THE THREE TYPES OF GLIOBLASTOMA

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The problem of glioblastoma multiforme is an ever present one in the neurosurgical clinic. In Cushing's\(^3\) material of intracranial tumors the glioblastomas amounted to 10.4 per cent. While the problem therefore is of importance numerically, problems of diagnosis, of treatment and of purely human consideration are no less. In some clinics the tendency has been to give up, as far as this group of tumors is concerned, and the surgical problem has been transformed into a purely diagnostic one. It was hoped that the demonstration of arteriovenous anastomoses by angiography (Tön- nis\(^13\)) would aid the diagnosis, but it was soon found that this sign was present in only a certain number of cases.

In the Copenhagen clinic we have followed the principle of always operating in these cases whenever the general state of the patient allowed it—in the first years because we felt that our experience was too meagre to warrant a certain diagnosis, and later on because it became apparent that some patients with glioblastoma had a sufficiently long useful survival to justify operation. Growing experience seemed to show that long postoperative survivals were combined with certain macroscopical and microscopical features, and in this report we have tried to correlate these findings for the glioblastomas in our first 1000 intracranial tumors—102 patients. In the pathological report and in some tables, 31 later cases have been added. The survival periods and the pathological findings were not compared until the two parts of the work were finished.

PATHOGENESIS

The gliomas commonly are thought to be ectodermal tumors caused by dysontogenetic factors, some cells arrested at an embryonal stage becoming mother cells of the tumors. Ostertag\(^12\) and others have shown that even in the normal subject unripe cells are to be found in certain localizations, e.g. the gyrus cinguli and the corpus callosum, where glioblastomas frequently occur. The factors which “set off” the cells to sudden blastomatous growth are, however, unknown. In some gliomas, moreover, processes of both differentiation and of de-differentiation occur and a polymorphous or “multiform” picture is found, as in the glioblastomas. The marked degeneration phenomena, the fact that glioblastomas never metastasize and the rapid explosive growth have led some to assume that the glioblastomas really are degenerative processes and no true tumors at all.

In 1938 to 1944 Einarson and Neel,\(^6,7,8\) and Einarson, Neel and Ström- gren\(^9\) in a series of papers put forward a working hypothesis which may make it possible to combine the two theories and which may bring the solution.
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Working on the different forms of diffuse sclerosis, diffuse gliomatosis and glioblastomatosis they found that the differences might be due to varying constellations of the same four factors:

1. The dystrophic tissue factor: a constitutional insufficiency of the interfascicular oligodendroglia in dealing with the nutrition of the myelin sheaths.

2. The dyscatabolic tissue factor: an insufficiency of the microglia in dealing with the abnormal metabolic prelipoids and degeneration products of the myelin sheaths.

3. The histochemical tissue factor: the biological (stimulating resp. inhibiting) actions of the atypical metabolic degeneration products on the astrocytic apparatus.

4. The dysplastic tissue factor: the individual inherent tendency of the macroglia to proliferation and blastomatous growth.

Most probably the dystrophic factor is a hereditary conditio sine qua non for the development of the vast demyelinization characteristic of diffuse sclerosis (recessive inheritance). Based on this tissue factor hypothesis the authors introduced a new quantitative-histological classification of the cases of diffuse sclerosis.

The causal release of the first three tissue factors is thought to take place through influences exogenous to the brain (infections, trauma, intoxications, anoxia, dietary deficiencies, disturbances in lipid metabolism, endocrine anomalies, formation of a myelolytic agent). Furthermore the first three tissue factors are considered to possess the ability of actuating or releasing the fourth "intrinsic" tissue factor, and hence they may appropriately be termed "extrinsic." The use of these designations should, however, be strictly limited to this special conception. In their cases of diffuse glioblastomatosis the authors thus consider the intrinsic dysplastic factor the dominant one, while in other cases, characterized mainly by demyelinization and a milder form of reactive cellular gliosis, they think primarily of the 1st and 2nd factors, the 3rd factor only secondarily stimulating the cells to blastomatous growth. Only then does the 4th factor become of importance; in glioblastomatosis it is "intrinsic" with respect to the others.

