Clinicopathological Study of Brain Tumor Radiotherapy

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Summary

A clinicopathological study was made on 45 autopsy cases of brain tumors treated with radiotherapy. Morphological changes after radiotherapy were classified into six categories: 1) tumor disappearance, 2) small residual tumor, 3) extensive tumor necrosis, 4) proliferative tumor growth, 5) mixed glioblastoma and fibrosarcoma, and 6) no remarkable change. When the tumors are primarily radiosensitive, tumor disappearance or small residual tumors might occur. Germinomas, some of lymphomas and medulloblastomas were representative of primary radiosensitivity. When the tumors are secondarily radiosensitive, or tumor cell necrosis is brought about by blood vessel degeneration caused by radiation, there might be extensive tumor necrosis. About one a half of the astrocytic tumors and glioblastomas were thought to have a combination of primary and secondary radiosensitivity. One case of oligodendroglioma, two cases of ependymoblastoma, two cases of malignant lymphoma and two cases of metastatic tumor also showed extensive tumor necrosis. The other half of the astrocytic tumors and glioblastomas showed proliferative tumor growth. They seemed to be less radiosensitive. Two cases of glioblastoma at the time of the operation changed into mixed glioblastoma and fibrosarcoma in the autopsy. No remarkable changes were observed in cases of teratoma and pineocytoma which were mature benign tumors with little blood vessel supply.

No definite correlations were observed between the pathological changes and therapies such as the degree of resection, doses of irradiation and chemotherapy in astrocytic tumors and glioblastomas. There were, however, some tendencies for small residual tumors and extensive tumor necrosis to be brought about by extensive tumor resection, full courses of radiotherapy and intensive chemotherapy.

Key words: Brain tumor, radiation therapy, radionecrosis

Introduction

Radiation therapy is one of the most useful aids for the management of malignant tumors of the brain. It is universally believed that some tumors, such as medulloblastomas and germinomas, are the most radiosensitive. However, glioblastomas are thought to be less radiosensitive. The degree of radiosensitivity is variable even in the same histopathological group from one case to another. There have been only a few cases on record in which there is unquestionable histological proof that primary cerebral tumors disappeared completely following radiotherapy.\(^3\)\(^-\)\(^5\) In recent reports, extensive tumor necrosis with residual tumor cells has been discovered after radiotherapy.\(^9\)

We have tried to analyse the effect of radiotherapy on tumors and surrounding brain tissue from large histological preparations obtained from autopsy materials.

Materials and Methods

Forty-five cases of brain tumor which had been treated by radiation therapy and autopsied at the Gunma University Hospital from 1967 to 1977 were analysed. They included 15 cases of glioblastoma, 14 of astrocytoma and anaplastic astrocytoma, one of ependymoblastoma, one of oligodendroglioma, three of medullo-
blastoma, four of pineal region tumor, three of malignant lymphoma, two of metastatic brain tumor, and two of unverified necrotic tissue. Radiation therapy with 10 MV linac X rays (Toshiba) was applied to the tumor at doses of 5,000 to 6,000 rads. Radiation doses amounted to more than 10,000 rads in some recurrent cases. Chemotherapy using such drugs as CCNU, methyl-CCNU, ACNU, bleomycin and futrafual, and immunotherapy with OK-432 (Chugai) were sometimes added to the radiotherapy. The brains were cut coronally, sagitally, or horizontally according to the site of the tumor. Large histological preparations were made to analyse the microscopical changes of the tumor itself and of the surrounding brain tissue. They were prepared using H.E., Mallory and Klüver-Barrera stains.

