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A complicated form of spontaneous aortic atherosclerosis in an African green monkeys (*Chlorocebus aethiops sabaeus*) male Clinical case

Forma complicada de ateroesclerosis en un macho de mono verde africano (*Chlorocebus aethiops sabaeus*) Caso clínico

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ABSTRACT

Atherosclerosis is the mechanistic basis of cardiovascular disorders manifested by damage to the walls of the aorta, coronary, cerebral and peripheral arteries, leading to the development of acute or chronic ischemia of internal organs and tissues. This publication describes a case of spontaneous atherosclerotic lesion of the aorta with the formation of a dissecting aneurysm in an African green monkey male. The ancestors were introduced from Ethiopia and Europe. The case monkey was housed as a family group in an outdoor enclosure with attached smaller room equipped with heating system. It lived 16.4 years. Pathological diagnosis was established through complete autopsy and histopathology. Main disease was chronic atrophic gastroenterocolitis in exacerbation complicated with alimentary dystrophy, cachexia (brown atrophy of the myocardium, liver, skeletal muscles). The concomitant diseases: complicated atherosclerosis of the aorta, dissecting abdominal aortic aneurysm with a large cylindrical organized thrombus in the aneurysm area, stenosing atherosclerosis of the renal arteries, vascular wrinkled left kidney; focal atherosclerosis of the coronary arteries and their branches with small foci of atherosclerotic cardiosclerosis and arteriosclerosis of cerebral arteries. The revealed changes indicate a significant similarity in the pathomorphogenesis of atherosclerotic lesions in African green monkey and humans. It allows us to consider this genus of primates as a promising laboratory model for studying the pathogenesis and mechanisms of regression as well as the effectiveness of therapeutic approaches to the treatment of atherosclerosis and its complications.

Key words: Atherosclerosis; aneurysm; kidney diseases; primates; monkeys

RESUMEN

La aterosclerosis es la base mecánica de los trastornos cardiovasculares, que se manifiestan en el daño a las paredes de la aorta y las arterias coronarias, cerebrales y periféricas, lo cual lleva a la isquemia aguda o crónica de órganos y tejidos internos. La publicación describe un caso de lesión ateroesclerótica espontánea de la aorta, con la formación de un aneurisma disecante en un mono verde africano macho. Los antepasados fueron introducidos desde Etiopía y Europa. El mono descrito en este estudio de caso fue alojado por un grupo familiar en un recinto al aire libre con una habitación adjunta más pequeña equipada con un sistema de calefacción. Vivió 16,4 años. El diagnóstico patológico se estableció mediante autopsia completa e histopatología. La enfermedad principal fue gastroenterocolitis atrófica crónica con exacerbación complicada con distrofia alimentaria, caquexia (atrofia parda del miocardio, hígado y músculos esqueléticos). Las enfermedades concomitantes: aterosclerosis complicada de la aorta, aneurisma disecante de la aorta abdominal con un gran trombo cilíndrico organizado en la zona del aneurisma, aterosclerosis estenosante de las arterias renales, riñón izquierdo vascular arrugado; aterosclerosis focal de las arterias coronarias y sus ramas con pequeños focos de cardiosclerosis aterosclerótica y arteriosclerosis de las arterias cerebrales. Los cambios detectados indican una similitud significativa en la patomorfosis de las lesiones ateroescleróticas en el mono verde africano y en los humanos. Esto nos permite considerar este género de primates como un modelo de laboratorio prometedor para estudiar la patogénesis y los mecanismos de regresión, así como la eficacia de enfoques terapéuticos para el tratamiento de la ateroesclerosis y sus complicaciones.

