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Characterization of Spontaneous Subclavian Steal Phenomenon in a Female Rhesus Macaque (*Macaca mulatta*)

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In subclavian steal phenomenon (SSP), the subclavian artery develops a stenoocclusive disease proximal to the origin of the vertebral artery, leading to pronounced hemodynamic changes such as arterial flow reversal. Although SSP is a common echographic finding in humans, the phenomenon occurs only rarely in animals; consequently its physiologic features have not been reported previously. Here we describe the clinical and morphologic features of a spontaneous left SSP that was an incidental finding in an 18-y-old female rhesus macaque (*Macaca mulatta*). Our findings were documented through high-quality imaging studies obtained by using a computerized 3D tomography apparatus and clinical assessment of systolic and diastolic blood pressures.

Abbreviations: SSS, subclavian steal syndrome; SSP, subclavian steal phenomenon; BP, blood pressure; TB, tuberculosis tests; CAT, computed axial tomography–angiography.

The medical term 'subclavian steal' is used to describe retrograde filling of the vertebral artery, associated with either occlusion or stenosis of the proximal subclavian artery.[4,6,7,13] The subclavian steal designation was coined in 1961,[7] along with reports of 2 human cases of this uncommon condition.[25] The causes leading to this rather complex clinical subclavian stenosis may be congenital, acquired, or surgically induced in laboratory animals.[3,5,14,16,20,24,25] Peripheral arteriopathy, atherosclerosis, syndromes such as neurovascular twisting or stretching, and metabolic diseases such as diabetes, hypertension, and cholesterolemia have been suggested to predispose the development of this condition.[5,6,10,17,20,23] Typically this hemodynamic phenomenon presents unilaterally, affecting the left subclavian artery.[3,4,19,20]

Given the position that nonhuman primates occupy within the evolutionary tree, these species have the nearest phylogenetic relationship to humans.[8,11,27] In particular, the vascular systems of humans and rhesus macaques have analogous anatomic structures and similar physiologic functions. In humans and rhesus macaques, the right subclavian artery arises from the brachiocephalic artery, whereas the left subclavian arises from the convexity of the aortic arch. The left subclavian artery then travels below and behind the clavicle until reaching the external border of the first rib, where it becomes the axillary artery.[1,13]

In light of the potential clinical influence of subclavian steal phenomenon (SSP) and the novelty of this condition in animal models, we here describe the diagnosis and characterization of a left subclavian steal phenomenon that was an incidental finding on a routine computerized axial tomography (CAT) scan of an 18-y-old female rhesus macaque.

Clinical Case

During the annual health monitoring of the monkey colony at our institution (Centro de Investigación Proyecto Camina AC), random CAT scan studies with clinical assessments are performed in the primate population, leading to the incidental discovery of a significant reduction in the diameter of the left subclavian artery (Figures 1 and 2) in an 18-y-old female rhesus macaque (*Macaca mulatta*; weight, 8500 g). Clinical evaluation revealed reduced blood pressure (systolic/diastolic, 91/47 mm Hg) in the left forelimb. The macaque seemed lethargic and slightly underweight, and blood pressure in the right forelimb was 117/68. The decreased blood pressure in the left forelimb was remarkable, given that the normal for rhesus macaques is approximately 125/75 mm Hg.[9,18]

The affected macaque has been housed in this colony since her birth and showed no prior or suggestive symptoms of this disease. The colony comprises 68 macaques (34 female, 24 male; age, 0 to 27 y) maintained in group housing. The facilities contain 4 sections, where all social groups are kept stable to promote animal wellbeing, grooming, and interaction. Buildings include 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 access to morning sun and a natural photoperiod. Roofs provide a safe, waterproof covering along the corrals, and steel doors provided with security latches keep macaques from escaping and personnel safe. Daily animal care includes restricted (4% body weight) twice-daily feeding of pelleted diet (Monkey Diet 5038, PMI Nutrition International, St Louis, MO) containing 25% protein and provided in 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. Medi-