**Table 1** Glioblastoma—15 cases

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Extensive necrosis (4 cases)</th>
<th>Small residual tumor (4 cases)</th>
<th>Proliferative tumor growth (5 cases)</th>
<th>Mixed glioblastoma &amp; fibrosarcoma (2 cases)</th>
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<tr>
<td>extensive resection</td>
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<td>partial resection</td>
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<td>Irradiation (rad)</td>
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<td>4,900</td>
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<td>5,000–9,900</td>
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<td>10,000+</td>
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<td>Chemotherapy</td>
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<td>CCNU, Me-CCNU, ACNU</td>
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<td>Futrafual</td>
<td>4</td>
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<td>Bleomycin</td>
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<td>Immunotherapy</td>
<td>OK-432</td>
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Proliferative growth and mixed glioblastoma and fibrosarcoma might be the less effective ones. In the effective group, the postoperative median survival time was 18.3 months with a 3 to 43 month range, and in the less effective group, it was 10.3 months with a 2 to 19 month range. No definite correlations were observed between the pathological effectiveness and therapies such as degree of resection, doses of irradiation and chemotherapy. However, there seemed to be an inclination toward extensive tumor necrosis or small residual tumors in cases given intensive radio- and chemotherapy. Representative cases are described briefly.

**Case 1: Glioblastoma. Extensive tumor necrosis**

A 57 year-old male was diagnosed as having a bilateral frontal lobe tumor. The tumor was partially resected and histologically diagnosed as glioblastoma. He was given 6,000 rads of Linac X ray radiotherapy, delivered in 33 fractions over 49 days. He was given in addition 1,200 mg of methyl-CCNU over 4 months and 400 mg of futrafual daily for 4 months. He expired 1 year after the operation. Autopsy disclosed widespread tumor necrosis in the bilateral frontal lobe (Fig. 1A). Histologically the tumor tissue showed extensive coagulative tumor necrosis with an admixture of proteinous fluid and fibrin filaments (Fig. 1B). Incomplete tumor necrosis was observed in the marginal zone of the tumor (Fig. 1C). Blood vessels in the tumor necrosis were necrotic, while some vessels in the marginal zone of the tumor showed endothelial and adventitial proliferations.

**Case 2: Glioblastoma. Small residual tumor**

A man aged 36 was admitted to the hospital with the diagnosis of a left temporal lobe tumor. The tumor was partially resected and histologically diagnosed as glioblastoma. Linac irradiation was applied to the left hemisphere at a tumor dose of 6,050 rads, delivered in 33 fractions over 50 days. He was given 1,200 mg of futrafual daily for 4 months. The patient died of status epilepticus 4 months after the operation. The autopsy disclosed a small residual tumor and coagulative tumor necrosis in the left temporal lobe (Fig. 1D). Some

**Results**

I. Glioblastomas (Table 1)

Fifteen cases of glioblastoma were analysed. Extensive tumor necrosis was observed in four cases, small residual tumors in four, proliferative tumor growth in five, and mixed glioblastoma and fibrosarcoma in two. From the pathological viewpoint, extensive tumor necrosis and small residual tumors were thought to be the effective results of radiotherapy.
Fig. 1  A: Case 1. Bilateral frontal lobe glioblastoma. Extensive tumor necrosis.  
B: Case 1. Coagulative tumor necrosis with admixture of proteinous fluid and fibrin filaments.  
C: Case 1. Incomplete tumor necrosis in the marginal zone of the tumor.  
D: Case 2. Left temporal lobe glioblastoma. Small residual tumor (t) and coagulative tumor necrosis (n).  
E: Case 3. Left temporal lobe tumor. Mixed glioblastoma (g) and fibrosarcoma (f).  
F: Case 3. Histology of the sarcomatous part.  
G: Case 3. Necrotic region in the glioblastomatous area.
vessel walls in the border zone between the residual tumor and tumor necrosis showed adventitial fibrosis and hyalinosis. White matter surrounding the tumor showed a spongy necrobiosis state with reactive astrocytes and fat-laden macrophages.

Case 3: Mixed glioblastoma and fibrosarcoma
A left temporal lobe tumor in a 15 year-old boy was partially resected and followed by two courses of radiotherapy of 5,600 rads and 6,000 rads. The operative specimen was histologically diagnosed as glioblastoma. He was given 400 mg of futraful daily for 1 month and methyl-CCNU at a total dose of 1,350 mg over 9 months. He expired 13 months after the operation. In the autopsy, the tumor occupied the left temporal lobe with an extension into the posterior fossa (Fig. 1E). The tumor was partially necrotic, and was histologically mixed glioblastoma and fibrosarcoma (Fig. 1F, G). Necrotic and thrombotic vessels were found within and around the tumor necrosis.