An apparently significant argument in favor of this theory is the authors' claim to have definitely established the true existence of a glioblastomatous form of diffuse sclerosis, and to have shown that there actually do occur transitional cases between diffuse sclerosis (a degenerative process) and diffuse glioma (a true tumor); we refer especially to their Cases 7 and 8 (Einarson and Neel7) and Case 13 (Einarson, Neel and Strömgren9).

While this theory—or rather synthesis of theories—cannot as yet be considered proven, there are so many points which seem relevant to our problem that this short summary seems justified.

PATHOLOGY

While some authors have subdivided the classical glioma groups of Bailey and Cushing1, others have tried to simplify this grouping. Thus, Bergstrand2
divided the gliomas, with the exception of oligodendrogliomas and ependymomas, into two groups, called astrocytoma and glioblastoma respectively. Each group comprised three sub-groups (astrocytoma fibrillare, protoplasmaticum, gigantocellulare—glioblastoma multiforme, fusiforme, protoplasmaticum). This and other attempts at simplification have had no success and most neuropathologists find the Bailey-Cushing scheme indispensable. OsterTAG13 and others mention that the glioblastomas morphologically may be subdivided, but that a division is of no practical importance. Deery,4,5 however, dividing the glioblastomas into three groups according to the maturity of cells (fibril formation and number of mitoses) finds that there is an appreciable difference in the lengths of history before operation (9.5, 17.5 and

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**Fig. 1. Bilateral angionecrotic glioblastoma**

("butterfly" type)

12 patients

Age: 36-37-38-42-44-54-58-59-60-61-61-63 years

History: 1-2-3-4-4-4-4-5-7-12-13-60 (?) months

Typical psychosomatic state .................................. 11/12

Papilledema .................................................. 12/12

Hemianopia ................................................... 1/12

Triple symptom ............................................... 1/12

Aphasia .......................................................... 5/12

Impaired sphincteric control ................................. 9/12

Deaths without operation ................................... 2/12

Operative deaths* ............................................. 6/12

Postoperative survival time: 1-1-2-2 months

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* Operative deaths = All deaths after operation irrespective of cause of death.

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**Fig. 2. Bilateral angionecrotic glioblastoma**

("S-type")

3 cases

Age: 37-50-65 years

History: 6-9-9 months

Typical psychosomatic state .................................. 3/3

Papilledema .................................................. 2/3

Hemianopia ................................................... 0/3

Triple symptom ............................................... 0/3

Aphasia .......................................................... 0/3

Impaired sphincteric control ................................. 1/3

Deaths without operation ................................... 2/3

Operative deaths ............................................. 1/3

Postoperative survival time: None
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Fig. 3. Angioneurotic glioblastoma in one temporal lobe
4 patients
Age: 43-48-53-54 years
History: 2-3-3-4 months
Typical psychosomatic state: 3/4
Papilledema: 1/4
Hemianopia: 2/4
Triple symptom: 1/4
Aphasia: 3/4
Impaired sphincteric control: 1/4
Deaths without operation: 0/4
Operative deaths: 0/4
Postoperative survival time: 2-4-13-18 months

Fig. 4. Angioneurotic glioblastoma in posterior part of one hemisphere
21 patients
History: 1-1-2-2-2-2-2-2-3-3-3-4-4-4-4-4-4-4-5-5-9 months
Typical psychosomatic state: 19/21
Papilledema: 14/21
Hemianopia: 13/21
Triple symptom: 12/21
Aphasia: 5/21
Impaired sphincteric control: 7/21
Deaths without operation: 6/21
Operative deaths: 3/21
Postoperative survival time: 1-2-2-4-4-5-6-7-7-11-17-18 months
42 months respectively). He does not follow up this finding as to postoperative survival time.

