Natural history of cerebral saccular aneurysms

F. I. Ojini

Institute of Neurology, University College London,
Queen square, London WC1N 3BG
Department of Medicine, College of Medicine,
University of Lagos. P. M. B. 12003, Lagos, Nigeria.
E-mail: fojinif@yahoo.co.uk

Summary

Cerebral saccular aneurysms are relatively common, and are most commonly located at the branching points of large arteries of the circle of Willis. Many are asymptomatic and only discovered incidentally.

Available evidence suggests that these aneurysms develop as a result of a combination of congenital or inherited defects weakening the arterial wall, and acquired degenerative vascular disease.

It appears that most untreated cerebral aneurysms will get larger, and that all aneurysms have the potential to rupture. The only consistent significant predictor of aneurysmal rupture in most studies is the size of an aneurysm. Aneurysms less than 5mm have a very low rupture rate while those greater than 10mm have a significant risk of subsequent rupture. There is no consensus on the influence of the other reported risk factors such as hypertension, cigarette smoking and aneurysm location, on aneurysmal rupture.

Those who have suffered a ruptured aneurysm are at a high risk for a recurrent haemorrhage shortly after the initial one.

Keywords: Natural history, Cerebral saccular aneurysm, Aneurysmal rupture.

Résumé

Anevrismes cérébrum sacculaires sont assez courant, et le plus souvent situés aux points embranchment des grandes artères du circle de Willis. Beaucoup sont asymptomatiques et seulement découvert incidemment. Des preuves disponibles évoquent que ces anévrismes développent à la suite d'une combinaison des défauts congénitaux ou hérités faiblissant la paroi artérielle et la maladie vasculaire dégérative acquise.

Il paraît que la plupart des anévrismes cérébraux non traités seront élargi, et que tous le cas d'anévrismes ouvrent de grandes possibilités de se faire éclater. Le prédicteur important le plus logique de la rupture d'anévrismes dans la plupart des études est la taille d'un anévrisme. Des anévrismes qui sont moins de 5mm ont un taux de rupture beaucoup plus bas tandis que ceux de plus de 10mm ont un risque important de la rupture subseqüente. On n'arrive pas à un consensus sur l'influence d'autre facteur de risque rapportés tels que l'hypertension, fumée de cigarette et l'emplACEMENT d'anévrisme, sur la rupture d'anévrisme ceux qui avaient souffert d'anévrisme rupture sont à haut risque pour une hémorragie périodique peu après le premier.

Introduction

Cerebral aneurysms, often referred to as berry or saccular aneurysms, are outpouchings on arteries most commonly located at the branching points of large arteries of the circle of Willis at the base of the brain. These intracranial aneurysms are probably caused by a combination of congenital defects in the vascular wall and degenerative changes. Much less often, cerebral aneurysms are caused by arterial dissection through the adventitia of arterial walls, embolism of infected or myxomatous material to the vasa vasorum of distal cerebral arteries (mycotic aneurysms), and degenerative, atherosclerotic, elongation and tortuosity of arteries (fusiform aneurysms). These 'acquired' aneurysms are not part of this review.

With improvement in imaging techniques, unruptured intracranial aneurysms are diagnosed with greater frequency, and with improved surgical techniques, surgical treatment is becoming the order of the day. However, the management of these aneurysms remains controversial because of incomplete and conflicting data about the natural history of these lesions, and the risks associated with their repair.

This paper reviews the available literature on the natural history of cerebral saccular aneurysms with a view to highlighting those factors that have been found to be associated with mortality and morbidity. It is hoped that in making a decision on the management of patients with unruptured intracranial aneurysms, the risks of the natural history would be compared with the risks of repair for each patient.

Incidence of cerebral aneurysms

The reported incidence of cerebral saccular aneurysms shows a wide variation in different parts of the world. The prevalence of incidental cerebral aneurysms among adults undergoing cerebral angiography in Europe and North America is reported as between 0.5 and 1 percent. Autopsy series from there report a prevalence of 0.2 to 9.9 percent, with mean of approximately 5 percent. The higher prevalence in the autopsy series is due to small aneurysms undetected by cerebral angiography.