Palabras clave: Arteriosclerosis; aneurisma; enfermedades renales; primates; mono

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INTRODUCTION

Atherosclerosis is the main cause of morbidity and mortality of patients with cardiovascular disease which is caused by damage to the coronary, cerebral and peripheral arteries, leading to the development of heart attacks, strokes, and ischemic organ damage [1, 2, 3]. Initial atherosclerotic lesions are detected already in the second decade of a human life. However, obvious clinical manifestations usually appear many decades later [4, 5]. The pathomorphological substrate of atherosclerosis includes in early stages fatty dots and streaks, but later atheromas (lipid and fibrous atherosclerotic plaques) appear in the arterial wall. Hence, the complicated course of the latter with calcification, rupture and thrombosis, intraplaque hemorrhages, fragmentation, and weakening of the vascular wall leads to obvious clinical manifestations. They depend on progressing vascular wall rigidity, narrowing of the arterial lumen (due to thrombi and spasms caused by vasoconstriction autacoids generated by unstable atheroma), embolism and aneurysms [4, 5, 6]. Both environmental factors and genetic predisposition contribute greatly to the development of atherosclerosis [5, 6, 7].

Atherosclerosis is observed in animals also. Some animal species, including rabbits (*Oryctolagus cuniculus*), pigs (*Sus scrofa domesticus*), and monkeys (New World monkeys: *Saimiri* spp., *Callithrix* spp.; Old World monkeys: *Macaca mulatta, Macaca fascicularis*, *Papio* spp., *Chlorocebus aethiops* ssp.), are well–established laboratory models of atherosclerosis, while others, such as dogs (*Canis lupus familiaris*), hamsters (*Cricetinae*), mice (*Mus musculus*), rats (*Rattus norvegicus*), cats (*Felis catus*), guinea pigs (*Cavia porcellus*), are less susceptible to developing atherosclerosis and have been used to a lesser extent or after genetic modifications and/or under certain additional conditions only [8, 9, 10]. Among them, a special place is occupied by nonhuman primates, which have the greatest phylogenetic similarity with humans compared to other species [9, 10]. Nonhuman primates were extensively used to study dietary (high fat, high cholesterol, etc.) induced atherosclerosis and are well characterized as the model [10]. However, there is an alternative point of view, according to which the atherosclerotic lesions in humans and most of animals have a completely different etiology, pathogenesis, a different macroscopic appearance and location/distribution within the arteries, as well as different structure of the fibrous capsule [11].

Publications about the manifestations of spontaneous atherosclerosis in animals exist but are rare [12, 13]. Thus, in dogs, spontaneous atherosclerosis is rarely registered, with one study reporting it only in 30 out of 6300 dogs (0.5%, autopsy data). Among the affected dogs, sixteen had normal serum cholesterol levels without any identified endocrinopathies, suggesting a role for some other factors in the development of spontaneous atherosclerosis in them [14]. Therefore, descriptive studies of the manifestations of spontaneous atherosclerosis in animals are of significant value for the formation of the true concept on the etiology and pathogenesis of this disease in both humans and animals.

The paper presents case of a pathomorphological study of a *Chlorocebus aethiops sabaeus* male monkey with spontaneous complicated form of aortic atherosclerosis: a widespread atherosclerotic lesion of the aorta with the formation of a dissecting aneurysm, stenosing atherosclerosis of the renal arteries and a vascular wrinkled kidney.

MATERIALS AND METHODS

Animals

The study was performed on archival (study of autopsy reports) and current pathological and clinical veterinary material of the family (TABLE I) of African green monkeys (*Chlorocebus aethiops sabaeus*).

TABLE I
Closest relatives of the Proband

Inventory No	Kinship	Date of birth	Date of death	Longevity, years
35138	Proband	27/05/2003	03/11/2019	16.4
1500	Mother	14/05/1984	09/01/2006	21.7
32108	Father	27/09/1995	23/08/2007	11.9
34368	Brother	13/06/2001	30/10/2012	11.4
36246	Brother	20/06/2005	09/01/2006	0.6
40386	Child, male	22/10/2012	31/07/2014	1.8
44260	Child, female	18/07/2017	alive	5 years old at the study time
45403	Child, male	12/11/2018	alive	4 years old at the study time

Proband – male inv. No. 35138 was born on May 27, 2003, healthy, full–term, but small for date (TABLE II). Throughout his life, it was healthy according to regular veterinary examinations. At the age of 6 years, on November 24, 2009, it was treated for a laceration of the scalp (blood test dated November 27, 2009 – red blood cells $3.8 \times 10^{12} \cdot L^{-1}$, white blood cells $5.1 \times 10^{9} \cdot L^{-1}$, erythrocyte sedimentation rate 8 mm/h), was discharged from veterinary unit on December 12, 2009 being clinically healthy. It died on November 3, 2019 at the age of 16.4 years. At the time of death, the emaciation was registered.