II. Astrocytomas and anaplastic astrocytomas
(Table 2)
Fourteen cases of astrocytomas and anaplastic astrocytomas were analysed. Extensive tumor necrosis was observed in six cases, a small residual tumor in one, and proliferative tumor growth in seven case. In the treatment, the degree of resection, doses of irradiation, and chemotherapy were not basically different in these groups. There were, however, some tendencies for extensive tumor necrosis and small residual tumors to be observed in cases with extensive resection, full courses of radiotherapy, and intensive chemotherapy. Those with extensive tumor necrosis and small residual tumors were thought to be sensitive to radiotherapy, and those with proliferative tumor growth were found to be less sensitive. The median survival time of the former group was 18 months with a 3 to 36 month range, and that of the latter group was 8 months with a 2 to 12 month range.

Case 4: Anaplastic astrocytoma. Extensive tumor necrosis
A thirteen year-old girl was admitted to the hospital with a diagnosis of a right basal ganglia tumor. No operation was performed, but irradiation was applied at a tumor dose of 6,000 rads delivered in 38 fractions over 55 days. She was given 800 mg of futraful daily for 13 days and expired 2 months later. An autopsy revealed a hen's egg size tumor in the right basal ganglia (Fig. 2A). Histologically, the tumor consisted mainly of coagulative necrosis with densely matted fibrin filaments (Fig. 2B). Small amounts of residual ballooning tumor cells were observed in the marginal zone of the tumor and in the perivascular area within the tumor. Exudative changes and hyaline thickening of the vessel walls were found in the tumor but not in the surrounding brain.

Case 5: Anaplastic astrocytoma. Small residual tumor with adjacent brain necrosis
A man aged 54 was diagnosed as having a right thalamic tumor. He was treated by radiation therapy at a tumor dose of 5,950 rads, delivered in 45 fractions over 122 days. Methyl-CCNU was added at a total dose of 900 mg over 5 months. He expired 9 months after the treatment. The autopsy revealed a small residual tumor restricted to the posterior thalamus surrounded by necrotic white matter (Fig. 2C). Histologically, the tumor was composed of an anaplastic astrocytoma and

<table>
<thead>
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<th>Table 2 Astrocytoma and anaplastic astrocytoma—14 cases</th>
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<tr>
<td>Extensive necrosis (6 cases)</td>
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<td>Surgery</td>
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<td>Chemotherapy</td>
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<td>Futraful</td>
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Fig. 2  A: Case 4. Right basal ganglia tumor (anaplastic astrocytoma). Extensive tumor necrosis.
B: Case 4. Coagulative tumor necrosis. Dilated blood vessel showing fibrous degeneration.
C: Case 5. Right thalamic tumor (anaplastic astrocytoma). Small residual tumor (t) and surrounding brain necrosis (n).
F: Case 10. Coagulative tumor necrosis showing a perivascular pseudorosette.
tumor necrosis. White matter adjacent to the tumor necrosis showed a spongy state with reactive astrocytes and small amounts of fat-laden macrophages. Hyaline thickening of the vessel walls and narrowing of their lumen were found in the tumor necrosis but not in the surrounding white matter.

Case 6: Anaplastic astrocytoma. Proliferative tumor growth
A girl aged 5 was admitted to the hospital with a diagnosis of a temporal lobe tumor. The tumor was partially resected, and postoperative irradiation was performed at a tumor dose of 5,600 rads, delivered in 29 fractions over 38 days. She expired 5 months after the treatment. An autopsy showed a tumor extending to the thalamus and basal ganglia with ventricular tumor dissemination. Histologically, the tumor was an anaplastic astrocytoma and only a microscopic necrotic area was observed. Vascular changes were not conspicuous.

III. Medulloblastoma (Table 3)
All of the three cases of medulloblastoma were thought to be sensitive to radiotherapy from a pathological viewpoint. One case showed large extensive tumor necrosis and the other two showed small residual tumors at the original sites. Each case had widespread meningeal tumor dissemination.