A lower incidence of cerebral aneurysms has been reported from many parts of Africa and the Indian subcontinent, both from autopsy series and angiographic studies. This has given rise to speculations that there may be racial differences in the incidence of aneurysms. Ohaegbulam et al. found whites twice more prone to having aneurysms than the black population in their study of intracranial aneurysms at a hospital in the American state of Michigan. It has been suggested that the incidence of congenital defects in the media of cerebral vessels may differ with various racial groups. However, due to the wide variations in published reports, it is not possible to conclusively support the observations that Asian and African countries have a lower incidence of cerebral aneurysms as compared to
their European counterparts.

Pathogenesis of cerebral aneurysms

The reasons for the development of cerebral aneurysms are not clear, but three main aetiopathogenetic factors have been considered by most studies: congenital or inherited defects weakening the arterial wall, hypertension, and atherosclerosis. Crawford, in his pathological study of ruptured and unruptured cerebral aneurysms, observed that cerebral arteries have poorly developed media and external elastic lamina, and that developmental faults occur quite commonly in the media at the points of arterial junctions. These ‘congenital’ or developmental features are believed to render such arteries particularly prone to aneurysm formation.

Several lines of evidence suggest that acquired factors have an important role in the pathogenesis of intracranial aneurysms. For example, intracranial aneurysms are very rare in children and tend to increase in incidence with age. Hypertension and atherosclerosis are the two main acquired factors that have been identified as being important in aneurysm formation. Some studies however, have not shown an increased risk of cerebral aneurysms with hypertension.

Considerable evidence also support the role of genetic factors in the pathogenesis of cerebral aneurysms. The two main ones are the familial occurrence of aneurysms, and their association with heritable connective tissue disorders such as autosomal dominant polycystic kidney disease and Ehlers-Danlos syndrome type IV.

Stehbens, however, argues forcefully against a congenital or developmental theory of aneurysm formation. According to him, the available evidence overwhelmingly favours causation of aneurysms by ‘haemodynamically induced degenerative vascular disease’, although he did accept that there is probably a predisposition to aneurysm formation in cases of connective tissue disorders in which mural fragility develops.

Growth of cerebral aneurysms

Most workers are of the view that once started, aneurysms tend to enlarge slowly but relentlessly. There is however, considerable evidence in the growth rate of aneurysms. Juvela et al found a growth rate of between 1 and 344 percent per year in their groups of patients. Growth rate was maximal in the aneurysms that ruptured while those that did not rupture during the follow-up period changed little in size. They also found that growth rate was independent of patient’s age, blood pressure, or initial size of the aneurysm. Similar findings were reported by Alcock and Canham.

Aneurysms usually begin to produce clinical effects when they attain a diameter of 6mm to 15mm, and then tend to produce symptoms of mass effect. The most common symptom of an aneurysmal mass effect is headache, and the most common sign is a palsy of the third nerve caused by an aneurysm at the junction of the carotid artery and the posterior communicating artery, or an aneurysm of the upper end of the basilar artery.

However, the most devastating consequence of an aneurysm is spontaneous rupture, which results in the clinical picture of subarachnoid haemorrhage, intracerebral haemorrhage, or both. Unruptured cerebral aneurysms causing a mass effect carry a high risk of subsequent rupture.

Rupture of cerebral aneurysms

The incidence of aneurysmal subarachnoid haemorrhage in the western world is reported as approximately 10 cases per 100,000 per year. This is less than the frequency of 0.5 to 1 percent of incidental cerebral aneurysms among adults undergoing cerebral angiography, or the average frequency of 5 percent in autopsy series. This discrepancy suggests that most cerebral aneurysms do not rupture.