TABLE II
Body weight of Proband in different periods of life

Date	12/08/2003	19/10/2006	09/06/2017	03/11/2019
Age, years	0.2	3.4	14.0	16.4
Body weight, kg	0.4	3.8	6.7	3.8*
Reference body weight range for males, kg [15]	0.4–1.2	5.0–7.8	6.6–10.6	7.3–9.2

*: Body weight at autopsy

Husbandry

The colony of African green monkeys of Kurchatov Complex of Medical Primatology (formerly Research Institute of Medical Primatology, Sochi, Russia) accounts 42 male and 90 female monkeys. The Proband family originated from Ethiopia and Europe. The Proband belongs to second generation born in the colony after introduction of originating monkeys. The Proband family was housed as group in outdoor enclosure with 9 m^2 floor area and 2.75 m high fenced with metal mesh and attached smaller room equipped with heating system

to provide protection from bad weather and during the cold season. The animals were fed standard pelleted breeding diet prepared according to the Altromin (Lage, Germany) technique. The pelleted base diet was enriched with fresh vegetables, fruits. Tap water was available *ad libitum*.

Pathomorphological investigation

The Proband animal was subjected to a complete autopsy. Tissue samples were fixed in 10% neutral formalin solution, standard histological processing of the material was carried out in isopropyl alcohol, followed by embedding in HISTOMIX paraffin medium (LLC BioVitrum, St. Petersburg, Russia). Tissue sections 5-7 μm thick were prepared and stained with hematoxylin and eosin (H&E). Morphological analysis was performed on a biological microscope AXIO LAB.A1 (Carl Zeiss Microscopy GmbH, Germany) with digital camera Axiocam 105 color (Carl Zeiss Microscopy GmbH, Germany).

Blood analysis

Blood samples were taken at morning from fasted animals without sedation from the brachial vein into vacuum tubes with K_2EDTA or clotting activator with separation gel. Hematological analysis was performed on a HumaCount 30TS analyzer (Human, Germany). Biochemical analysis of blood serum was performed on a Cobas 6000 analyzer (Roche Diagnostics International Ltd, Switzerland) using commercial kits.

RESULTS AND DISCUSSION

Detailed pathological diagnosis was established for the Proband: The main disease was chronic atrophic gastroenterocolitis, in exacerbation. Complications of the underlying disease were: alimentary dystrophy, cachexia (brown atrophy of the myocardium, liver, skeletal muscles); with the concomitant diseases: complicated atherosclerosis of the aorta, dissecting abdominal aortic aneurysm with a large cylindrical organized thrombus in the aneurysm area, stenosing atherosclerosis of the renal arteries, vascular wrinkled left kidney; focal atherosclerosis of the coronary arteries and their branches with small foci of atherosclerotic cardiosclerosis and arteriosclerosis of cerebral arteries.

Gross anatomical examination revealed that the intima of the aorta was light yellow in color, with gray–yellow spots, stripes and plaques in the thoracic and abdominal portions. In the abdominal aorta, there was an intimal defect with blood penetration into the degeneratively changed media, forming an intramural hematoma with longitudinal dissection of the aortic wall and formation of a large cylindrical thrombus with the signs of its organization. The aneurysmal expansion in this area is clearly visible both on the native preparation and after fixation of the preparation (FIG. 1).

Gerota's fasciae of both kidneys were hardly removable, exposing uneven, fine-grained gray–red surfaces. On section, the kidneys were gray–red in color, with the boundaries of the cortical and medulla layers poorly distinguishable. The left kidney was significantly reduced in size (2.5 × 1.8 × 0.9 cm). The right one was 5.0 × 3.5 × 2.0 cm in size.