Case 7: Medulloblastoma. Extensive tumor necrosis
A 1-year and 6-month old boy was diagnosed as having a superior vermis tumor. No direct operation was performed, but a ventriculoperitoneal shunt was made. He received three courses of radiotherapy when the tumor seemed recurrent; the doses were 5,750 rads, 5,000 rads and 3,000 rads. Twelve months after the initiation of radiotherapy he expired. The tumor was bigger than a hen’s egg and situated in the superior medial part of the cerebellum (Fig. 2D). Histologically, the tumor showed extensive coagulative necrosis except for microscopically vital cells of the medulloblastoma in the marginal zone of the tumor and in the perivascular area within the tumor. Vascular changes were not remarkable.

Case 8: Medulloblastoma. Small residual tumor
A 5-year-old boy was diagnosed as having a cerebellar vermis tumor. The tumor was partially resected and this was followed by irradiation at a tumor dose of 4,050 rads, delivered in 28 fractions over 57 days. He expired 9 months after the operation. In the autopsy, the original tumor site showed no tumor tissue except in the tumor margins. Spinal meningeal tumor dissemination was observed.

IV. Oligodendroglioma
Case 9: Extensive tumor necrosis
A 44-year-old female was diagnosed as having a right parietal lobe tumor. She had partial resection of the tumor three times and six courses of radiotherapy totaling 28,100 rads over 11 years and 9 months. An autopsy revealed extensive tumor necrosis with surrounding brain necrosis. Histologically, the tumor was mostly coagulative tumor necrosis with an amorphous proteinous substance and fibrin filaments. Some perforating vessels within the tumor were necrotic or thrombotic, while other vessels showed hyalineous thickening of the walls.

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Extensive necrosis (1 case)</th>
<th>Small tumor with meningeal dissemination (2 cases)</th>
</tr>
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<tr>
<td>Irradiation (rad)</td>
<td>-5,000</td>
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<td>13,750</td>
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Table 3 Medulloblastoma—3 cases

| Germinoma | 3,000 | disappearance of (2 cases) 5,000 rads tumor |
| Teratoma | 5,800 | no effect (1 case) |
| Pineocytoma | 5,650 | no effect (1 case) |

Table 4 Tumors of pineal region—4 cases
Fig. 3  A: Case 11. Germinoma in the pineal and suprasellar region. No tumor but cystic changes were observed.
   B: Case 11. Complete disappearance of tumor cells. Cysts were surrounded by reactive astrocytosis.
   C: Case 19. Upper brain stem lesion showing unverified necrotic tissue due to radiotherapy.
   D: Case 19. Necrotic brain tissue with telangiectatic vessels and calcified vessel walls.
V. Ependymoblastoma
A case of fourth ventricle ependymoblastoma and a case of cerebral ependymoblastoma were included. Both cases showed extensive tumor necrosis at autopsy.

Case 10: Extensive tumor necrosis
A 9-year-old boy had a fourth ventricle tumor which was partially resected and diagnosed histologically as ependymoblastoma. He was given three courses of radiotherapy totaling 12,200 rads at the original site, while 3,000 rads were applied to the whole brain and spinal axis. The patient died of peritoneal tumor metastases via the ventriculoperitoneal shunt 22 months after the operation. The autopsy showed a necrotic and hemorrhagic tumor at the original site (Fig. 2E). Histologically, the tumor showed mostly coagulative necrosis (Fig. 2F) with small perivascular vital cell cuffing. Dense hyalinous collagenous tissue and hyalinous thickening of small vessels within the tumor were observed.

VI. Pineal region tumor (Table 4)
Tumors in this region were found in four cases: two cases of germinomas, one case of teratoma, and one case of pineocytoma.

Case 11: Germinoma. Complete disappearance of the tumor
A patient aged 19 was clinically and pneumoencephalographically diagnosed as having a germinoma in the pineal and suprasellar region. He was given radiotherapy at doses of 3,150 rads in the tumor region, 1,800 rads over the whole brain and 3,450 rads along the spinal axis. He expired 10 months after radiotherapy. In the autopsy there was no tumor but cystic changes were observed in the pineal region and in the anterior third ventricle (Fig. 3A). Histologically, the cyst wall was composed of astroglial tissue surrounded by edematous white matter (Fig. 3B). Vascular changes were not remarkable.

