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CLINICOPATHOLOGICAL STUDY OF CEREBRAL SUBCORTICAL CAVERNOUS ANGIOMA AS EPILEPTOGENIC FOCUS

SHIGERU TSUNODA[1], TOSHISUKE SAKAKI[2], TETSUYA MORIMOTO,[2]
HIROYUKI NAKASE[2], HIROYUKI HASHIMOTO[2], KAZUO GODA,[1]
SHOZO KAWAI[3], HIDEYUKI OHNISHI[4] and MANABU HISANAGA[5]

1) *Department of Neurosurgery, Saiseikai-chuwa Hospital*
2) *Department of Neurosurgery, Nara Medical University*
3) *Department of Neurosurgery, Osaka Prefectural Hospital*
4) *Department of Neurosurgery, Osaka Neurological Institute*
5) *Department of Neurosurgery, Senboku National Hospital*

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Summary : The authors conducted a comparative histological study of two groups of patients with cerebral subcortical cavernous angioma. One group was composed of 5 asymptomatic cases detected accidentally. The other group was composed of 4 patients presenting as epilepsy. The results obtained may be summarized as follows ; 1) Hemosiderin deposit and gliosis were seen in all cases examined ; 2) Granulomatous change was a histological finding associated with epileptogenesis ; 3) The histological changes, starting with proliferation of collagen fibers and leading to hyaline degeneration, calcification, and then hemangioma calcificans, seem to represent a course of spontaneous healing, when viewed from epileptogenesis

Index Terms

cavernous angioma, epilepsy, hemosiderin, hemangioma calcificans

INTRODUCTION

With magnetic resonance imaging, which has recently begun to be used clinically, most cerebral subcortical cavernous angiomas are demarcated with a low-signal ring on T_2-weighted images indicative of hemosiderin deposit.[1] Therefore, it is now impossible to argue about the mechanism for epilepsy based on hemosiderin deposit alone. Bearing this in mind, the authors conducted a histological comparison between two groups of patients with cerebral subcortical cavernous angioma. One group was asymptomatic, and the other group presented as epilepsy.

SUBJECTS and METHODS

The study included 8 cases of cerebral subcortical cavernous angioma excluding the occipital lobe. Five of them were asymptomatic and the other 4 presented as epilepsy. The latter group did not include cases in which subcortical hemorrhage was detected by CT even though epilepsy was observed. Mass effect was confirmed radiologically in all 9 cases. As for asymptomatic cases, operations were carried out to rule out tumors such as astrocytoma and oligodendroglioma. Cases presenting as epilepsy were also operated to relieve epilepsy. Surgically removed tissue from each case was histologically examined under a microscope.

RESULTS

Histological examination of the brain tissue around angioma revealed gliosis in all cases, but provided no other noteworthy findings. Therefore, cavernous angioma itself was histologically examined in detail.

As shown in Table 1, hemosiderin deposit was observed in all 9 cases. Histological responses could be divided into three types; lymphocyte and macrophage infiltration accompanied by proliferation of fibroblasts and new vessels (granulomatous type or Type G), proliferation of collagen fibers occasionally accompanied by hyaline degeneration or calcification (collagenous type or Type C), and coexistence of both responses to a similar degree (intermediate type or Type I).

There were 3 cases of type G, 2 cases of Type I and 4 cases of Type C. The incidence of epilepsy was 3/3 in Type G, 1/2 in Type I and 0/4 in Type C.

REPRESENTATIVE CASES

Case 8:

A 56-year-old male patient was admitted complaining of epileptic attacks. Plain CT revealed a small isodense tumor in the right parietal area (Fig. 1-A), and enhanced CT showed a homogeneous enhancement (Fig. 1-B). The tumor was removed via right parieto-occipital craniotomy.

Histological examination revealed cavernous angioma of granulomatous type (Fig. 2).