Pathohistological examination revealed atherosclerotic changes in the coronary arteries (FIG. 2a–b), perivascular cardiosclerosis and hypertrophy, combined with granular degeneration of cardiomyocytes (FIG. 2c), kidney glomerulosclerosis (FIG. 2 d), arteriosclerosis of cerebral vessels (FIG. 2e–f). In the coronary artery (FIG. 2 b), all layers demonstrated

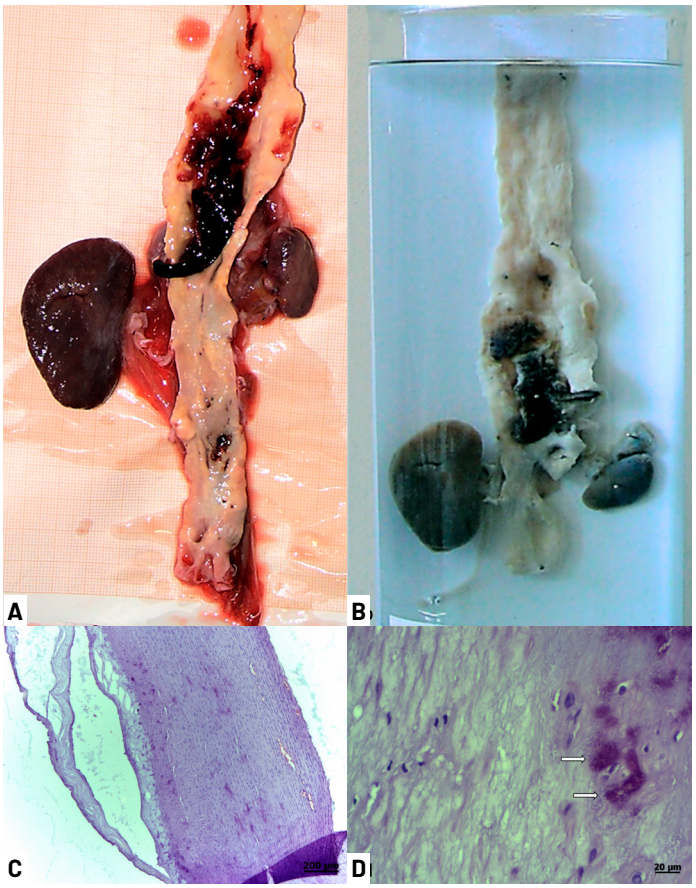

FIGURE 1. Close-up of a pathological specimen and microphotographs of atherosclerotic changes in the aorta. A: Gross specimen of the abdominal aorta and kidneys with atherosclerotic dissecting aneurysm and large cylindrical organizing thrombus. B: Vascular wrinkled left kidney ("small red kidney"). C: Aortic wall of abdominal region. Atherosclerotic plaque. Cleavage of the internal elastic membrane, fragmentation of its fibers, swelling of individual sections of the elastic fiber, H&E staining, 50×. D: Higher magnification of C, 400×, the structure of vascular wall is completely lost at plaque boundary with calcium deposits in the aortic wall (indicated with an arrows)

an altered histoarchitectonics. The intima with endothelium and a relatively wide subendothelial layer had an uneven surface protruding into the vessel lumen. The subendothelial layer was poorly defined. The media consisted of the circular bundles of smooth muscle cells. Collagen fibers of the loose fibrous connective tissue of the adventitia were oxyphilic. The vasa vasorum were located in the adventitia. Clearly, the proliferation of connective tissue is a direct continuation of the inner layer of the intima with the involvement of the media.

Family anamnesis of the Proband was available. The closest relatives of Proband, according to archival data of anatomical pathology department, also suffered from several inflammatory and metabolic diseases. The mother of Proband, who lived for 21 years, was diagnosed with catarrhal colitis, amyloidosis of the liver and kidneys. The father, who lived for 11 years, died of cirrhosis of the liver, and chronic atrophic gastritis which was also established as the concomitant disorder. Proband had two brothers: a male inv. No. 34368 that lived for 11 years (the cause of its death was acute enterocolitis) and male inv. No. 36246, who died of pneumonia in early childhood, being just 7 months old. Proband had offspring (3 animals). These are: a male inv. No. 40386 lived – 1.8 years, died of pneumonia