As we had some surprisingly long postoperative survivals following operation for glioblastoma we suspected error in diagnosis and consequently revised our preparations. This led to a subdivision of the glioblastoma group into three types, which had much in common, the differences still warranting a division. We have become accustomed to speaking of an angionecrotic, a multicellular and a magnocellular type (glioblastoma angionecroticum, gl. multicellularare, gl. magnocellularare), the term glioblastoma multiforme covering the whole group, and we shall try to give an impression of our findings.

The angionecrotic type was found in 60/133 patients (37 men, 23 women). The cerebral localization of these tumors is shown in Figs. 1-4: 26 affected the right, 19 the left hemisphere only, while 15 were bilateral. Involvement of the corpus callosum was noted in 18 while possible in several others—this question can sometimes only be ascertained at autopsy, which was performed in 24 cases. Only about one third of the tumors were localized in the anterior part of the brain. All the tumors had their chief localization in the white matter; in 10 cases, however, there was macroscopical infiltration of the cortex and in 4 cases the tumor infiltrated the dura, which was confirmed microscopically. At operation these tumors were of the characteristic grey to yellow color. Ten contained one big cyst of the degenerative type with xanthochromic, jelly-like contents, while 6 contained numerous smaller cysts. In all the tumors necroses and hemorrhages were found. In 11 of the tumors calcifications, mostly of the gritty kind, were found macro- or microscopically.

Microscopically the picture is characterized by polymorphism of cells, differentiated and undifferentiated cells at random, necroses, hemorrhages, and vascularity with proliferation of intima and adventitia. The vessels frequently are lying in smaller or larger conglomerates and one gets the impression that they are integral parts of the tumor itself. Thromboses, fibrous and hyaline degenerations are common with the consequent necroses and "pseudo-rosettes," and areas of regeneration by connective tissue are always to be found. The cells themselves differ considerably in size and form—spongioblasts in various stages of differentiation, protoplasmic and fibrillary astrocytes mixed with giant cells, some with one, others with several nuclei. The vascular phenomena and the resulting changes are so characteristic that the name angionecrotic glioblastoma seemed natural (Figs. 5 and 6).

While the described picture sometimes is to be found in some places in our other two types, and especially the vascular changes in various degrees are met within all three types, the picture in other respects is different:

The multicellular type was found in 46/133 patients (33 men, 13 women). This type seems less infiltrating in mode of growth—less diffuse—than the angionecrotic type. Involvement of the corpus callosum was found in 10, invasion of the cortex in 23 and of the dura in 4. Most of the tumors were localized in the anterior part of the brain (Figs. 7 to 10). Parts of the tumors
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Fig. 5. NK 3386. Glioblastoma, angioneerotic type. (Hematoxylin)

Fig. 6. NK 909. Glioblastoma, angioneerotic type. (Hematoxylin)
Fig. 7. Bilateral multicellular glioblastoma
5 patients

Age: 34-44-45-46-47 years
History: 2-3-6-12-70 (?) months

Typical psychosomatic state .................. 5/5
Papilledema ........................................ 4/5
Hemianopia ........................................... 0/5
Triple symptom .................................... 0/5
Aphasia .................................................. 1/5
Impaired sphincteric control ................. 4/5
Deaths without operation ..................... 0/5
Operative deaths ................................. 3/5
Postoperative survival time: 1-28 months

Fig. 8. Multicellular glioblastoma in one frontal lobe
19 patients

History: 1-1-2-2-2-2-3-3-3-3-5-8-9-9-9-16-18-24-24-36-36 months

Typical psychosomatic state .................. 12/19
Papilledema ......................................... 14/19
Hemianopia ........................................... 1/19
Triple symptom .................................... 2/19
Aphasia ............................................. 5/19
Impaired sphincteric control ................. 3/19
Deaths without operation ..................... 2/19
Operative deaths ................................. 3/19
Postoperative survival time*: 2-2-3-5-6-12-14-24-2.5-28-30-33-38-64 months