Case 1:

A 36-year-old female patient was incidentally discovered to have a calcification in the left parietal area in the skull X rays (Fig. 3-A). Plain CT revealed a small calcified tumor in the left parietal subcortical area (Fig. 3-B). The tumor was removed via left fronto-parietal

Table 1. Histological study on cerebral subcortical cavernous angioma

Case No.	1	2	3	4	5	6	7	8	9
Age(yrs), Sex	36 F	13 M	38 M	35 M	40 M	33 M	25 M	56 M	52 M
Location[1]	Lt P	Lt F	Lt F	Lt T	Rt F	Rt F	Rt T	Rt P	Rt F
Epilepsy	(−)	(+)	(+)	(−)	(−)	(−)	(+)	(+)	(−)
Hemosiderin deposit	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)
Infiltration of lymphocytes and macrophages	(−)	(±)	(±)	(−)	(+)	(+)	(±)	(±)	(+)
Proliferation of fibroblasts	(−)	(±)	(±)	(−)	(+)	(+)	(±)	(±)	(+)
Newly formed blood vessels	(−)	(±)	(±)	(−)	(+)	(+)	(±)	(±)	(+)
Proliferation of collagen fibers	(±)	(+)	(+)	(±)	(+)	(±)	(±)	(+)	(±)
Hyaline degeneration	(±)	(+)	(+)	(+)	(+)	(±)	(±)	(+)	(±)
Calcification	(±)	(−)	(−)	(−)	(−)	(+)	(±)	(+)	(−)
Histological[2]	C	G	G	C	I	C	I	G	C

1) F: frontal, P: parietal
2) G: granulomatous type, I: intermediate type, C: collagenous type

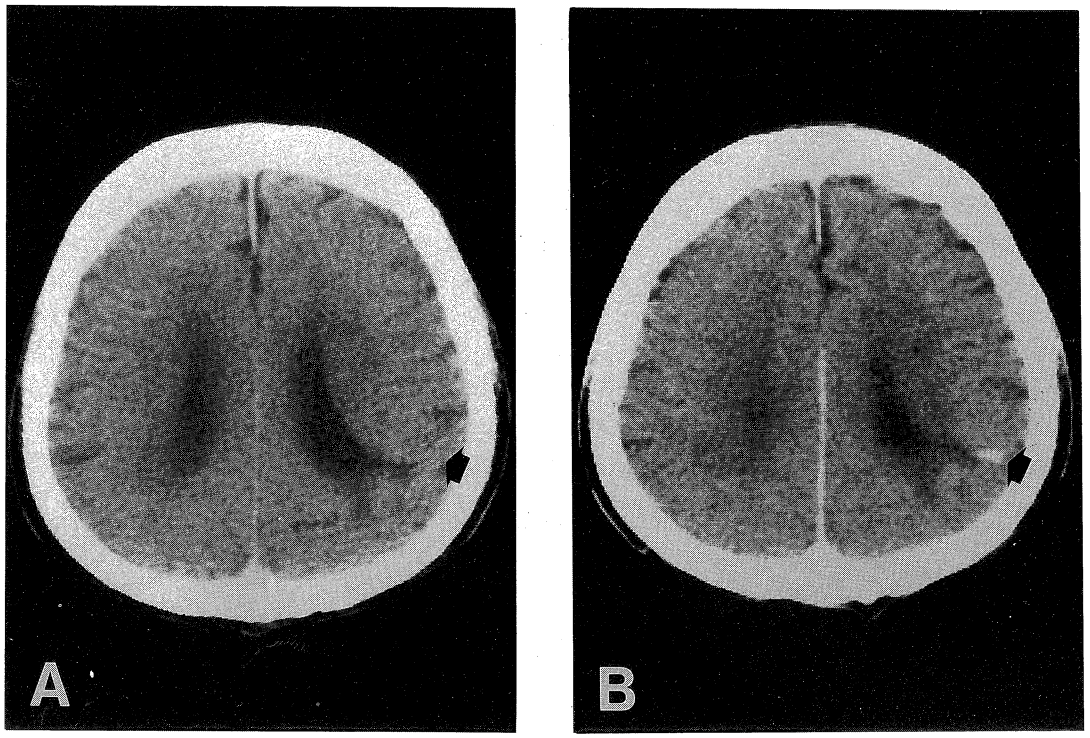

Fig. 1. A. Plain CT revealed small isodense tumor in the right parietal area (arrow).
B. Enhanced CT revealed a homogeneous enhancement (arrow).

