THE ROLE OF SMALL ANGIOMATOUS MALFORMATIONS IN THE PRODUCTION OF INTRACEREBRAL HEMATOMAS

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(Received for publication May 10, 1951)

The etiologic background of intracerebral hemorrhage falls readily into certain well defined categories, which include hypertensive-arteriosclerotic apoplexy, aneurysms of the berry or medial-defect type, angiomatous malformations, trauma, blood dyscrasias, and neoplasms. But in any series of cerebral hemorrhages one invariably encounters a group of unknown etiology. To this group certain features are common, namely:

1) occurrence in a relatively young age group;
2) absence of any known predisposing factors, except an occasional history of trauma;
3) suddenness of onset, usually with headache;
4) delayed loss of consciousness;
5) location of the bleeding usually within the white matter;
6) absence of a demonstrable anatomic cause for the bleeding.

Several excellent reviews have presented detailed discussions of all of the etiologic factors postulated for these hemorrhages. The various concepts dealing with the pathogenesis of apoplexy have been considered, but the age-distribution and the absence of significant arteriosclerosis in this group argue convincingly against vascular degenerative disease being the common background for these lesions. The relationship to trauma is inconstant, remote, and often equivocal. Infectious and toxic agents have been excluded in carefully studied cases. Most reports ascribe no definite causative factor. It is of historical interest that Hawthorne was impressed by their occurrence in apparently healthy children and adolescents.

The relationship of large vascular anomalies to cerebral hemorrhage is well known, an incidence of 50 per cent being reported by Olivecrona and Riives, and a frequency of 41 per cent being found in a review of Dandy limited to arteriovenous aneurysms. But the role of small angiomatous formations in the production of intracranial hemorrhage is less well known. Three examples of bleeding from small macroscopic lesions have been reported from the clinic of Olivecrona. Hawkins and Rewell described 2 cases, and Bagley another, of fatal hemorrhage related to cavernous...
angiomas that were demonstrable only at a microscopic level. Kidd and Cumings\(^{10}\) discussed a family presenting a history of 10 deaths in two generations from cerebrovascular accidents occurring in youth. Two of these subjects were autopsied, one showing a hemorrhage associated with an angioma revealed in sections, the other presenting old and recent hematomas without a demonstrable background.

A survey\(^ {16}\) of the problem of intracranial hemorrhage currently being undertaken at Duke Hospital has indicated (1) that a considerable proportion of hemorrhages are without demonstrable cause and (2) that small angiomatous malformations may play a more significant role than usually recognized. Over a 20-year period 14 hematomas of unknown etiology and 9 instances of hemorrhage from angiomatous malformations have been found, compared with 55 cases of hypertensive-arteriosclerotic apoplexy and 29 hematomas resulting from ruptured berry aneurysms.

Six fatal hematomas related to vascular malformations were studied at autopsy. Four were found to have been produced by rupture of small lesions. The minute size of one of these, the difficulty in demonstrating the second, and the deep-seated situation of the others point to their possible role in the production of so-called spontaneous intracranial hemorrhage. The incidental finding of two other examples of cerebral vascular lesions susceptible of being obliterated by related hemorrhage again emphasizes this possibility. These cases are being reported in this aspect.

CASE REPORTS

Two examples of massive fatal intracranial hemorrhage arose from vascular malformations that were not evident grossly. In Case 1, a tiny arteriovenous angioma was demonstrated only after multiple sections of the wall of a subcortical hematoma had been studied. In Case 2, a pontine lesion was so nearly destroyed by the related hemorrhage that its classification as a cavernous angioma is difficult. With neither of these lesions was the afferent or efferent circulation demonstrable.

Case 1. J. B., a 12-year-old white male, had sudden onset of a headache during a contest with his playmates “to see who could blow a harmonica the loudest.” The child became progressively less responsive and vomited frequently.

On admission 12 hours later temperature was 37\(^\circ\)C., pulse 96, respirations 22, and B. P. 118/66. The principal neurological findings included semicoma, left hyperreflexia, and a left Babinski sign. The CSF was clear and free of RBC; the pressure was not recorded. Bilateral pyramidal signs developed and death occurred on the 4th day of illness.

