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Tetralogy of Fallot in a Japanese Macaque (*Macaca fuscata*)

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Only a few case reports have described heart diseases in monkeys, and most cases have involved postmortem diagnosis. A newborn female Japanese macaque showed weakness immediately after birth and died 1 d thereafter. Necropsy revealed that the animal had tetralogy of Fallot and patent ductus arteriosus. This report is the first description of tetralogy of Fallot in a monkey.

Abbreviations: PDA, patent ductus arteriosus; VSD, ventricular septal defect

To date, reported cases of congenital heart disease in monkeys have comprised ventricular septal defect (VSD) in a chimpanzee,[2] orangutan,[3] rhesus monkeys,[9,12] hamadryad baboon,[9] cynomolgus monkeys,[7,8] and African green monkey;[7] atrial septal defect (ASD) in a chimpanzee,[6] bonnet macaque,[1] Schmidt's white-nosed monkey,[4] stump-tailed monkey,[7] African green monkey,[7] and hybrid macaque;[9] and patent ductus arteriosus (PDA) in stump-tailed monkey.[7] Cases of multiple congenital heart diseases include atrial septal defect and PDA in cynomolgus and rhesus monkeys[7] and the combination of VSD and PDA in cynomolgus and African green monkeys.[7] Despite these reports of congenital heart diseases, tetralogy of Fallot[10] in a monkey has not been reported previously.

The Japan Wild Animal Research Center maintains and breeds Japanese monkeys (688 as of February 2006) in a closed environment. A newborn animal showed weakness immediately after birth and did not cling to the mother. The neonate was transferred immediately to an intensive care environment but was found dead in the cage the next day. The neonate was female, weighing 472 g; normal newborn Japanese macaques weigh about 500 g. This animal showed normal growth but slightly decreased weight. Clinical chemistry, radiographic evaluation, and thoracic auscultation were not performed prior to death.

External inspection of the cadaver revealed contusion of the head. In addition, the external contours of the heart showed overall expansion. The internal surface of the heart showed severe right ventricular hypertrophy and enlargement of the right atrium, with congenital VSD, overriding aorta, stenosis of the pulmonary valve, and PDA (Figure 1). In light of these findings, this animal was diagnosed as having tetralogy of Fallot and PDA. The head contusion was thought to have been the result of oppression during the parturient canal passage.

The length and width of the heart were 2 cm and weight was 5 g. Necropsy of the heart revealed remarkable pulmonary stenosis. The opening of the arterial duct was extremely large. Therefore, high-volume flow from the left to right short-circuit through the arterial duct may have occurred at birth. These conditions lead to a severe elevation of pulmonary artery pressure, consequently decreasing penetration at the pulmonary artery periphery. The gas exchange in the lungs, which starts immediately after birth, might have been insufficient in this animal. In addition, this animal had a large VSD and concentric hyper-

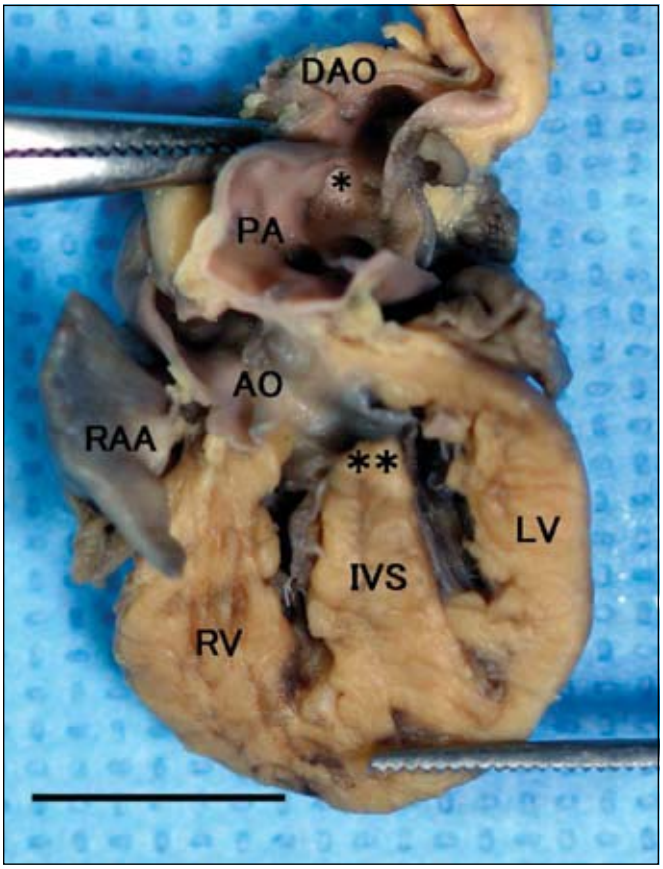

Figure 1. Section along the long axis of the heart of this case. Overriding aorta, right ventricle hypertrophy, pulmonary stenosis, pulmonary artery postvalvular dilation, right auricular dilation, patent ductus arteriosus, and ventricular septal defect were confirmed. AO, aorta; DAO, descending aorta; PA, pulmonary artery; RAA, right atrium and auricle; RV, right ventricle; IVS, interventricular septum; *, ductus arteriosus; **, ventricular septal defect. Bar, 1 cm.

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trophy of the right ventricle. Therefore, the pressure in the right ventricle might have exceeded that in the left ventricle, with subsequent flow of venous blood to the systemic circulation.

In humans, surgery (the Blalock–Taussig method) is performed in cases of tetralogy of Fallot to increase pulmonary blood flow.[11] This technique is a by-pass procedure in which an artificial blood vessel is placed between the arteria subclavia and pulmonary artery to secure an adequate volume blood circulating to the lungs. In the reported animal, blood flowed into the pulmonary artery from the aorta because of the PDA. This state was similar to the circulation established by the Blalock–Taussig method. However, because the opening of the arterial duct was extremely large, it might have lead to pulmonary hypertension at birth.

The frameshift mutation of GATA4 is considered to be a cause of inherited interatrial septal defect and VSD in humans.[5] Genetic examination of the reported animal was not performed. Neither the parents nor other relatives of this monkey showed clinical conditions suggesting heart disease.

Heart diseases in monkeys have not been investigated in detail. In particular, congenital and acquired heart diseases in the Japanese macaque are rare. These monkeys are important in regard to extrapolation to humans in the medical field. Therefore, an investigation of heritable heart diseases in a large-scale Japanese macaque-breeding colony is scheduled.

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