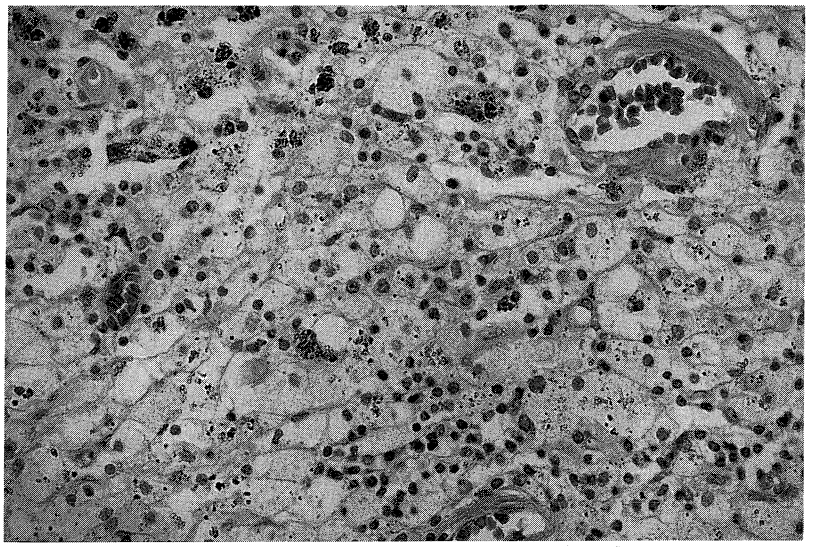

Fig. 2. Granulomatous type. Histological findings showed lymphocyte and macrophage infiltration accompanied by proliferation of fibroblasts and new vessels. (HE×100)

