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Radiographic Incidence of Spinal Osteopathologies in Captive Rhesus Monkeys (*Macaca mulatta*)

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Degenerative spinal disease is a leading cause of chronic disability both in humans and animals. Although widely seen as a normal occurrence of aging, degenerative spinal disease can be caused by various genetic, iatrogenic, inflammatory, and congenital factors. The objective of this study was to characterize the degenerative spine-related diseases and the age at onset in a random subpopulation of 20 captive rhesus monkeys (*Macaca mulatta*; male, 13; female, 7; age: range, 4 to 27 y; median, 18.5 y). Spinal radiographic evaluation (left lateral, right lateral, and ventrodorsal views) of the spinal column (C1 to S1) was performed, and spinal degenerative disease was scored. The incidence of osteopathology was higher in the 14- to 18-y-old group, but incidence did not differ according to sex. In the studied population, degenerative changes were present in monkeys as young as 9 y of age.

Degenerative spine disease comprises several abnormalities, including the formation of osteophytes, narrowing of the intervertebral space by disc collapse, and facetary arthrosis, which involves the facetary and intervertebral joints, and is affected by the torsion forces and axial load generated in the lumbar spine.[2] The bipedal posture of humans has prompted various anatomic modifications, generating compensatory changes that become functionally inadequate later in life. This adaptation has resulted in excessive tension in the lumbosacral region, producing accelerated aging and degenerative changes on the column.[15,19] Degenerative spinal disease has diverse causes, including genetic, congenic, inflammatory, and iatrogenic. These osteopathologies frequently appear in conjunction with motility deficits or functional disorders. The degree of deterioration depends on the specific problem and the severity at onset.[8,18] Several researchers have developed models of degenerative spine disease in various species.[1,9,10,11,14,16,17,22,23] The principal objective of the current study was to determine the degenerative changes and age at onset in a captive rhesus monkey (*Macaca mulatta*) population in which the animals were 4 to 27 y of age.

Materials and Methods

This research was undertaken in adherence of the NOM-062-ZOO-1999[20] and was approved by our local IACUC and by the Ethics and Research Commission of the Investigation Center Proyecto CAMINA para Curar la Parálisis AC (Civil Association). This study involved a random subpopulation of 20 rhesus macaques (7 female: age, 10 to 27 y; weight, 5.50 to 9.50 kg; 13 male: age, 4 to 21 y; weight, 3.57 to 10.70 kg). All the research animals were donated by the Centro de Investigación Proyecto CAMINA para Curar la Parálisis AC (Mexico City, Mexico).

The monkey colony from which the study population derived consists of 68 macaques (34 female; 24 male; age, 0 to 27 y) maintained in group-housing conditions; the facilities contains 4 sections where all social groups are kept stable to promote animal wellbeing, grooming, and interaction. Building materials consist of seamless concrete flooring, and all interior surfaces are covered with high-impact ceramic tiles. External walls are made of cyclone-fence mesh firmly anchored to walls and floors, to allow the macaques access to morning sun and a natural photoperiod. Roofs provide a safe waterproof covering along the corrals, and steel doors are provided with security latches to keep monkeys from escaping and personnel safe. Daily animal care includes restricted (4% per body weight) twice-daily feeding of pelleted diet (Monkey Diet 5038, PMI Nutrition International, St Louis, MO) containing 25% protein, provided through ad libitum food dispensers designed to avoid physical contact of pellets with feces and urine; fresh water is provided ad libitum by means of an automatic watering system. Medical veterinary care is provided regularly and in adherence to the Mexican NOM-062-ZOO.[20] Tuberculosis testing is performed twice annually, as is routine parasite monitoring.

Radiology. Animals were restrained by using tiletamine–zolazepam (4 mg/kg IM; Zoletil, Virbac Laboratories, Carros, France) to avoid false-positive disk images and to maintain the spine in a single, homogeneous position during the radiology studies.[5,12] Heart rate, temperature, and respiratory frequency were monitored to detect and avoid any hemodynamic alteration during the sedation time.

The protocol for the radiographic studies was based on NOM-157-SSA[21] and we obtained left lateral, right lateral, and ventrodorsal x-ray projections of the spine (C1 to S1; Siregraphs CF,

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Figure 1. (A) A ventrodorsal lumbar radiograph of a 15-y-old, female rhesus monkey with lumbar scoliosis (circled). (B) A ventrodorsal chest radiograph of a 15-y-old, male rhesus monkey with thoracic scoliosis (circled).

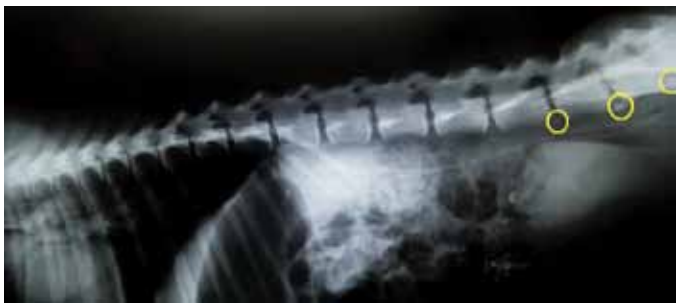

Figure 2. Right lateral radiograph of the lumbar spine of a 10-y-old, male rhesus monkey, with osteophytes (circled) in L6 to L7 and S1.