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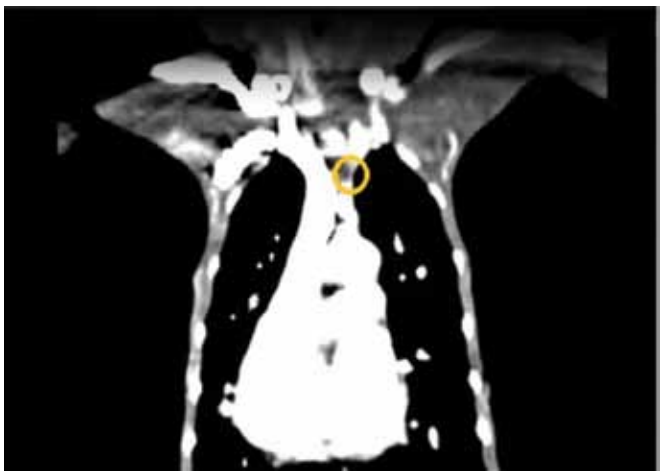

Figure 1. Ventrodorsal chest tomographic image of an 18-y-old, female rhesus monkey with SSP. The circle indicates stenosis of the subclavian artery.

cal veterinary care is provided regularly and in adherence to Mexican NOM-062-ZOO.[21] Tuberculosis testing is performed twice annually, with negative results, as is routine parasite monitoring. All experimental manipulations were performed according to NOM-062-ZOO-1999[21] and were approved by our local IACUC and the Ethics and Research Commission of the CAMINA Research Center.

To confirm this arterial pathology, the macaque was anesthetized lightly with tiletamine–zolazepam (4 mg/kg IM; Zoletil, Virbac Laboratories, Carros, France) and assessed with computerized tomography angiography.[2,9,21]

Tomographic technique. Once the macaque was restrained, scans of the lateral superior cervical spine region were obtained by using computerized 3D tomography equipment (Somaton Sensation, 3D model, Siemens Medical Solutions USA, Malvern, PA) according to guidelines of the NOM-157-SSA1-1996.[22] Briefly, the macaque was placed on a resting board in supine position; the cephalic vein was cannulated by using a 22-gauge catheter (Insyte 0.9 × 25 mm, Becton Dickinson, Franklin Lakes, NJ), followed by slow administration of nonionic contrast medium (0.3 to 0.5 mL/kg; Iopamidol, Iopamiro 370, Schering AG, Berlin, Germany).

Angiographic study and parameters. For image reconstruction, we used specialized software (Sensation S64, Siemens Medical Solutions USA) calibrated to the following parameters: slice collimation, 32 × 0.6 mm; gantry rotation time, 0.33 s; 120 kV; 135 mA; and distance, 60 and 80 cm. An anterior mediastinal window and a single medium-soft filter (B30f Kernel, Somaton Sensation, 3D model, Siemens Medical Solutions USA) were used to enhance image quality.

Visual observation of the obstructive condition in the tomograph (Figure 2), combined with knowledge of the blood pressure deviations encountered in both limbs, confirmed the diagnosis of left SSP secondary to severe stenosis of the proximal left subclavian artery.

Discussion

SSP is considered a rare syndrome and can be classified according to the resulting hemodynamic alterations in the vertebral artery.[19] Furthermore, SSP can be defined into 4 types according to the territory from which blood is 'stolen': vertebrovertebral, carotid–basilar, external carotid–vertebral, and carotid–subclavian (which occurs only after occlusion of the brachiocephalic artery).[26] Another classification system is based on vertebral artery hemodynamics and establishes 3 phases of abnormalities, ranging from stage I to III, which indicate increasing subclavian artery occlusion.[4] Early proximal stenosis of the subclavial artery diminishes systolic blood flow at the ipsilateral vertebral artery; the condition worsens with time and is followed by systolic and diastolic retrograde flow of the vertebral artery. These signs are a clear indicator of high-degree subclavian arterial stenosis or occlusion, resulting in decreased blood pressure in the arm distal to the stenoocclusive disease.[15,24,25] The macaque we present demonstrated a noticeable decrease in the arterial blood pressure of the left forelimb (91/47 mm Hg), in comparison to the near-normal pressure registered for its right forelimb (117/68 mm Hg). Definitive diagnosis of SSP in this macaque rested on physical exam findings combined with appropriate anamnesis and clinical observations to detect deviations from normal ambulatory patterns and behavior. Finally, the macaque's abnormality was assessed by using noninvasive imaging studies including CAT scans, from which hemodynamic and angiographic findings were evaluated carefully. Other diagnostic tools include Doppler ultrasound examination of the neck arteries, aided with contrast studies and magnetic resonance imaging.[10,12,15,17] Because SSP is a morphologic defect, most occurrences are asymptomatic in animals, even though much information about SSP in humans has been reported.[12] In our macaque case, SSP was an incidental finding that presented during annual health monitoring routines. Our literature search failed to yield any previously documented case of spontaneous SSP in laboratory nonhuman primates.