1) Extracerebral lumps of tumor

* Italics indicate that the patient is still living.
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Fig. 9. Multicellular glioblastoma in one temporal lobe
6 patients
Age: 23-31-36-40-52-63 years
History: 3-3-10-12-12-36 months

Typical psychosomatic state........................................ 5/6
Papilledema.......................................................... 3/6
Hemianopia.......................................................... 1/6
Triple symptom.................................................... 0/6
Aphasia............................................................... 3/6
Impaired sphincteric control........................................ 2/6
Deaths without operation........................................... 0/6
Operative deaths.................................................... 1/6
Postoperative survival time: 3-3-11-24-27 months

Fig. 10. Multicellular glioblastoma in posterior part of one hemisphere
7 cases
Age: 13-27-29-40-50-51-52 years
History: 4-6-6-9-13-18-23 months

Typical psychosomatic state........................................ 4/7
Papilledema.......................................................... 3/7
Hemianopia.......................................................... 2/7
Triple symptom.................................................... 1/7
Aphasia............................................................... 2/7
Impaired sphincteric control........................................ 0/7
Deaths without operation........................................... 0/7
Operative deaths.................................................... 1/7
Postoperative survival time: 17-18-18-22-23-28 months
were soft, resembling the angioneurotic type; other parts were firm and more fleshy. In 12, single degenerative cysts were found and in 23, several smaller cysts. The color at operation was similar to that of the angioneurotic type, but necroses and hemorrhages were less frequent. At operation the tumor seems more circumscribed, and between the tumor and the brain two zones are frequently to be found—an edematous zone similar to that found surrounding the angioneurotic type, and a peripheral zone of firm glial reaction, microscopically containing no tumor cells; this latter zone was excised with

![Figure 11. NK 4090. Glioblastoma, multicellular type. (Hematoxylin)](image)

the tumor whenever possible. Microscopy showed that this zone was in part to be found in the preparations in 37 cases, tallying with the impression of the operator, who deemed “macroscopical total excision” to have been carried out in 20, which occurred in none of the angioneurotic cases.

The multicellular type is microscopically vascular, but less so than the angioneurotic type; the typical proliferation of intima and adventitia is nearly always present. The characteristic feature of this type seems less to be polymorphism of cells than richdum in cells, large areas of well preserved rather closely lying fusiform or smaller glial cells being found. This tumor in parts resembles a spongioblastoma somewhat (Figs. 11 and 12), but may be distinguished by more polymorphous cells, areas of edema and necroses, and by the vascular changes which, if less conspicuous than in the angioneurotic type, are still to be found.

The magnocellular type was found in 27/133 patients (22 men, 5 women). These tumors are still more circumscribed than the previous type. Only one
involved the corpus callosum, while 5 invaded the cortex, and 1 the dura. Their localization is shown in Figs. 13 to 16. Macroscopically this type is rather fleshy, in places tough, and the color usually a light red-brown. In 2, single degenerative cysts were found; in 9, several smaller cysts. Calcifications have been found only microscopically (4 cases), while the peripheral zone of glial reaction was recognized in the microscopical preparations in 16.

The dominant feature microscopically is the big, plump cells (Figs. 17 and 18), usually with one excentric nucleus; multinuclear giant cells are perhaps somewhat more frequent than in the other two types. In between the big cells are seen areas of spongioblasts and astrocytes of different sizes and in different stages of development, and these areas with the typical vascular changes, which if less frequent still are to be found, serve to distinguish the magnocellular glioblastoma from the astrocytoma gemistocyticum.

When experience has been gained the diagnosis between the three types can usually be made at operation. Several times, however, a multicellular glioblastoma has been taken for an angionecrotic one, while the angionecrotic type has never been taken for anything else. The magnocellular type has occasionally been mistaken for a metastatic tumor, but is usually considerably larger than the average metastasis.