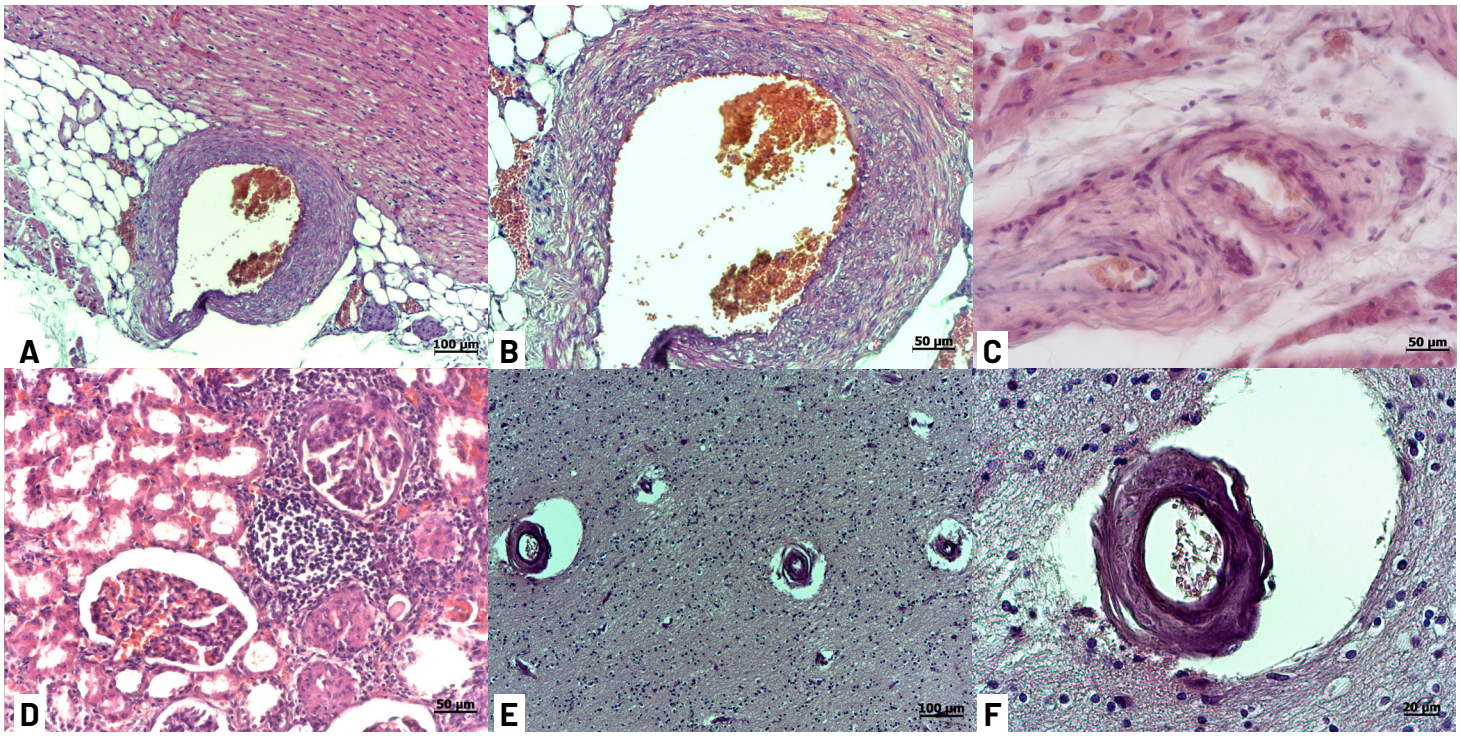

FIGURE 2. Microphotographs of the arteries and kidney. A: The anterior interventricular superficial branch of the left coronary artery (ramus interventricularis anterior arteriae coronariae sinistrae). Uneven thickening of the vessel wall, moderately severe coronary atherosclerosis, H&E staining, 100×. B: Higher magnification of A, 200×, the intima with endothelium and a relatively wide subendothelial layer has an uneven surface protruding into the vessel lumen. C: The anterior wall of the left cardiac ventricle. Perivascular cardiosclerosis and hypertrophy, combined with severe granular degeneration of cardiomyocytes. H&E staining, 200×. D: Right kidney. Glomerulosclerosis. Focal lymphocytic infiltration in the stroma, H&E staining, 200×. E: Prominent arteriosclerosis of the walls of the vessels of the brain tissue substance – uneven thickening, splitting of the walls and narrowing of the lumen of the vessels. H&E staining, 100×. F: Higher magnification of E, 400×, compaction and thickening of the artery wall due to growth of fibrous tissue

and 2 more descendants alive at the time of the study: inv. No. 44260, a female, age at the time of the study – 5 years and inv. No. 45403, a male, age at the time of the study – 4 years. Both living descendants of Proband are clinically healthy. They were subjected to blood sampling for hematological and biochemical tests (TABLE III).

The analysis of lipid profile showed that the daughter of Proband had a severe hypertriglyceridemia – 142.5 mg·dl^{-1}, while the reference data for a population comparable in age and sex are 46.5 ± 18.1 mg·dl^{-1}. Total cholesterol level (182.09 mg·dL^{-1}) was above upper limit of reference values.

TABLE III
Data of hematological and biochemical analysis of blood of Proband's descendants

Index	The examined animals		Reference values (x̄ ± SD)	
	Inv. No. 44260, female	Inv. No. 45403, male	females	males