The overall annual rupture rate of cerebral aneurysms from most large studies is 1 to 2 percent per year. The International Study of Unruptured Intracranial Aneurysms Investigators, in their multi-centre study of unruptured cerebral aneurysms found an unusually low rupture rate of 0.5 percent per year. However this arm of their study was retrospective, while the whole study also had so many exclusion criteria, which may have introduced some systemic bias.

There is much less information on ruptured intracranial aneurysms and subarachnoid haemorrhage from the developing world. However, the available studies suggest a lower incidence of both entities than in the developed countries.

A low incidence of risk factors such as atherosclerosis and cigarette smoking has been proposed as reasons for this low incidence.

Risk factors for rupture of cerebral aneurysms

The only consistent significant predictor for aneurysm rupture appears to be the size of an aneurysm. However, there is considerable disagreement in the literature concerning the critical size for aneurysmal rupture. Data presented by Wiebers and colleagues suggest that only cerebral aneurysms that are 10mm or larger in diameter carry a significant risk of subsequent rupture. The ISUIA reported similar findings, with an exceedingly low rupture rate in patients with aneurysms that were less than 10mm in diameter.

Juvela et al could not find any critical diameter above which the risk of rupture increased, but noted a linear association between the risk of rupture and aneurysm size. The critical size for rupture reported by most other studies varied between 5mm and 10mm. McCormick and colleagues, and Kassell and Torner, found the critical size for rupture of aneurysms to be 5mm. Rosentorn et al assessed aneurysmal size in 1044 cases of ruptured aneurysms, and found that the maximum diameter was less than 5mm in 18.4 percent, between 5mm and 10mm in 50.2 percent, and more than 10mm in 31.4 percent cases.

Most of these studies, however, did not properly address the issue of growth of aneurysms. It appears that most untreated cerebral aneurysms will get larger, but there is very little information about the growth rate of these lesions.

Therefore, prediction of which smaller aneurysm will stay below a claimed critical size and which will grow by 5mm this size is quite impossible, and so, an exact probability of rupture cannot be made for a given aneurysm, with a given size, in a given patient.
Another reported predictor of aneurysmal rupture is cigarette smoking. Several studies have found that cigarette smoking is an independent predictor of aneurysm rupture. A meta-analysis of 32 separate studies by Shinton and Beevers found strong evidence of an excess risk of subarachnoid haemorrhage among cigarette smokers. Similarly, the multicentre co-operative aneurysm study involving 3441 patients found smoking a significant risk factor for ruptured aneurysms. The mechanism of this significant association is not clear. It is known that smoking causes an acute increase in blood pressure for approximately 3 hours. This transient increase in blood pressure may contribute to the rupture of an aneurysm. It is also possible that long-term smoking can cause formation of an aneurysm by weakening the vessel walls of cerebral arteries, or increase the size of an aneurysm by the same mechanism.

Studies of hypertension and its role in aneurysm rupture have generally given conflicting results. Phillips et al reviewed the records of all residents of Rochester, Minnesota, who experienced subarachnoid haemorrhage within a 30-year period. They found the prevalence of hypertension in these patients to be similar to the prevalence of hypertension in a normal population of the same age.

Sacco et al, on the other hand, in a similar community-based study, reported that the mean systolic and diastolic blood pressures of subjects who developed subarachnoid haemorrhage in a 26-year prospective follow-up of residents of Framingham, Massachusetts, were significantly higher than for those who did not.

There is similarly no consensus in autopsy studies on the influence of hypertension on aneurysmal rupture. McCormick and Schmalstieg found no significant difference in the prevalence of hypertension in autopsy series of patients with unruptured cerebral aneurysms, ruptured aneurysms, and without aneurysms. de la Monte et al, in a case-control autopsy study, found a high degree of correlation between severe 'acute' hypertension and aneurysm rupture, although the method of defining 'acute' hypertension was not reported. Juvela et al and Wiebers et al, in prospective studies of patients with unruptured cerebral aneurysms followed-up for at least 10 years and 5 years after diagnosis respectively, found that systolic and diastolic blood pressures at the time of aneurysm diagnosis were not significant predictors of subsequent rupture.