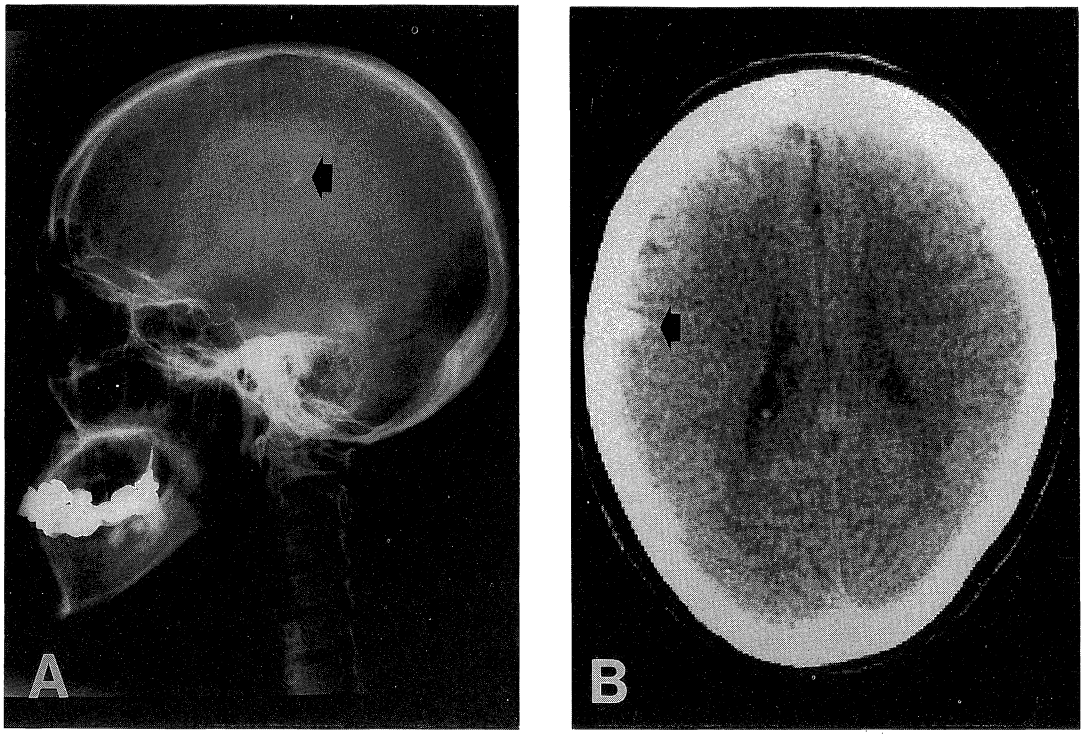

Fig. 3. A. Skull X ray revealed a calcification in the left parietal area (arrow).
B. Plain CT revealed a small calcified tumor in the left parietal subcortical area (arrow).

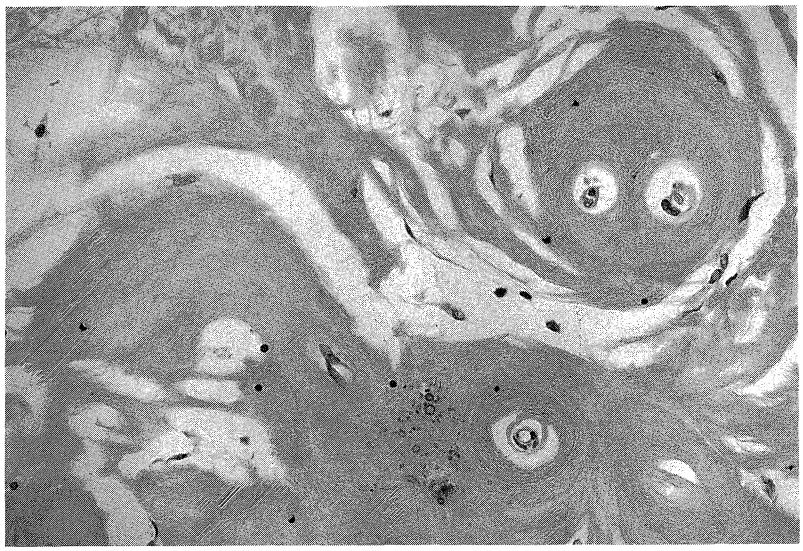

Fig. 4. Collagenous type. Histological findings showed proliferation of collagen fibers accompanied by hyaline degeneration and calcification. (HE×100)

craniotomy. Histological examination revealed cavernous angioma of collagenous type (Fig. 4).

DISCUSSION

Since the report of Jackson[2], epilepsy has been regarded as a condition induced by synchronized excessive discharge from nerve cells. About one-third of cases with cavernous angioma are said to present as epilepsy[3]. However, it is unknown which histological findings are associated with such synchronized excessive discharge. Willmore et al.[4)5)] prepared a model of traumatic epilepsy by injecting iron salts into rat cerebral cortex, and suggested that hemosiderin in also associated with epilepsy. However, it was difficult to explain why only about one-third of patients with cavernous angioma presented as epilepsy in spite of detection of hemosiderin deposit by MRI in most cases of cavernous angioma.

In the present study, patients with cavernous angioma were clinically divided into two groups (asymptomatic and epileptic) and histologically classified into 3 types (Type G, Type I and Type C). The comparison of the incidence of epilepsy between histological types (3/3 in Type G, 1/2 in Type I and 0/4 in Type C) yielded the interesting finding that granulomatous change correlates with epilepsy, and that the incidence of epilepsy decreases as collagen fibers increase ($P<0.05$). The results from this study suggest that the histological changes, starting with proliferation of collagen fibers and leading to hyaline degeneration, calcification (partial), and then hemangioma calcificans, seem to represent a course of spontaneous healing, when viewed from epileptogenesis. It was additionally suggested that epileptic cases of cavernous angioma, apparently representing hemangioma calcificans, must possess granulomatous change somewhere.

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