CLINICAL SYMPTOMS, TREATMENT, AND RESULTS

Sex. In most materials of glioblastomas the male sex preponderates. In our series of 133 patients 92 were men, and 41 women.
Fig. 13. Bilateral magnocellular glioblastoma
2 patients
Age: 24–30 years
History: 3–6 months
- Typical psychosomatic state: 0/2
- Papilledema: 2/2
- Hemianopia: 0/2
- Triple symptom: 0/2
- Aphasia: 0/2
- Impaired sphincteric control: 1/2
- Deaths without operation: 0/2
- Operative deaths: 0/2
- Postoperative survival time: 15–27 months

Fig. 14. Magnocellular glioblastoma in one frontal lobe
8 patients
Age: 18–27-29-30-31-34-35-36 years
History: 2-2-2-7-12-18-24-26 months
- Typical psychosomatic state: 4/8
- Papilledema: 6/8
- Hemianopia: 0/8
- Triple symptom: 0/8
- Aphasia: 1/8
- Impaired sphincteric control: 3/8
- Deaths without operation: 0/8
- Operative deaths: 0/8

* This patient was operated upon for a recurrence 58 months after the first operation.
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Fig. 15. Magnocellular glioblastoma in one temporal lobe
11 patients
History: 1-2-2-2-3-4-4-5-7-24-24 months
Typical psychosomatic state ........................................ 9/11
Papilledema ........................................................... 8/11
Hemianopia ............................................................. 3/11
Triple symptom ......................................................... 2/11
Aphasia ................................................................. 3/11
Impaired sphincteric control ......................................... 3/11
Deaths without operation ............................................. 0/11
Operative deaths ....................................................... 3/11
Postoperative survival time: 4-6-12-12-17-36-33-34 months

Fig. 16. Magnocellular glioblastoma in posterior part of one hemisphere
4 patients
Age: 22-30-36-36 years
History: 2-3-3-4-60 months
Typical psychosomatic state ......................................... 3/4
Papilledema ............................................................ 3/4
Hemianopia ............................................................ 1/4
Triple symptom ....................................................... 1/4
Aphasia ................................................................. 2/4
Impaired sphincteric control ........................................ 1/4
Deaths without operation .......................................... 0/4
Operative deaths ..................................................... 0/4
Postoperative survival time: 5-22-27-38 months
Fig. 17. NK 118. Glioblastoma, magnocellular type. (Hematoxylin)

Fig. 18. NK 8533. Glioblastoma, magnocellular type. (Hematoxylin)
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Age. The average age of our first 102 patients does not differ markedly from that in other materials. Dividing the patients into the three groups we find that the average age for the angioneurotic type was 49.5 years at time of admission, while for the multilayered and the magnocellular groups it was 39.6 and 36.4 respectively, so it seems safe to assume a real difference as to age for the three types (Fig. 19).

Length of History. While a short history is typical of glioblastoma, Deery\(^5\) found marked difference when he divided the glioblastomas into three types (see above). Long and fairly long histories (Fig. 20) are especially seen in our last two groups; while the average history for the angioneurotic type was 5.5 months, we find 12.2 and 10.9 for the multilayered and the magnocellular groups. The difference in this respect is, however, not so striking as in the ages of the patients. While one feels somewhat sceptical as to the very long histories (60 months, 2 cases; 70 months, 1 case), one still cannot help thinking of the theory of Einarson and Neel;\(^5\) following this theory it could be assumed that some factor extrinsic to the brain could suddenly activate a quiescent anlage or a slowly growing tumor, but as to proof of this pathogenesis, we have none.