Case 12: Teratoma. No radiation effect
A boy aged 12 had a pineal region tumor and was treated by irradiation at a dose of 5,800 rads, delivered in 29 fractions over 40 days. He expired 5 months after the therapy. An autopsy revealed a pineal region tumor with a metastatic nodule at the medulla oblongata and lumbar spinal cord. Histologically, the pineal region tumor was thought to be a mixture of a teratoma and embryonal carcinoma, and the latter component disappeared from the original site but was metastasized to the medulla oblongata and lumbar subarachnoid space.

Case 13: Pineocytoma. No radiation effect
A 35-year-old female was diagnosed as having a pineal region tumor and was treated by irradiation at a dose of 5,900 rads, delivered in 26 fractions over 49 days. She died 9 months after the treatment. The autopsy revealed a tumor of pigeon's egg size located in the pineal region. It was histologically a pineocytoma with no internal necrosis. Vascular changes were not conspicuous.

VII. Primary malignant lymphomas of the brain
Two cases of reticulum cell sarcoma and one case of lymphosarcoma were analysed.

Case 14: Reticulum cell sarcoma. Coagulative necrosis with a residual tumor
A 52-year-old male had a left frontal lobe tumor subtotally resected. The tumor was histologically a reticulum cell sarcoma. He received three courses of radiotherapy totaling 11,600 rads. The patient expired 9 months after the treatment. In the autopsy, the frontal lobe tumor was mostly necrotic and extended to the basal ganglia and corpus callosum. Histologically, the tumor was revealed to be necrotic or necrobiotic with a perivascular vital cell growth pattern in some areas. Vascular changes, such as angionecrosis and thrombosis, were conspicuous.

Case 15: Reticulum cell sarcoma. Disappearance of the tumor
A 31-year-old female had a right cerebellar tumor resected. It was histologically diagnosed as a reticulum cell sarcoma. She was given four courses of radiotherapy totaling 19,050 rads. She received two courses of vincristine sulfate at a total dose of 20 mg. She expired 5 years and 11 months after the operation. In the autopsy no tumor tissue was present but a cystic glial scar was observed.
**Case 16: Lymphosarcoma. Coagulative necrosis with a residual tumor**
A 10-year-old boy had a thoracic epidural tumor partially resected. It was histologically a lymphosarcoma. He was given radiotherapy at a tumor dose of 1,800 rads. He expired 5 months later. An autopsy revealed coagulative tumor necrosis with some invasion of the paravertebral soft tissue.

**VIII. Metastatic brain tumor**
Two cases of metastatic brain tumor were analysed. One was a small cell carcinoma of the lung, and the other was a malignant melanoma originally occurring in the epidermis of the back. Radiotherapy was thought to be moderately effective in these two cases.

**Case 17: Metastatic small cell carcinoma. Coagulative necrosis**
A 35-year-old male was diagnosed as having a small cell carcinoma of the right lung and he was operated on. Six months later he showed increased intracranial pressure, and was treated by two courses of whole brain irradiation amounting to 7,900 rads. Intrathecal methotrexate at a total dose of 44 mg was also given. He expired 22 months after the radiotherapy. An autopsy revealed tumors in the right parietal and left temporal lobes, both showing necrosis. Microscopically vital tumor cells were noted in the marginal zone of the tumor. Many vessels within the tumor or in the peripheral zone showed angionecrosis, hyalinous thickening, thrombosis, and adventitial fibrosis.

**Case 18: Metastatic malignant melanoma. Brain necrosis without tumor**
A 63-year-old male had a metastatic malignant melanoma in the left frontal lobe. It was removed totally and this was followed by radiotherapy at a tumor dose of 5,900 rads, delivered in 26 fractions over 38 days. He expired 15 months after the operation. The autopsy revealed no residual tumor at the original site. Microscopically the white matter around the lesion showed necrosis and a spongy state with scattered reactive astrocytes. Adventitial fibrosis of perforating vessels was recognized in the white matter.