White blood cells × 10^{9}·L^{-1}	13.44	6.80	8.10 ± 3.32 ¥	6.15 ± 1.97 ¥
Red blood cells × 10^{12}·L^{-1}	5.79	7.30	5.61 ± 0.64 ¥	6.18 ± 0.57 ¥
ALT, U·L^{-1}	62.10	24.70	19.54 ± 14.23 ¥	28.44 ± 14.74 ¥
AST, U·L^{-1}	41.70	26.10	27.88 ± 16.71 ¥	33.40 ± 24.31 ¥
Alkaline phosphatase, U·L^{-1}	201.00	94.00	312.56 ± 168.36 ¥	259.02 ± 108.04 ¥
Urea, mmol·L^{-1} (urea nitrogen, mg·dL^{-1})	5.80 (16.2 mg·dL^{-1})	7.50 (21.0 mg·dL^{-1})	20.1 ± 5.1 mg·dL^{-1} §	19.8 ± 4.4 mg·dL^{-1} §
Triglycerides, mmol·L^{-1}	1.61 (142.5 mg·dL^{-1})	0.39 (34.5 mg·dL^{-1})	46.5 ± 18.1 mg·dL^{-1} §	38.7 ± 15.4 mg·dL^{-1} §
Cholesterol total (A), mmol·L^{-1}	4.71 (182.09 mg·dL^{-1})	3.54 (136.86 mg·dL^{-1})	127.79 ± 18.49 mg·dL^{-1} ¥ 131.7 ± 18.9 mg·dL^{-1} §	124.47 ± 15.76 mg·dL^{-1} ¥ 114.9 ± 18.4 mg·dL^{-1} §
Cholesterol HDLP (B), mmol·L^{-1}	2.23	2.42	–	–
Cholesterol LDLP (C), mmol·L^{-1}	1.75	0.94	–	–
Atherogenic coefficient = (A-C)/B	1.11	0.46	–	–

¥:data for females aged 3–4 years and for males aged 5–6 years [16], §:data for animals weighing from 1.5 to 7.5 kg without indicated age [17], data in parentheses have been converted from mmol·L^{-1} to mg·dL^{-1}.

African green monkeys, also called "vervets" or "grivets", include several closely related species, are characterized by a lifespan in captivity of up to 32 years. Females reach sexual maturity at 2 years, and males at 5 years. African green monkeys appear to have a moderate prevalence of spontaneous atherosclerosis in the form of aortic fatty dots and streaks. Thus, out of 61 adults, fatty streaks were found in 48%, and among 21 adolescents, in 14%. The foci were characterized by a diameter up to 2 mm, and were localized around the orifices of the branches of the vessels [18]. According to internal data in the colony of African green monkeys of the institution, the atherosclerosis was found in 33% of autopsies of animals over the age of 15 years of both sexes. Main findings were aortic fatty dots and streaks.

