ANATOMIC CORRELATION BETWEEN INTIMAL PATHOLOGY AND CEREBRAL VASOSPASM FOLLOWING SUBARACHNOID HEMORRHAGE

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ABSTRACT

Subarachnoid hemorrhage (SAH) resulting from a ruptured intracranial aneurysm can induce cerebral vasospasm with subsequent reduction in cerebral blood flow (CBF). The present study examines the pathological alterations in the wall of human cerebral arteries at autopsy, especially with regard to intimal pathology, following aneurysmal SAH. Arterial segments from the circle of Willis were fixed in 10% formalin, embedded in paraffin, sectioned at 4μ and stained with hematoxylin-eosin or toluidine blue. Similar numbers of sectioned vessels were also examined in control material. The areas of intima, lumen and the length of internal elastic lamina were compared with those from control sections. Pathological changes such as myonecrosis and fibrosis in muscular layers associated with a possible loss of compliance and elasticity of the vessel wall were also noted. The average luminal area decreased to 56.8% ± 12.5% compared to comparable controls (p<0.005). The tunica intima was the most abnormal component of the arterial wall with cellular proliferation which was made up predominantly of collagen fibers and loose fibroblasts. These pathological findings are mainly due to myonecrotic changes and intimal proliferation with the resultant luminal constriction and CBF impairment which might explain the high incidence of cerebral infarction in cases of SAH.

Keywords: Subarachnoid Hemorrhage, Cerebral Vasospasm, Intimal Pathology.

INTRODUCTION

Subarachnoid hemorrhage (SAH) usually occurs when an intracranial berry aneurysm ruptures and bleeds into the subarachnoid space.5,6,11,14,15 It is a serious disease with high morbidity (20% to 30%) and mortality (40% to 50%) rates. Despite the progress that has occurred in medical and surgical treatment, the incidence of SAH remains unchanged.5,16,17

The most complicated and disastrous outcome of aneurysmal SAH is mainly due to the development of long-term cerebral arterial narrowing known as "cerebral vasospasm".5,14,15 This can lead to decreased cerebral blood flow, resulting in neurological deficits, cerebral ischemia or infarction, and death. Cerebral arterial spasm is time-dependent, rarely occurs before the 3rd day and reaches its peak around 7-10 days after the bleed.1,11,16,23

The pathoanatomical changes that appear in the major
Intimal Pathology and Cerebral Vasospasm After SAH

Fig. 1. Ventral view of the brain from autopsyed cases of control showing the arterial patterns. Note the anterior cerebral (arrowhead) and middle cerebral (curved arrow) arteries.

cerebral arteries of patients who died at different time intervals following SAH, specifically associated with cerebral vasospasm, have been studied for many years. However, the purpose of this study was two-fold: 1) to examine the histopathological changes of the cerebral arterial wall from the autopsied cases of patients dying after two weeks post-SAH; and 2) to determine the morphometric correlation between the intimal pathology and arterial narrowing which usually occurs following aneurysmal rupture. To our knowledge, this is the first morphometric study of cerebral arterial segments from autopsied cases.

MATERIALS AND METHODS

For light microscopy and morphometry, arterial segments from the circle of Willis of 2 control and 4 autopsied cases of patients who died after two weeks following SAH were fixed in 10% formalin. After several days, they were dehydrated in graded ethanol dehydration prior to embedding in paraffin. Then, the blocks were cut transversely into 4 micron sections, and stained with 1% toluidine blue or hematoxylin-eosin. The light microscopic slides were finally coverslipped and examined by a conventional light microscope. Five sections were taken proximal and distal to the site of aneurysmal rupture from both right and left middle cerebral arteries (M1 portions) and the anterior cerebral arteries (A1 portions) (Fig. 1). The length of the circumference of the internal elastic lamina, and the area of the intima and of the lumen of each human arterial section were measured using a Calcomp 2000 (Anaheim, CA) digitizer interfaced to a BBC computer.