Siemens Medical Solutions USA, Malvern, PA). After the studies were finished, all animals were closely monitored in individual stainless steel cages (40 × 70 × 60 in.) until total recovery, after which they were reintroduced into their original social group and frequently observed to prevent any aggression.

SPSS for Windows 16 software (SPSS, Chicago, IL) was used for all statistical analyses. A *P* value of less than 0.05 defined statistical significance.

Results

In the study population of 20 rhesus macaques (age, 4 to 27 y), we noted several age-associated vertebral spine pathologies among the older animals, particularly those older than 9 y. The screened population 5 y of age and younger did not present any sort of osteopathy.

Among the 75% of monkeys (8 male [average age, 13 y] and 7 female [average age, 14 y]) showing some degree of osteopathology, scoliosis was the most frequent disease (Figure 1), affecting 46.6% of the population studied. The second most prevalent finding was osteophytosis, which was detected in nearly 40% of the macaques. (Figure 2), Spondylosis and osteoporosis each achieved an incidence of 26.7% (Figures 3 and 4). Of the 15 total animals with osteopathology, 6 monkeys (3 male [average age, 15 y] and 3 female [average age, 19 y]) had multiple osteopathies.

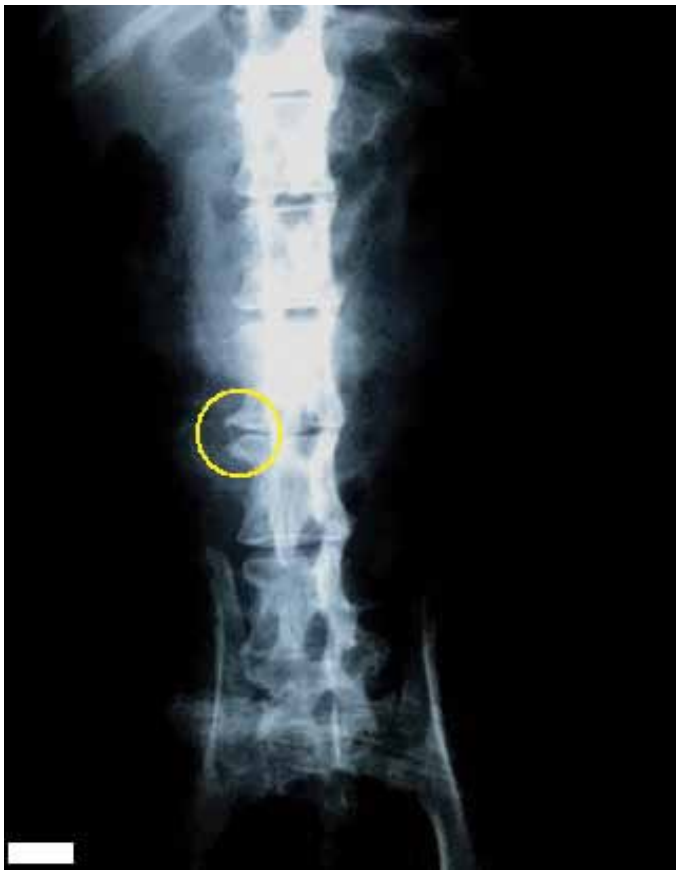

Figure 3. A ventrodorsal radiograph of the lumbar spine of a 21-y-old, male rhesus monkey with right spondylosis (circled) of L4 to L5.

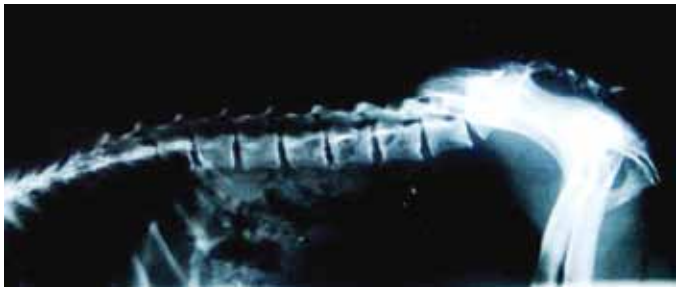

Figure 4. Right lateral radiograph of the lumbar spine of a 9-y-old, male rhesus monkey with osteoporosis (circled) in the lumbar vertebrae.

Pearson χ^2 tests revealed a statistically significant (degrees of freedom, 20; χ^2= 39.954, P = 0.005) difference in the incidence of osteopathology between middle-aged (14 to 18 y) and early middle-aged (9 to 13 y) macaques (Table 1). In contrast, the frequency of osteopathy did not differ (degrees of freedom, 20; χ^2= 6.580, P = 0.254) according to sex; that is, there was a balanced distribution between the appearance of osteopathologies and sex sex (Table 2).