**IX. Unverified necrotic tissue due to radiotherapy**
Two cases with no previous surgical biopsies revealed only degenerative brain changes without tumor tissue at autopsy.

**Case 19: Upper brain stem lesion**
A 27-year-old female was diagnosed clinically and pneumoencephalographically as having an upper brain stem tumor. She had two courses of radiotherapy totaling 8,800 rads. CCNU was given at a total dose of 1,620 mg. She expired 18 months after radiotherapy. An autopsy revealed brownish softening in the midbrain, third ventricle, and temporal lobe (Fig. 3C). Histologically, the lesion showed coagulative brain necrosis with a proteinous substance, slight bleeding, and degenerative vascular changes such as fibrinoid necrosis, endothelial thickening, thrombosis, athelomatous change and calcification deposits (Fig. 3D). No tumor tissue was found.

**Case 20: Pontine tegmentum lesion**
A pontine tumor was diagnosed in a man aged 21. He received three courses of radiotherapy totaling 15,800 rads over 6 years. He expired 9 years after the initial radiotherapy. The lesion was recognized in the dorsalpons and middle cerebellar peduncles. Telangiectatic vessels, hemorrhages, and small vessels impregnated with calcium were observed. The white matter adjacent to the lesion showed necrosis with small amounts of reactive astrocytes.

**Discussion**
Pathogenesis of radiation necrosis of brain tumors consists of two parts: 1) tumor cells are "primarily" or "directly" injured by ionizing radiation, and 2) tumor cell necrosis is brought about "secondarily" or "indirectly" by blood vessel changes caused by radiation. Medulloblastomas, germinomas and some kinds of lymphomas are primarily radiosensitive. Tumor cells usually regress or disappear without conspicuous vascular changes. However, case 7 with a medulloblastoma showed extensive tumor necrosis, and exudative vascular changes and thrombosis were confined to the necrotic region. This case of medulloblastoma was
exceptional but it suggested that if a tumor is large enough, tumor regression and disappearance rarely occur, and vascular changes are thought to be secondary to tumor necrosis since they occur in regions of tumor necrosis. Astrocytic tumors, glioblastomas, oligodendroglomas, ependymomas, some kinds of metastatic tumors and some of the lymphomas are thought to show a combination of primary and secondary radiosensitivity. Secondary radiosensitivity seems to play an important role in these tumor groups because angionecrotic or sclerotic changes in small perforating vessels are parallel to tumor necrosis in most cases. Pennybacker and Russell\(^8\) stated that the pathology of the necrosis appeared to be related to reactions in smaller vessels in which collagenous thickening, fibrinoid necrosis, and thrombosis were conspicuous. However, in cases in which small residual tumors were found, the tumor growth was suppressed, or even regressed, due to primary radiosensitivity without conspicuous vascular changes at autopsy.

Brain tumor radiotherapy is restricted for fear of radionecrosis of the normal brain. The limits of the brain's tolerance to radiation are not fully understood. The normal adult brain is relatively radioresistant.\(^1\) However, diseased or peritumoral edematous brain tissues are thought to be easily damaged by radiation. Lindgren\(^4\) published a modified Strandqvist's diagram showing two logarithmic curves: the upper line corresponds to the maximum dosage level above which the risk of cerebral necrosis is considerable; the lower line shows the lowest dosage level producing necrosis. From this diagram it is possible to read the size of a fractionated dose producing the same biological effect, i.e. cerebral necrosis, as a given unfractionated dose, and vice versa. Bouchard\(^1\) stated that there were no appreciable postradiation tissue changes observed beyond the tumor-bearing area, either immediately or even months to years later in cases in which the doses have been fractionated within the range of acceptable tissue doses. In two cases, we observed white matter degeneration adjacent to the brain tumor even within the range of acceptable tissue doses. Martins et al.\(^5\) stated that from their experience of delayed radiation necrosis the fraction size of radiation should not exceed 200 rads per day. Recently, in cases of glioblastomas, we tried to apply a tumor dose of 5,000 to 5,500 rads, delivered locally at 300 rads per day 3 times a week in expectation of efficacy. This method might increase the risk of radiation necrosis of the brain, but tumor necrosis can also be expected as benefit.