Autopsy findings were irrelevant except for the cerebral changes. A massive subcortical hematoma, 6×4×4 cm., was found in the left parietal lobe, confined to the white matter (Fig. 1A). No subarachnoid bleeding was present. No gross source of the bleeding was demonstrated, and study of the lesion with a dissecting microscope gave no further indication of the background of the hematoma. The parenchyma in the wall of the hemorrhage was unaltered except for congestion and multiple small hemorrhages.
Fig. 1. Case 1. (A) Coronal section of brain showing large hematoma in left parietal lobe. No gross vascular malformation was demonstrable. (B) Complexly branching vessels of venous structure showing abrupt thinning of walls. Masson, ×69.

Of many blocks selected from the hematoma wall, one revealed a tiny arterio-venous angioma contained largely within the meninges of a single sulcus and 3 to 5 mm. of parenchyma bordering the hemorrhage. The most superficial vessels were tortuous arteries, altered by fibrous intimal plaques and zones of thinning and fibrosis of the muscularis. Deeper in the sulcus sinuous and straight vessels of venous character entered the brain parenchyma, branched complexly and were dispersed. Abrupt thinning occurred in the walls of some of these vessels, the media giving way suddenly to a thin endothelial lining (Fig. 1B). The parenchyma related to the vessels presented a few foci of gliosis; there was no evidence of an older hemorrhage.
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Case 2. M. R. C., a 2½-year-old white female, fell from a swing 40 hours prior to admission and struck the left frontotemporal region. There was no loss of consciousness. Four hours later the child began complaining of generalized headache; after 12 hours the headache became more severe and cerebration became progressively slower until stupor supervened. On the morning of admission left ptosis and left hemiparesis were observed. Bloody CSF had been found by the referring physician.

On admission temperature was 37.8°C., pulse 124, respirations 24, and B. P. 90/66. X-rays of the skull were negative. The principal neurologic findings included stupor, a slightly stiff neck, left ptosis and dilated pupils which reacted to light. There was paresis of all extraocular muscles. Left hemiparesis and hyperreflexia were present. Subsequently, there developed a right peripheral 7th nerve paralysis, and respiratory embarrassment, and the patient expired 3 days after onset.

Autopsy revealed no disease outside of the central nervous system. The caudal portion of the pons was greatly expanded and virtually destroyed by a circumscribed hematoma, 3X2X2 cm. (Fig. 2A). A few smaller hemorrhages bordered the larger lesion, but no gross traces of an older hemorrhage were observed. Slight subarachnoid bleeding was present. There was no gross evidence of an abnormal vascular pattern in the parenchyma or meninges related to the lesion.

Sections demonstrated the lesion from which the bleeding had its origin, virtually destroyed by the hemorrhage. At some borders of the hematoma there were small numbers of collapsed cavernous vessels with thin walls, consisting of a single layer of endothelium and basement membrane, or a rim of hyaline connective tissue (Fig. 2B). The lesion was confined entirely to the parenchyma. Older small hemorrhages were evident at the periphery of the lesion, where gliosis, hemosiderin pigment within histiocytes, and basophilic depositions upon the basement membrane of telangiectatic vessels were observed.

Two examples of massive fatal cerebral hemorrhage arose from deep-seated small venous malformations. In neither of these was the afferent circulation discovered. In one the venous drainage to an internal cerebral vein was demonstrated. These cases are reported below.

Case 3. S. P., a 7-year-old white female, fell from a chair while in school and remained stuporous until admission 24 hours later. She complained of right frontal headache and vomited several times. A left hemiparesis was noted soon after onset. The patient had struck her head against the door 2 days prior to her present illness with no loss of consciousness or immediate sequelae. Two to 3 years previously she had experienced an episode of severe right-sided headache, nausea and vomiting lasting 2 to 3 days.

On admission temperature was 37.4°C., pulse 100, respirations 22, and B. P. 110/80. The patient was semicomatose. Her neck was supple. A left hemiparesis was present, most marked in the arm. The CSF was clear, and contained no RBC; the pressure was 170 mm. of H2O. Deep coma supervened, decerebrate attacks developed, and death occurred on the 4th day of illness.