Many species of nonhuman primates develop atherosclerosis in a way similar to that in humans. So, the lesions develop first in the abdominal aorta, and then in the thoracic aorta subsequently affecting the proximal sections of the main branches of the epicardial coronary arteries, the common carotid arteries, and finally the cerebral arteries [10]. African green monkeys are susceptible to the development of atherosclerosis when fed the diets with a relatively high amount of cholesterol (0.5–0.8 mg·kcal^{-1}) for a long time (3–5 years). At the same time, diet-induced atherosclerotic lesions in African green monkeys can be complex, and morphologically and biochemically are quite similar to those in humans [10]. The development of lesions occurs approximately twice as intensively in the abdominal portion of aorta than in the thoracic one. Atherosclerosis of the coronary arteries mainly occurs in the proximal sections of the main coronary arteries [10].

The development of the atherosclerotic process in Proband corresponds to the pattern described above according cited references. In the study, Proband showed a pronounced lesion of the abdominal aorta with an atherosclerotic dissecting aneurysm, a large cylindrical organizing thrombus and a vascular wrinkled left kidney due to atherosclerotic damage to the orifice of the renal artery. Less pronounced atherosclerotic changes were in the thoracic aorta and coronary arteries. Arteriosclerosis of cerebral arteries also was found and probably indicates age-related pathology.

The pathomorphological picture of the aneurysm revealed in Proband is similar to that described in humans. Thus, local expansion of a part of the vascular wall is associated with type IV, V, and VI atherosclerotic lesions in humans. Distinct localized external bulges or vascular aneurysms are usually associated with type VI lesions in which the intimal surface is highly eroded. Aneurysms often contain parietal thrombi, both fresh and remnants of old ones. With long-existing aneurysms, thrombotic deposits are usually layered, thrombolysis or thrombi intramural inclusion due to collagen organization are uncommon [19]. Spontaneous bleeding and rupture of the vessel wall is considered an extremely rare phenomenon in large animal models of atherosclerosis and have only been described in coronary arteries of pigs with hereditary LDL hypercholesterolemia or in pigs fed with cholesterol along with streptozotocin-induced diabetes [20, 21].

Formation of aneurysms in experimental diet-induced atherosclerosis was reported in cynomolgus and rhesus monkeys. Aneurysms formed in 13% of cynomolgus monkeys (4 of 31) and 1% (1 of 107) rhesus monkeys on an atherogenic regimen for 16 to 24 months [22]. However, these findings were criticized as authors did not demonstrate aneurysmal dilation in any animal but rather, they reported an increase in the cross-sectional area of the abdominal aortic lumen at one specific site [23].

African green monkeys may be considered as a unique model for spontaneous human atherosclerosis, even among the other nonhuman primates. So, when comparing the metabolism of lipoproteins and their size in rhesus monkeys, cynomolgus monkeys and African green monkeys fed with atherogenic diet with human beings it is in African green monkeys that the change in the lipoprotein profile and the size of lipoproteins is closest to that in humans [10]. Also, effects of diet enriched in saturated fat, monounsaturated fat or polyunsaturated fat on plasma lipoproteins was similar to those seen in humans in this nonhuman primate model [24]. Compared to squirrel monkeys and macaques, African green monkeys have only small increase in liver cholesterol content after long-term feeding of atherogenic diets [25, 26].

It is well known that there are significant individual differences in the development of atherosclerosis under identical conditions in all animal models, including monkeys. The plasma cholesterol response to atherogenic diets among primate species can be low, moderate, or high [27]. This individual variability is thought to be primarily due to genetic factors [10].

In addition, there are significant sex differences in the progression rates of atherosclerosis in African green monkeys. Thus, the area of atherosclerotic plaques in the coronary arteries was significantly larger in male than in female monkeys after 5 years of eating a cholesterol-containing diet, enriched with either saturated or polyunsaturated fats. Female monkeys fed a polyunsaturated fat diet showed no signs of coronary artery atherosclerosis [28]. This fact has been linked to the protective effect of estrogens [29].

