	2	43	
Ornithomimidae			
Struthiomimus	2	25	
Archaeornithomimus	9	118	
Dromiceiomimus	1	1	
Ovoraptosauridae			
Chirostenotes	3	50	
Dromaeosauridae			
Deinonychus	7	67	
Saurornitholestes	2+	130	
Utahraptor	1	58	
Troodonidae			
Troodon	3+	47	
Megalosauridae			
Carcharodontosaurus	4	4	
Allosauridae			
Allosaurus	39+	1,091	
Spinosauridae			
Spinosaurus	5	6	
Acrocanthosaurus	6	38	

Table 1 (continued)

	Minimum no. of individuals	No. of vertebrae	No. of individuals with tumors
Ceratosauridae			
Ceratosaurus	4	38	
Dryptosauridae			
Dryptosaurus	2	2	
Tyrannosauridae			
Tyrannosaurus	4	58	
Gorgosaurus	5	46	
Daspletosaurus	4	47	
Albertosaurus	6	56	
Albertosaurid	1	6	
Tyrannosaurid	18	130	
Non-specific small theropods	?	36	
Order Ornithischia			
Suborder Ornithopoda			
Hypsilophodontidae			
Tenontosaurus	39	614	
Orodromeus	2	50	
Thescelosaurus	6	77	
Othnielia	1	22	
Non-speciated	2+	50	
Iguanodontidae			
Camptosaurus	33	348	
Non-specific	2	13	
Dryosauridae			
Dryosaurus	5	86	
Suborder Ceratopsia			
Psittacosauridae			
Psittacosaurus	4	66	
Protoceratopsidae			
Protoceratops	6	104	
Leptoceratops	2	25	
Ceratopsidae			
Brachyceratops	3	98	
Centrosaurus	5	206	
Monoclonius [b]	5	64	
Chasmosaurus	7	150	
Triceratops	27	195	
Pachyrhinosaurus	?	180	
Pentaceratops	1	9	
Styracosaurus	1	23	
Einiosaurus	2	32	
Achelousaurus	3	35	
Non-specific ceratopsian	13	48	
Suborder Ankylosauria			
Nodosauridae			
Edmontonia	5	16	
Sauropelta	13	199	
Silvisaurus	1	8	
Non-specific	2+	102	
Ankylosauridae			
Ankylosaurus	1	22	
Euplocephalus	12	87	
Anodontosaurus (=*Euplocephalus*)	1	1	
Non-speciated Ankylosauria	4	23	
Suborder Pachycephalosauria			
Pachycephalosauridae			
Pachycephalosaurus	?	46	
Suborder Stegosauria			
Stegosauridae			
Stegosaurus	43+	738	
TOTAL NON-HADROSAURAN	611	7,475	

[a] Number indicates number of individuals of that genus with each variety of tumor, if any; B = osteoblastoma; D= desmoplastic; H = hemangioma; M = metastatic cancer

[b] While *Monoclonius* is now classified as *Centrosaurus*, the horn bases in these individuals differed from that of classic *Centrosaurus*

neoplastic) new bone. A malaligned infected fracture was actually responsible for the cauliflower-like growth.

Discussion

While tumors have previously been recognized in dinosaurs (Rothschild et al. 1998, 1999), their epidemiology has been unclear. This radio-epidemiologic study documents the apparent restriction of tumor occurrence to hadrosaurs. While Wade Miller at Brigham Young University and Leon Goldman at the San Diego Naval Hospital have suggested that a "cauliflower-like" growth on a 135–150-million-year-old theropod (probably *Allosaurus* or *Torvosaurus*) humerus might represent a type of cartilage cancer called a chondrosarcoma (Taylor 1992),personal examination of the specimen revealed that it was simply an infected fracture. Such lesions are not uncommon in the fossil record (Molnar 2001).

Although samples sizes are small for most species of dinosaurs, the combined sample is large and a relatively high occurrence of hemangiomas in hadrosaurs, coupled with their absence in other kinds of dinosaurs, warrants an explanation. It may, of course, be a genetic predilection towards hemangioma. If so, it would be basic to the hadrosaurs, as it is present in both flat-headed and crested forms.

Hypothetical considerations

Causality of tumors is a contentious subject, even in humans. The implications of the restriction of this type of pathology to a very narrow subset of the dinosaur radiation deserve an explanation. One of the features of hadrosaur biology that might be considered is their diet. Stomach contents of *Edmontosaurus*, known from the famous "mummies," include conifers. This diet may be unique to hadrosaurs (Barrett and Upchurch 2001; Krauss 2001). Hadrosaur physiology might also differ from that of other dinosaurs. Chinsamy (Chinsamy 1994; Chinsamy and Dodson 1995) noted that hadrosaurs show bone structure that she felt was suggestive of endothermic metabolism. These structures were demonstrated by Chinsamy not to exist in a wide variety of other dinosaurs, including theropods.

Diagnosis of tumors

Hemangiomas have an almost pathognomonic x-ray appearance: coarse vertical (cephalad–caudad) striations (thick trabecular struts), separated by relatively lucent zones, replacing normal trabeculae (Boye et al. 2001; Chew 1997; Mohan et al. 1981; Resnick 2002; Rothschild and Martin 1993; Schmorl and Junghanns 1971; Sherman and Wilner 1961; Yochum et al. 1993). The permeative edges of metastatic cancer are also easily recognizable.