Conclusion

This report emphasizes that although veterinary clinical care is provided to our colony on a daily basis, a comprehensive evaluation of each monkey takes place only periodically, leaving unnoticed and unattended potential ischemic events derived from SSP or any other subtle pathology that could be expected in light of the subject's age. In humans, clear signs of SSP and other potential ischemic events, including dizziness, unsteadiness, vertigo, and vision changes, become apparent after 50 y of age and typically are related to vertebrobasilar and posterior cerebral ischemia.[20] Conversely in animals, specific signs related to SSP are rare, perhaps masked by mild clinical changes and frequently going unnoticed. Therefore, observation of a lethargic animal with an unexplained motor motion among a small cohort of monkeys is incomplete in the absence of modern diagnostic tools such as 3D CAT scans, which provide comprehensive, accurate anatomic information. The present work demonstrates the advantages derived from using current imaging methods for precise diagnosis of highly infrequent pathologies such as SSP in nonhuman primates and stresses the need for further monitoring of descendants of our original foundation stock (imported from India in the late 1970s), given that an inbreeding factor could be involved.

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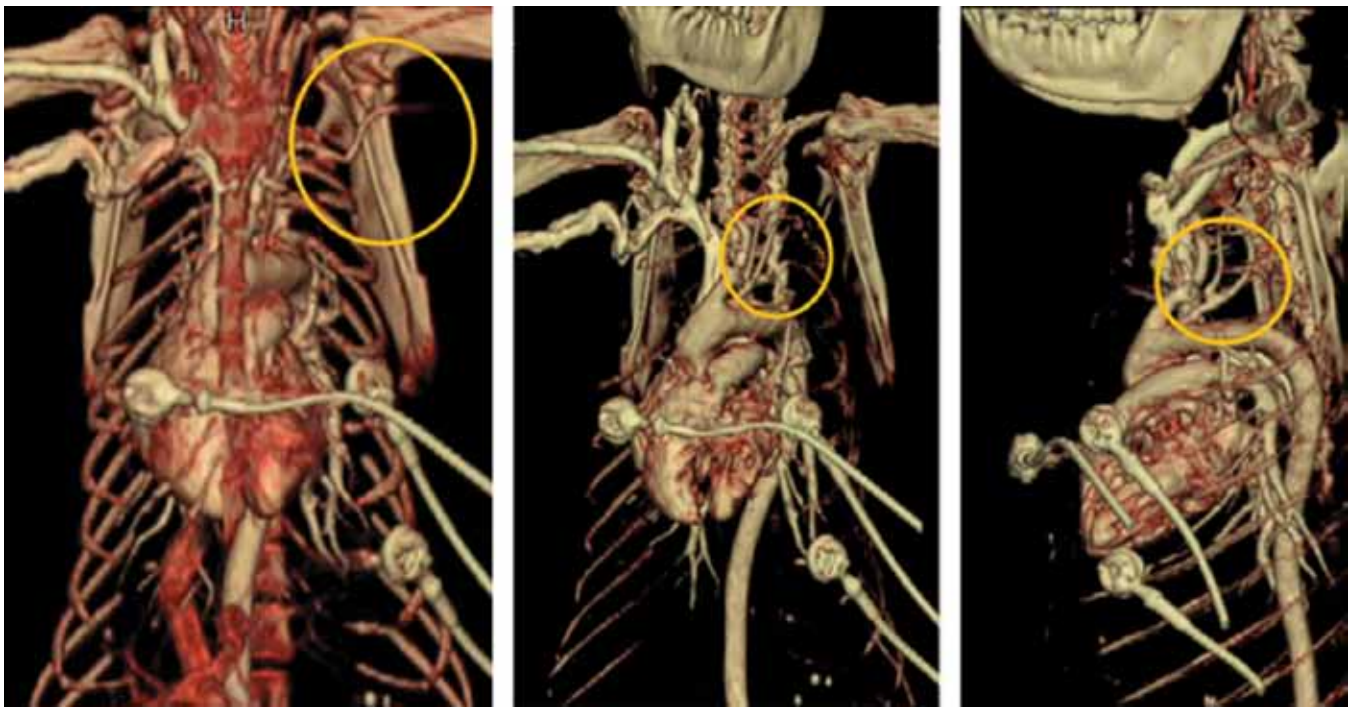

Figure 2. CAT scan showing stenosis of the left subclavian artery in an 18-y-old-female rhesus macaque.

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