Cerebral Localization. All of the glioblastomas in our cases have been localized in the cerebrum, while none were localized infratentorially. We have tried roughly to localize the tumors in certain groups, but want to em-

![Fig. 19. Age of 102 patients with the three types of glioblastoma.](image-url)
phasize that the projectional markings in the schematical drawings are to be taken with several grains of salt, since the markings of these tumors can be only approximate. The “butterfly” type (12 cases) seems typical of the angionecrotic group. The bilateral tumors of the multi- and magnocellular groups are quite different; in both groups the tumors tend to grow into the interhemispherical cistern and only a smaller part is to be found in the brain itself. The “S-type”—crossing through the corpus callosum from the anterior part of one hemisphere into the posterior part of the other—has been found only in the angionecrotic group. All three groups have been found in the posterior part of one hemisphere and in one temporal lobe, while we in no case found an angionecrotic glioblastoma in one frontal lobe. In this location the multicellular type tends to grow subpially outside the brain substance and can be found in fleshy lumps along the base of the frontal lobe or growing into the cisterns. While this type frequently is found in the most anterior part of the frontal lobe, the magnocellular type seems to favor the premotor region, but our material is still too small to make this certain.

Clinical Symptoms. A discussion of the clinical symptoms falls outside the scope of this report. Some symptoms have been summarized below the schematical drawings and only a short commentary will be added here. By

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**The 3 Types of Glioblastoma.**

*History in months.*

![Graph](image)

**Fig. 20.** Length of history of 102 patients with the three types of glioblastoma.
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"typical psychosomatic state" we mean the nearly pathognomonic state described by Olivecrona\textsuperscript{10} and others and familiar to all neurosurgeons—the intoxicated, "rotten" appearance and the turbid psyche. This state is seen most frequently and markedly in cases of bilateral angionecrotic tumors, but is by no means uncommon in other types and localizations and may give some slight support to the assumption of active factors extrinsic to the brain. We had hoped that the triple symptom (some motor and some sensory involvement with a hemianopsia) would be a help in diagnosing the angionecrotic type, but this was found unreliable. A frequent symptom is impaired sphincteric control which, however, is a common symptom in many cases of tumors in the anterior part of the brain, even meningiomas (Olivecrona\textsuperscript{11}) and is, moreover, dependent on the psychical state of the patient.

In most of our cases the preoperative diagnosis was glioblastoma, with the usual percentage of error (subdural hematoma, abscess, metastasis), but it was found impossible to make a reliable "type-diagnosis" on the clinical symptoms alone.

The only real help to a "type-diagnosis" has been cerebral angiography. Arteriovenous anastomoses (Fig. 21) were found in 21 of 33 angionecrotic

![Fig. 21. NK 3945. Glioblastoma, angionecrotic type. Angiography showing the typical arteriovenous anastomoses.](image)
glioblastomas, in only 1 of 24 multicellular tumors (and even then not quite typical), and in none of 17 patients with magnocellular glioblastoma. The investigation consequently is of help when positive, but fails in a certain number of angionecrotic tumors, presumably because no anastomoses are patent at the time of angiography. Still, this method has been of real help in making a decision as to operation in some patients in bad general condition: If anastomoses are seen, the tendency will be to discourage operation. We want to stress, however, that in our opinion the indication for operation must in every case be an individual one.

Surgical Technic. In our first cases we tried to carry out lobectomies, but soon discontinued this unsatisfactory procedure for these tumors, and made as clean an excision of the tumor alone as was possible without damaging important centres. In the angionecrotic type this was most frequently done by means of suction with subsequent coagulation of the vessels. In some rare cases of the angionecrotic type and in most tumors of the other two types a zone of edematous brain tissue with tumor invasion was surrounded by yet another zone of firm, glial reaction without invasion; in these cases the excision of this last-mentioned layer, which, however, may not be present all the way around the tumor, was carried out as far as possible. A "macroscopical total excision" was felt to have been carried out in 20 of 37 multicellular glioblastomas, in 14 of 25 magnocellular tumors and in none of the angionecrotic group. The dura usually was closed and the bone flap replaced without decompression. The cavities generally were drained for 24 hours through a separate wound.