Autopsy revealed no pertinent changes outside the central nervous system. In the right cerebral hemisphere a massive hematoma, 12X6X4 cm., occupied most of the centrum semiovale, extending from a retrolenticular level nearly to the frontal pole (Fig. 3A). The hemorrhage was recent, and was sharply delimited, especially at the external margin of the putamen, where it had cleaved the parenchyma, rather than destroying it in its dissection. No intraventricular or subarachnoid bleeding had
occurred. The source of the hemorrhage was a small venous angioma at the inferomedial margin of the hematoma (Fig. 8A). This lesion, which consisted of small, widely dispersed vessels, occupied a zone of white matter approximately 1.5 cm. in each dimension. These vessels, the largest of which measured 1 mm. in diameter,
Fig. 3. Case 3. (A) Coronal section of brain showing massive hematoma in right centrum semiovale. At the inferomedial border the venous angioma is seen, and below this the cystic remnant of an older hemorrhage. (B) Varied-sized vessels of venous structure within white matter. Hematoxylin-eosin, X31.
diminished progressively in size and number at the margins of the lesion, being lost anteriorly in the white matter and posteriorly within the caudate nucleus. There were no abnormalities of arterial or venous pattern in the related parenchyma or meninges to indicate the afferent or efferent circulation of the lesion. At the anterior margin of the malformation a cleft-shaped zone of encephalomalacia in the medullary core of the right gyrus rectus, bordered by brown-stained parenchyma, gave evidence of an older hemorrhage.

The microscopic pattern of the lesion presented widely scattered vessels within an unaltered parenchyma. The vessels varied from muscular veins to thin-walled venules (Fig. 3B); no arterial structures were observed. Irregular hyaline plaques produced advanced narrowing of some lumina. The wall of the recent hematoma contained many necrotic, thrombosed vessels, and ring- and ball-shaped hemorrhages. The older hemorrhage, remote from the recent bleeding, presented areas of cyst formation, fibrous gliosis, and hemosiderin pigmentation both within histiocytes and upon the cell bodies of large astrocytes.

Case 4. V. R., a 29-year-old white female, had onset of right retro-orbital pain 16 hours prior to admission. This progressed in severity and 2 hours later a left hemiparesis was noted. Forty-five minutes thereafter the patient became comatose.

On admission, temperature was 37.4°C, pulse 52, respirations 16, and B. P. 100/70. The principal neurological findings included semicoma, left hemiparesis, and slight nuchal rigidity. The right pupil became fixed to light. The state of consciousness remained unchanged. Sudden respiratory death occurred 44 hours after onset.

Autopsy demonstrated the absence of evidence of kidney disease, hypertension, or significant atherosclerosis. In the left cerebral hemisphere a hematoma, 4 cm. in each dimension, occupied the frontal lobe anterior to the basal ganglia (Fig. 4A). It approached the anterior tip of the lateral ventricle, but the ventricles and subarachnoid space were free of gross bleeding. At the ragged medial margin of the hemorrhage a venous angioma was observed (Fig. 4A). This consisted of a network of small, thick-walled vessels, distributed sparsely within the otherwise normal parenchyma. The lesion was limited to the frontal portion of the lenticular nucleus, and the adjacent internal capsule and corona radiata. The caliber of the vessels measured 1 mm. or less. Presenting upon the lateral wall of the left lateral ventricle a dilated tortuous venous channel, 8 mm. in diameter, passed into a dilated internal cerebral vein, then into the great cerebral vein. Through these veins retrograde injection could be freely made into the vascular malformation and into the cavity of the hemorrhage. There were no abnormalities in the pattern of the related arterial circulation.

Sections of the lesion showed diffusely scattered vessels, with walls varying from thin endothelial linings to thick fibrous and muscular coats, but most were of venous composition (Fig. 4B). Mural plaques were prominent, ranging from fibrous focal thickening to massive collagenous proliferation that produced near occlusion, especially of some of the largest vessels. A perivascular astrocytic proliferation was prominent but no evidence of older hemorrhage about any of the vessels was observed.