An important factor determining the development of atherosclerosis in monkeys is the sociopsychological one. Thus, in social groups in dominant females of long-tailed macaques fed with a high cholesterol diet, the development of atherosclerosis actually not observed, and in subordinate individuals of a lower rank, atherogenesis was at the level observed in males, and in such females the hypercortisolemia, behavioral dysfunction and impaired ovarian function were detected [29].

The presence of endocrinopathy is also an important factor contributing to atherogenesis in animals. When streptozotocin-induced diabetes mellitus was combined with the use of high cholesterol diet in Yorkshire pigs, a 2-fold increase in the risk of atherosclerosis was observed compared with a use of high cholesterol diet alone. The development of atherosclerotic lesions in the aorta, coronary and femoral arteries also accelerated [9]. First successful attempt to obtain atherosclerosis model in carnivores (dogs) was achieved only after high cholesterol diet in them was combined with hypothyroidism [30].

African green monkeys develop abdominal obesity associated with changes in insulin sensitivity and plasma lipid profile, thus clearly demonstrating interactions between metabolic syndrome and cardiovascular diseases [31]. There is also evidence on more severe cardiovascular lesions in nonhuman primates infected with SIV and fed with high-fat diet. Still in African green monkeys SIV infection is nonpathogenic but was exacerbated by high-fat diet [32]. Trimethylamine-N-oxide, a microbial choline metabolism byproduct that is processed in the liver and excreted into circulation, was shown to be involved in the control of atherosclerosis in African green monkeys via miR-146-5p pathway [33]. A study utilizing novel computational approach using individually expression data demonstrated that immune cells, adipocytes, cardiomyocytes,

and smooth muscle cells played a synergistic role in cardiac and physical functions in the aged female African green vervet monkeys by regulation of the biological processes associated with metabolism, inflammation, and atherosclerosis [34].

There are no data on the social status of Proband and the presence of some endocrine pathology in it. In terms of nutrition, all the animals were kept on the same balanced base diet with addition of vegetables and fruits. This makes it possible to exclude the role of the nutritional factor in the development of atherosclerosis in Proband. To evaluate the role of the hereditary factor the available pathomorphological and laboratory studies data of the Proband's relatives were assessed. There were no data on atherosclerotic process among the deceased relatives. Living children of Proband have no clinical signs of obesity and glucose metabolism disorders. The female descendant of Proband alive at the time of the study had an increase in blood level of triglycerides (three times higher than the reference level) and of total cholesterol, which suggests the role of a hereditary factor.

CONCLUSION

Spontaneous atherosclerosis in African green monkeys can develop into pronounced clinical forms. The similarity of the pathomorphological pattern of atherosclerosis and its complications between African green monkeys and humans suggests that this species of primates may be a valuable model for evaluating the pathogenesis and mechanisms of regression, as well as the effectiveness of therapeutic interventions in atherosclerosis.

Availability of data and materials

All data is within the manuscript and available on request from the corresponding author.

Conflict interests statement

The authors declare that they have no conflicting interests.

Informed consent

The conditions for conducting the study on animals corresponded to the standards of the Bioethical Committee of the Federal State Budgetary Scientific Institution "RIMP", approved on the basis of the legal acts of the Russian Federation (GOST 33218–2014. Guidelines for accommodation and care of laboratory animals. Species-specific provisions for nonhumane primates doi: https://protect.gost.ru/document.aspx?control=7&id=202272; Model law on the treatment of animals. Resolution of the plenary meeting of the Interparliamentary Assembly of the CIS Member States No. 29 dated 10/31/2007 doi: https://docs.cntd.ru/document/902092614?marker) and the requirements of the European Convention for the Protection of Vertebrate Animals Used for Experiments or Other Purposes, ETS No. 123. For this article the archival material on animals was used. Blood samples were obtained as part of general veterinary health monitoring and prevention examinations. Additional approval of the study by the Institutional Bioethical Committee was not required.

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