Discussion

Nonhuman primates are valuable models for the study of spinal degeneration, including its contributing genetic or environmental factors involved in the complex mechanism of aging. Related

Table 1. Incidence (no. of cases) by age (y) of spinal osteopathology in 20 rhesus macaques

	Age (y)					
	4–8	9–13	14–18	19–23	24–28	Total no. of cases
Scoliosis	0	1	5	1	0	7
Spondylosis	0	1	2	0	1	4
Osteophytes	0	3	1	1	1	6
Osteoporosis	0	3	1	0	0	4
No pathology	5	0	0	0	0	5
Total no. of cases	5	8	9	2	2	26

Note that 6 macaques had multiple osteopathologies.

Table 2. Incidence (no. of cases) by sex of spinal osteopathology in 20 rhesus macaques

	Sex		
	Female	Male	Total
Scoliosis	2	5	7
Spondylosis	2	2	4
Osteophytes	4	2	6
Osteoporosis	2	2	4
No pathology	0	5	5
Total	10	16	26

Note that 6 macaques had multiple osteopathologies.

factors such as age, sex, familial tendency, number of pregnancies, hormonal imbalances, and metabolic bone disease (in which osteoclastic resorption of bone and formation of fibroosseous tissue is seen even in young macaques[25]) as well as undernourishment, poor nutrient metabolism, and diverse other factors may be involved in the manifestation of this disease.[2,3,9,13]

Body proportions and the associated biomechanics vary greatly among primate species. Primary differences reflect morphologic function, growth, maturation, composition, metabolism, and the biomechanical characteristics of the musculoskeletal tissues.[23] Humans walk in a bipedal manner whereas most other primates are quadrupeds, leading to the observed differences in locomotive structure and axial load.[19] In addition to genetic similarities, nonhuman primates have similar endocrinologic and reproductive cycles to those of humans.[4] Aging is associated with a gradual reduction of bone density in men and premenopausal women, starting around the fourth decade of life. In the present study, most of the macaques were aged adults (15 y and older); therefore, the observed loss of bone density or presence of osteopathology may reflect hormonal changes. Studies evaluating the effects of maturation and aging on the bone mineral content of female rhesus monkeys at sites analogous to those evaluated in humans revealed that through the first decade of life, bone mineral content actually increased in female macaques but subsequently decreased in older monkeys.[3,7]

Even though a number of studies have assessed the incidence and characteristics of spinal osteopathologies,[10,11,24] little is known about the age of onset of osteopathologies that accompany age-related changes in bone density in animal models.[4] One of the most common osteopathologies in baboons was a decrease in the bone mineral density.[13] This finding links degenerative changes caused by osteoporosis and aging in macaques; subsequent to osteoporosis, bone fragility develops, similar to that in humans.

The results of the present study show a clear relationship (χ^2 = 39.954, P = 0.005) between age and the appearance of various osteopathologies in rhesus macaques (Table 1). A discussion of the severity and complications that this complex degenerative disease can cause over time is beyond the scope of this report, primarily because we radiographically monitored only 20 monkeys. A common finding was that age plays a critical role in the development and incidence of the disease.

The first age-associated sex-independent osteopathology we noted was osteoporosis, appearing in male macaques as young as 10.5 y and in female monkeys as young as 13.5 y. This finding is consistent with earlier studies[9,10] that evaluated the relationship between age, hormonal factors (such as decreased steroids), and the presence of late osteoarthritis and osteoporosis in rhesus monkeys. We did not evaluate hormonal status in the current study, but the radiographic findings clearly demonstrated the appearance of osteoporosis corresponding to chronologic age. Another study[6] found that the lower thoracic and lumbar spine of aged rhesus monkeys have increased susceptibility to fractures because of increased fragility due to osteoporosis. The incidence of this osteopathology in the semicaptive animals of the earlier study[5] was similar to that we appreciated in captive animals.

Diverse methods have been used to study scoliosis in experimental animals. A comparative study of the muscle fibers of the dorsal rhomboid and cervical muscle in rhesus monkeys and humans was performed to determine the value of rhesus as an experimental model for idiopathic scoliosis.[2] Another study[23] investigated the presence of experimentally induced scoliosis in a group of macaques (*Macaca fascicularis*) and found that the most common anatomic site for scoliosis was the lumbar area of the spine. In our present study, scoliosis occurred mainly in male macaques, most often in the thoracic and lumbar regions. Interestingly, in the population we monitored, scoliosis was a noninduced, natural age-related defect that occurred both in male and female macaques, with the sole difference between the current study and that cited[23] being the area in which lesions occurred.

In conclusion, the importance of studying degenerative diseases of the spine lies in the prevention of potential complications. The degenerative changes that emerge in rhesus macaques are related to the age of the animal. In rhesus, spinal degeneration begins at approximately 9 y of age, thus showing clinical and chronologic similarities to osteopathologies in humans. These

similarities make rhesus macaques (and perhaps nonhuman primates in general) excellent experimental models for the application of new treatments.

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