Two small vascular lesions, incidental findings which had not given rise to gross hemorrhages, are presented because their small size illustrates the difficulty of finding the source of any major hemorrhage occurring from them. One of these certainly would have been completely destroyed by
hemorrhage of any consequence. The description of these lesions follows.

Case 5. M. S. This lesion was a small vascular malformation classified as a telangiectasis. It was an arc-shaped lesion, 2 mm. in thickness and about 2 cm. in its coronal and anteroposterior diameter (Fig. 5A), found in the brain of a 37-year-old colored female. The lesion paralleled the cortex in the upper margin of the left su-
Case 5. (A) Inconspicuous group of small vessels within medullary lamina of superior temporal gyrus. (B) Telangiectatic thin-walled vessels composing the lesion. Hematoxylin-eosin, X32.

perior temporal gyrus, and had the appearance of a zone of dilated congested vessels, pinpoint to 1 mm. in size, distributed within the otherwise normal white matter. The margins were vague and no feeding or draining vessels were demonstrable.

Sections at coronal levels through the lesion showed it to consist predominantly of dilated vessels which presented regular round cross-sections, appearing only infrequently in the longitudinal plane (Fig. 5B). Their coats were thin, most being composed solely of an endothelial lining. In a few, collagenous fibrous tissue was added to the walls. The vessels were spaced widely in the white matter and their
Fig. 6. Case 6. (A) Coronal section of brain showing small cavernous angioma adjacent to hippocampus. (B) Cavernous vascular spaces with collagenous septae. Masson, ×37.
numbers diminished rather gradually at the margin of the lesion. No old hemorrhage was observed in the parenchyma and only a slight gliosis was observed.

Case 6. J. C. In the brain of a 31-year-old white male, a single small cavernous angioma was discovered. This lesion, which was situated predominantly in the medullary core of the left hippocampal gyrus, measured 8 mm. in greatest diameter and was sharply marginated (Fig. 6A). It presented no gross evidence of past bleeding. No abnormalities in the circulation related to it were evident.

In sections, closely packed blood-filled cavernous spaces constituted the lesion (Fig. 6B). Many of the vessels lay wall to wall without intervening stroma or parenchyma. The walls of the vessels varied from a thin endothelial lining to a fibrous wall a few cell layers thick; in others the vessels were obliterated or replaced by laminae of hyalinized connective tissue. Intervening tissue consisted in some areas of a dense collagenous stroma. Traces of an old small hemorrhage were indicated by hemosiderin pigment within macrophages, and encrusting the cytoplasm of astrocytes and microglia which had proliferated at the borders of the lesion.

DISCUSSION

Except for the demonstration of the etiologic factor, these 4 hematomas bear a close resemblance to the spontaneous cerebral hemorrhages of unknown etiology. Their clinical aspects, and the type and location of hemorrhage differ in no significant way from 10 cases of intracerebral hematoma of undetermined origin diagnosed surgically, and 4 cases studied at autopsy at Duke Hospital. It is not possible to exclude a vascular malformation as an etiologic factor in those cases studied solely under operative conditions. Nor would angiography be likely to demonstrate minute lesions. Hawkins and Rewell have suggested that a careful search for angiomatosus formations be made in the walls of unexplained cerebral hemorrhages occurring in young people. Furthermore, the possibility of destruction or masking of the causative lesion by the hemorrhage has to be considered in cases studied at autopsy. The variety of cerebral vascular malformations and their embryologic background have been well documented. It is reasonable to regard all such lesions as potential sources of bleeding.

The delayed loss of consciousness common to hemorrhages of unknown etiology as well as to those related to vascular malformations has been explained on the basis of slow venous bleeding. But the location of these hematomas may be of more significance in this respect than their rate of development.

SUMMARY

Four cases of intracranial hematomas arising from rupture of small angiomatosus malformations are reported, along with 2 other lesions that did not bleed. The clinical and pathological features of these hemorrhages are described. The relationship of minute lesions of this nature to spontaneous cerebral hemorrhage of unknown etiology is suggested.
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REFERENCES