The International Study of Unruptured Intracranial Aneurysms reported that the location of aneurysm was a significant independent predictor of rupture. They found that aneurysms in the tip of the basilar artery, vertebrobasilar or posterior communicating artery were more likely to rupture than aneurysms at other sites. On the other hand, Yasui et al in their long-term follow up of 360 conservatively treated patients with unruptured cerebral aneurysms found no significant differences in the risk of rupture according to the aneurysm location.

Multiple cerebral aneurysms

Multiple cerebral aneurysms, usually two or three in number, are found in 20 to 30 percent of patients. Their incidence has been related to the accuracy and completeness of angiography or autopsy. Hypertension, female gender, age and cigarette smoking have all been reported as risk factors for multiple cerebral aneurysms. However, only cigarette smoking and female gender appear to be consistently linked.

In the study by Juvela et al, the presence of multiple unruptured aneurysms per se did not increase the risk of aneurysmal rupture. A similar finding was reported by the investigators in the International Study of Unruptured Intracranial Aneurysms.

Outcome following rupture of cerebral aneurysms

Subarachnoid haemorrhage from a ruptured cerebral aneurysm has a serious prognosis. Despite great progress in the diagnosis and surgical management of aneurysmal subarachnoid haemorrhage, the overall morbidity and mortality has not changed significantly. The overall case-fatality is still approximately 40 to 50 percent. In addition, 10 to 20 percent of patients will remain severely disabled and only approximately 40 percent of patients recover to an independent state after subarachnoid haemorrhage.

In the study of patients with ruptured aneurysm by Rosenon and Eskens, rupture of even the smallest aneurysm was associated with a grave prognosis. Mortality in their group of small aneurysms (47 percent) was nearly as high as in the large aneurysm group (51 percent).

Multiple cerebral aneurysms are reported to be associated with a less favourable outcome than are single aneurysms when rupture occurs. Rebleeding of ruptured cerebral aneurysms

Patients who have suffered a ruptured cerebral aneurysm are at very high risk for a recurrent haemorrhage shortly after the initial one. Lockley, reported on the rebleeding pattern of patients admitted to a co-operative aneurysm study. He reported that rebleeding occurred most commonly at the end of the first week and beginning of the second week after the initial haemorrhage. However, strict objective criteria for rebleeding (such as detection of blood in cerebrospinal fluid) were observed in only 60 to 70 percent of the cases in this study. Some of the reported rebleeding episodes may have actually represented neurologic deterioration on the basis of ischaemic complications of vasospasm, heart attacks, and pulmonary emboli.

Kassell et al, in a more recent co-operative aneurysm study where rebleeding was documented by either lumbar puncture or computerised tomographic scan, reported that 4.1 percent of the 2265 patients admitted to the study rebled during the first 24 hours after initial haemorrhage. The conclusion from this large study with objective criteria for rebleeding is that, the rate of recurrent haemorrhage is at least 4 percent within the first 24 hours, and between 1 and 2 percent per day for the first two weeks.

Conclusion

The natural history of cerebral saccular aneurysms is still incompletely understood. Questions about the development, growth, risk and risk factors of aneurysm rupture are still open.
Many aneurysms are asymptomatic and only discovered incidentally. Most data suggest that small, asymptomatic aneurysms have the lowest natural risk of rupture, with the risk of rupture increasing the greater the size of the aneurysm, especially if accompanied by symptoms of mass effect. Factors which probably further influence the risk of aneurysmal rupture are the presence of hypertension and cigarette smoking.

The presence or absence of the known risk factors for rupture in a patient with berry aneurysm should help in deciding whether to manage such a case conservatively with long term medical follow-up, or to actively manage with surgical repair or endovascular treatment.

The prognosis of subarachnoid haemorrhage from a ruptured cerebral aneurysm remains grave despite advances in the medical and surgical management of this condition.

References


Natural history of cerebral saccular aneurysms - F. I. Ojini