The repetition of a radiotherapy series over a period of one year or even much longer is sometimes very hazardous. In our series, seven out of eight cases treated with more than two series of radiotherapy totaling 10,000 rads showed extensive tumor necrosis or small residual tumors with adjacent white matter degeneration, in which the myelinated fibers became sparse or spongy with reactive astrocytes and gitter cells.

Vascular changes, such as fibrinoid necrosis, hyaline thickening, and periventricular fibrosis, were frequently observed in the area of brain tumor radionecrosis. Telangiectatic vessels and calcificiation of small perforating vessels recognized in cases 19 and 20 might also be caused by irradiation.

We classified the morphological changes of brain tumors after radiotherapy into six categories: 1) tumor disappearance; 2) small residual tumors with or without adjacent brain necrosis; 3) extensive tumor necrosis; 4) proliferative tumor growth; 5) mixed glioblastoma and fibrosarcoma (gliosarcoma); and 6) no remarkable change. These changes might also be influenced by the degree of operative resection and by chemotherapy.

Tumor disappearance: Two cases of germinoma and one case of malignant lymphoma belonged to this group in our series. Lindgren\(^4\) reported no residual primary tumors in four cases of medulloblastoma and one case of malignant ependymoma. Tumor cells must be primarily radiosensitive and be easily absorbed to fall into this group.

Small residual tumors with or without adjacent brain necrosis: In our series four cases of glioblastoma, one case of anaplastic astrocytoma and two cases of medulloblastoma showed this type of tumor change. Tumor cell growth might be supressed by radiotherapy. Most of the cases had extensive tumor resections and intensive radiotherapy. Tumor changes in this group were of the intermediate type between tumor disappearance and exten-
Extensive tumor necrosis: Extensive tumor necrosis was observed in four cases of glioblastoma, six cases of anaplastic astrocytoma, one case of medulloblastoma, one case of ependymoblastoma, and one case of oligodendroglioma. Malignant lymphomas and metastatic brain tumors also showed extensive tumor necrosis. All of the cases had small foci of vital tumor cells. Lindgren\(^4\) reported necrosis without any residual tumor in four cases of medulloblastoma and one case of malignant ependymoma. Pennybacker et al.,\(^8\) Lampert,\(^3\) and Nakamura et al.,\(^7\) reported similar cases of extensive and massive tumor necrosis without any residual tumors. Our case 19 with unverified necrotic tissue in the upper brain stem might be such a case, although there was not confirmation by biopsy before irradiation. Lindgren\(^4\) also reported massive necrosis and residual tumors in another six cases of gliomas. Extensive tumor necrosis might be brought about by primary and/or secondary radiosensitivity. Rubinstein\(^9\) pointed out that the most obvious effect of radiation on brain tumors is the development of extensive necrosis.

Proliferative tumor growth: Five out of 15 cases of glioblastoma and seven out of 14 cases of astrocytic tumor belonged to this group of proliferative tumor growth with or without partial necrosis. About one half of the astrocytic tumors, including glioblastomas, showed very restricted radiosensitivity or even radioinsensitivity. Blood vessel degeneration caused by radiotherapy was not remarkable in most cases of this group.

Mixed glioblastoma and fibrosarcoma: Two out of 15 cases of glioblastoma showed mixed glioblastoma and fibrosarcoma at autopsy. These two cases had only glioblastoma at the time of the operation. The operations were followed by radiotherapy and intensive chemotherapy. Morantz\(^6\) reported 24 cases of gliosarcoma, and stated gliosarcoma was present in 8% of all cases of multiform glioblastoma. Gliosarcoma appeared to have originated from neoplastic changes of markedly hyperplastic blood vessels within the anaplastic astrocytoma.\(^2\,^6\) Rubinstein\(^1\) reported that in three out of five cases of gliosarcoma, meningeal sarcoma promoted a malignant change in contiguous neuroglia.

No remarkable change: A case of teratoma and a case of pineocytoma showed no remarkable changes from irradiation in our series. We could not observe secondary radiation effects on mature benign tumors which have little blood vessel supply.

References