In addition to hemangiomas and metastatic cancer, two additional types of tumor have been discovered in dinosaurs in this study: osteoblastoma and desmoplastic fibroma. Osteoblastomas are radiologically lytic (radiolucent), very circumscribed lesions with sclerotic margins and very fine trabeculae. Desmoplastic fibroma was recognized on the basis of the characteristic trabeculated radiolucent defect. Desmoplastic fibromas are radiologically lucent lesions with honeycomb/soap-bubble patterns associated with endosteal erosion (Resnick 2002; Rothschild and Martin 1993). They are typically isolated phenomena. They are recognized radiologically in humans, but only minimally alter vertebral shape/contour and thus are usually not recognizable on macroscopic examination of intact bones. Thus, radiologic examination is essential for their detection.

Because the appearances of these tumors are unique, alternative diagnostic possibilities (see Table 2) are

Table 2 Distinguishing characteristics of osteoblastoma and desmoplastic fibroma from other bone pathologies[a]

Consideration	Differential finding	Osteoblastoma	Desmoplastic fibroma
Osteoporosis	Thin trabeculae	Thick trabeculae	Thick trabeculae
Giant cell tumor	Thin trabeculae	Thick trabeculae	Thick trabeculae
Aneurysmal bone cyst	Thin trabeculae	Thick trabeculae	Thick trabeculae
Cystic angiomatosis	Sclerotic margin	Non-sclerotic margin	Non-sclerotic margin
Hemangioendothelioma	Thin trabeculae Ill-defined margin	Thick trabeculae Sharply defined margin	Thick trabeculae Sharply defined margin
Hemangiopericytoma	Thin trabeculae	Thick trabeculae	Thick trabeculae
Paget's disease	Coarse trabecular pattern Fronts of resorption Woven bone	Thickened individual trabeculae No resorptive sites Lamellar bone	Thickened individual trabeculae No resorptive sites Lamellar bone
Metastatic disease	Ill-defined margin Thin trabeculae	Sharply defined margin Thick trabeculae	Sharply defined margin Thick trabeculae
Chondromyxoid fibroma	Endosteal sclerosis Coarse trabecular pattern	Non-sclerotic margin Thickened individual trabeculae	Non-sclerotic margin Thickened individual trabeculae

[a] Derived from Chew (1997), Resnick (2002), Rothschild et al. (1999), Rothschild and Martin (1993)

limited (Boye et al. 2001; Chew 1997; Mohan et al. 1981; Schmorl and Junghanns 1971; Sherman and Wilner 1961; Yochum et al 1993). Differential diagnosis includes osteoporosis, giant cell tumor, aneurysmal bone cyst, “brown tumor” of hyperparathyroidism, cystic angiomatosis, hemangioendothelioma, hemangiopericytoma, metastatic disease, Paget’s disease, and pseudotumors related to intra-osseous bleeding in hemophilia (Boye et al. 2001; Chew 1997; Mohan et al. 1981; Resnick 2002; Rothschild and Martin 1993; Schmorl and Junghanns 1971; Sherman and Wilner 1961; Yochum et al 1993).

Osteoporosis is characterized by a thinning, rather than a thickening, of the trabeculae. Giant cell tumors, aneurysmal bone cysts, and hemangiopericytoma are expansile disorders with thin, delicate trabeculae. Cystic angiomatosis lesions are surrounded by a rim of sclerotic bone (Resnick 2002; Rothschild and Martin 1993). Hemangioendotheliomas (also called angiosarcoma and hemangioendothelial sarcoma) are characterized by thinned trabeculae and ill-defined margins. Brown tumors and pseudotumors related to hemophilia appear as radiolucent areas without a recognizable internal structure (Resnick 2002). Radiologically lucent (lytic) lesions of metastatic cancer are usually not as sharply defined as in this case, and do not contain thick bridging trabeculae. Paget’s disease is associated with coarsening of trabecular patterns, typically with “blade of grass” fronts of resorption, and is characterized by woven bone. None of the above diagnostic considerations seemed applicable to the specimens reported here.

Metastatic cancer was extremely rare; found in less than 1% of *Edmontosaurus* vertebrae. The absence of tumors in other genera may simply reflect an inadequate sample, rather than species specificity. However, the absence of hemangiomas in sauropods, ceratopsians, stegosaurs, theropoda, orinthomimids, and ankylosaurs was statistically significant, suggesting family selectivity for this pathology. The absence in *Corythosaurus* is also statistically significant, suggesting that there may also be variable susceptibility within the Hadrosauridae. Osteoblastoma and desmoplastic fibroma were too rare for statistical comparisons to be done.

Given the size, geographic origins, and stratigraphic range of the sample examined, the predilection of hadrosaurs to tumors is unprecedented and unique. As only the caudal vertebrae were affected in susceptible species, C-arm-related size limitations would not limit the ability to confirm the presence of tumors in all but the very largest sauropods (e.g., *Seismosaurus*). Limitation of tumors to the caudal vertebrae of Late Cretaceous hadrosaurs warrants an explanation.

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