Spontaneous Saccular Cerebral Aneurysm in a Rat

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Summary

A saccular cerebral aneurysm was incidentally found at the bifurcation of a fenestrated anterior cerebral artery of 35-week-old Sprague-Dawley rat. The animal had been fed a normal laboratory diet. The internal lamina extended for a short distance into the neck of the aneurysm and then suddenly disappeared. The medial layer ended abruptly at the neck of the aneurysm. The aneurysmal wall consisted mainly of connective tissue, and of some poorly stained fragments of elastic lamina. No evidence of polyarteritis nodosa or any other inflammatory reaction was obtained. These findings were the same as those observed in man. Therefore, this aneurysm proved to be of truly spontaneous origin.

In contrast to experimental aneurysms in rats and in monkeys, in which aneurysms are observed very often, degenerative changes of the elastic lamina in spontaneous aneurysm in the rat were confined to the neck of the aneurysm. This fact may explain partly the difference in frequency between spontaneous and experimental aneurysms in animals. The present study indicates that degenerative changes of the elastic lamina play a very important role in the development of saccular cerebral aneurysms.

Keywords: Spontaneous aneurysm in animal; elastic lamina; degenerative changes; histopathology.

Introduction

Saccular cerebral aneurysms are extremely rare in animals. This rarity in animals may partly explain why the developmental mechanism of such aneurysms in man is still controversial. So far only 3 cases of spontaneous aneurysm in animals have been reported: 1 case respectively in a llama, in a cow, and in a chimpanzee. In case of the llama and the cow, however, no reliable macroscopic and microscopic descriptions and no details of aetiology were given. Eight cerebral aneurysms were found in the chimpanzee, combined with severe atherosclerotic changes in the cerebral arterial system. But those aneurysms appear not to be spontaneous aneurysms, because severe atherosclerotic changes in the cerebral arterial system were present and the aneurysms were multiple in number to an extraordinary extent. Therefore, it still remained questionable, if “spontaneous” saccular cerebral aneurysms occur in animals.

Recently, a saccular cerebral aneurysm was incidentally found at the bifurcation of a fenestrated anterior cerebral artery (ACA) in a rat whose arterial bifurcations were intended to be used as control in an experimental study. In the present study, histopathology and details of the finding are reported.

Material, Methods, and Results

Cerebral arterial bifurcations of a male Sprague-Dawley rat serving as a control animal, were histopathologically examined. The 35-week-old rat had been fed a standard laboratory diet. The rat was anaesthetized using sodium pantobarbital, 40 mg/Kg i.p. Perfusion was performed with heparinized saline from the descending aorta, followed by a mixed solution of 2% glutaraldehyde and 1.5% paraformaldehyde in 0.1 M phosphate buffer (pH 7.4). After perfusion fixation, the major arteries at the base of the brain were carefully dissected under a microscope. During the dissection, no apparent atherosclerotic or aneurysmal changes were observed in the arterial system. The distal ACA presented fenestration on its left side. The bifurcation of this fenestrated ACA and the bifurcations of the anterior cerebral artery and the olfactory (ACA-OA) of both sides were also dissected for histological examination. The specimens were immersed in 2.5% glutaraldehyde (pH 7.2) for 24 hours, then washed in 0.1 M phosphate buffer (pH 7.4) 3 times and postfixed in 1% osmium tetroxide for 1 hour. After dehydration and embedding in epoxy resin 1 µ semithin sections were stained with 1% toluidine blue.

On light microscopy, no apparent atherosclerotic or aneurysmal changes were observed at the bifurcations of both ACA-OA. At the bifurcation of the fenestrated ACA, a small saccular cerebral aneurysm was found. The internal elastic lamina extended into the neck of the aneurysm for a short distance, and then suddenly disappeared. The medial layer ended abruptly at the neck of the aneurysm. The wall of the aneurysm was thin and consisted mainly of connective tissue and poorly stained fragments of the elastic lamina. There was no evidence of polyarteritis nodosa or any other inflammatory reaction (Fig. 1).
Fig. 1. Spontaneous saccular cerebral aneurysm of the anterior cerebral artery in a rat. The internal elastic lamina extends into the neck of the aneurysm for a short distance then disappears suddenly. The medial layer ends abruptly at the neck. The aneurysmal wall consists mainly of connective tissue (toluidine blue, × 400).

Discussion

Saccular cerebral aneurysms are found in less than 5% of the population, and usually diagnosed in elder people mainly between the 5th and 7th decade \(^{23,26}\). High blood pressure which is rather specific for man, has also some influence on the development of cerebral aneurysms \(^{21}\). These factors may explain the rarity of saccular cerebral aneurysms in animals. Furthermore, to evaluate an accurate study of cerebral aneurysms in animals, it should be necessary to study histopathologically numerous arterial bifurcations of many animals after perfusion fixation. This has been carried out exceptionally with small numbers of animals but thorough and systemic studies have never been performed in spontaneously hypertensive rats. In the present study, a cerebral aneurysm was observed in a rat with the same histological features as the spontaneous saccular cerebral aneurysms found in man.

In the pathogenesis of saccular cerebral aneurysm, two main factors have been stressed: degenerative changes of the internal elastic lamina and the defect or the gap in the medial muscle layer \(^{4,5,8,9,24}\). It still remains debatable which factor plays the most important role in the development of the disease. For the elucidation of the developmental mechanism, many experiments have been carried out. Most of the experimental aneurysms were induced by damaging mechanically the arterial walls. However, saccular cerebral aneurysms at the arterial bifurcations have never been produced by these methods \(^{1,7,10,22,27}\). Without mechanical injuries of arterial walls, some aneurysms were unexpectedly induced in two chimpanzees, which had been fed a high coconut oil diet with cholesterol \(^{2}\). Originally aneurysms were found by chance and it is not certain that aneurysms are able to be induced invariably with these methods. These aneurysms were most likely atherosclerotic, and they might throw little light on the pathogenesis of spontaneous aneurysms. Saccular cerebral aneurysms were induced in rats \(^{11}\) and monkeys \(^{19}\) ligating common carotid artery unilaterally, making them hypertensive, and feeding them beta-aminopropionitrile. In this model, enhanced haemodynamic stress is thought to be essential for the induction of the lesion \(^{12,13,14,19,20}\). Attention must be paid to the fact that it was very difficult to find medial defects in cerebral arterial bifurcations in rats, and that the degenerative changes of the elastic lamina in experimental aneurysms did not correlate with pre-existing medial defects \(^{5,17,18}\). In experimental aneurysms, the elastic lamina in the parent artery was often damaged or disappeared extensively \(^{18,20}\). Therefore, it might be thought that augmented haemodynamic stress is related to diffuse degenerative changes of the internal elastic lamina, and that experimental aneurysms are induced rapidly and frequently in the presence of the diffusely degenerated elastic lamina. On the contrary, the defect of the elastic lamina in the reported spontaneous aneurysm in the rat proved to be confined to the neck of the aneurysm. The medial layer of the parent artery in both aneurysm types did not show any apparent difference. These findings suggest that the degenerative changes of the elastic lamina play a main role in the development of cerebral aneurysms.

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