RESULTS

Using light microscopy, the cerebral arteries from control autopsy cases were consistent in morphology with endothelium forming a continuous monolayer overlying a non-convoluted internal elastic lamina. No sign of smooth-
muscle proliferation or necrosis, or of adventitial inflammatory infiltrate was apparent in the control specimens (Fig. 2). Table I shows the mean length of the circumference of the internal elastic membrane, and the areas of the intima and of the lumen of the control arterial sections.

In all of the autopsy cases of SAH studied, pathological changes were found in the anterior and middle cerebral arteries (Figs. 3-5). The intimal cellular proliferation was the most obvious change observed, made up predominantly by the loose fibroblasts and collagen between the corrugated internal elastic membrane and arterial lumen (Figs. 3, 4). This pathological reaction was associated with a corresponding reduction in the area of the arterial lumen (Figs. 2, 6). The internal elastic lamina was frequently found to be abnormal, being markedly infolded and corrugated, but in some areas fragmented and displaced into the lumen (Figs. 3,4). Patchy areas of necrosis in the tunica media with disrupted muscle fibers were the other important findings (Fig. 5). Blood cell infiltration in the adventitia was also seen in most arterial specimens.

Morphometric results are summarized in Table I and in Fig. 6. The results indicated a 53% increase in intimal area, 15% increase in internal lamina length, but a 51% decrease in the luminal area of the arterial sections from autopsied cases of SAH, when compared with control values.

**DISCUSSION**

Today, cerebral vasospasm is recognized as the most important cause of disability and death in patients with SAH. It is time-dependent, as it rarely occurs before the 3rd day following the initial SAH, reaches a peak around the
end of the first week, and continues for two to three
weeks.11,15,20,21.23

In all of the SAH cases that we studied, pathological
changes were found in the tunica adventitia, media, and
intima. Myonecrosis with disrupted muscle fibers and
blood cell infiltration in the adventitia was a common
feature of this arteriopathy. However, the most prominent
change was the severe intimal cellular proliferation causing
eccentric narrowing of the lumen (approximately 55%).
Obviously, none of these vasculopathy changes were
observed in control arterial sections. Peerless et al. suggested
that cellular proliferation and fibrosis in the intima following
SAH indicates a fundamental arterial wall response to
various noxious stimuli. The results agree with the findings
of other investigators that significant intimal thickening is
usually not seen in the first week after hemorrhage, and is
still not prominent till a few weeks have passed.7,10,16 As we
have reported earlier, extensive ultrastructural studies
revealed that endothelial cells were the first to undergo
degeneration and necrosis following experimental SAH in
rats.12,13 However, in contrast to the findings in arterial
sections from autopsied cases of SAH, only mild intimal
thickening, mainly due to the increased amount of
amorphous material within the internal elastic membrane,
was noticed. This may indicate that the mode of
pathoanatomical changes following SAH is different in
rats compared to autopsied cases.

From their classic investigation, Hughes and Schianchi
found that in patients surviving 17 days or less from
aneurysm rupture, the tunica intima was only slightly
swollen, whereas in those surviving longer the intima
became the most abnormal component of the arterial wall
with concentric thickening due to fibroblast cells, collagen
fibers, and macrophages. The same cellular components,
except macrophages, were also observed in the present
study. Therefore, it seems that the delayed appearance of
intimal proliferation (>2 weeks) does not correlate with the
time-course of vasospasm in humans which begins a few
days after the onset of hemorrhage. It is likely that
pathological responses related to the severity of the vessel
wall injury (e.g., endothelial and smooth muscle cell
necrosis) are directly related to the severity of vasospasm.
Whereas the intimal proliferative reaction which usually
occurs later during the course of vasospasm is a non-
specific reaction, it may alter the maintenance of vascular
physiological homeostasis.7,13,21

In summary, the pathological changes that were observed
in intracranial arteries two weeks after SAH are in agreement
with previous studies.7,8,10,15,16,21 In addition to this, our
morphometrical analysis showed a severe reduction in the
arterial lumen with hypertrophy of the intimal layer. This
certainly would affect the rate of blood flow to the cerebral
cortex.

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