Fatalities. These are recorded in the figures below the schematical drawings. Of the patients without operation (hopeless general condition) 10/40 died with angionecrotic tumors, 2/37 with multicellular tumors and none in the magnocellular groups. The operative deaths (mostly shock and pneumonia) were 10/30, 8/35 and 3/25 in the three groups respectively, making an operative mortality of 23.3 per cent for the whole series.

Postoperative Roentgen Therapy. This was given in most cases (3,600 r in 15 daily doses) and when possible the treatment was repeated after 3 and 6 months. While it is very difficult to judge of the effect of radiation in these cases, it is our impression that this therapy is of definite value. A half-hearted attempt of giving every other patient Roentgen therapy was never carried through as we felt ourselves unable to deprive the particular patient of what we felt was the best chance.

Recurrences. Three patients with recurrences of the multicellular type have been reoperated upon 14, 22 and 24 months after the first operation, with one death. Two with magnocellular recurrences were operated upon after 18 and 30 months, with no deaths. In no case of secondary operation has a "macroscopical total excision" been felt to have been carried out. In some late recurrences of these types, with the patient in bad general condition, radiation has been given, but has had no apparent effect. In the angionecrotic group no recurrence has been treated surgically, but radiation has sometimes been given, mostly solaminis causa on the wish of the relatives.
Postoperative Survivals. Fig. 22 seems to us to speak for itself. While only 20 per cent of the angionecrotic group lived 1 year after operation, this was the case with no less than 63 per cent of the multicellular and 77 per cent of the magnocellular groups (operative deaths deducted). And 1½ years after operation all patients harboring an angionecrotic glioblastoma were dead, while of the other groups nearly half of the multicellular and over half of the magnocellular groups were still living.

As to "useful life" (meaning that the patient is able to do some work, not necessarily his usual work, and to move about without too much discomfort and to partake to some extent in usual life), the figures are:

<table>
<thead>
<tr>
<th>Type</th>
<th>No. of Postoperative Survivals</th>
<th>Useful Life for more than ½ Year</th>
<th>Useful Life for more than 1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angionecrotic</td>
<td>30</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Multicellular</td>
<td>27</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>Magnocellular</td>
<td>22</td>
<td>13</td>
<td>10</td>
</tr>
</tbody>
</table>

Fig. 22. Postoperative survival time for 69 patients with the three types of glioblastoma.
Some of these patients are able to live a quite useful life, but we feel incapable of judging if anyone has been definitely cured. It not infrequently has happened that a patient who has visited us some months or weeks before and been found quite well and without symptoms, suddenly has been struck down with a recurrence and has died within a couple of days. Happily the end mostly comes suddenly, the patient being unconscious from the start, presumably from a sudden hemorrhage in the tumor as we have found in some brains (again one cannot help thinking of Einarson and Neel’s factors extrinsic to the brain changing the milieu of the tumor). In other cases the end is long in coming and the patient is an object of pity and a cause of despair to his relatives. In judging results it must always be remembered that in Fig. 22 all deaths without and from operation have been subtracted and that these failures amount to one third of the 102 patients who originally sought our help. Still, in many cases valuable living time may be saved for the patient and we certainly feel that the surgical treatment of glioblastomas, especially of the multi- and magnocellular groups, is worth while.

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When we think of the differences in the three types of glioblastoma as to macroscopical and microscopical pathology, as to age of the patients at time of admission, as to length of history, cerebral localization and, last but not least, as to postoperative survival time, we feel fairly certain that the difference between these three types is real and certainly established. Some objections, however, immediately present themselves:

1. The multi- and the magnocellular glioblastomas are not glioblastomas at all. On revising our preparations, however, we still feel that we must maintain our diagnosis. Moreover, if this was the case we should have an increase in our number of glioblastomas and a decrease in some other glioma group, especially perhaps the spongioblastoma polare. This, however, seems not to be the case when we compare Cushing’s percentages of classified gliomas (687) with our own (409 classified gliomas of our first 1000 verified intracranial tumors):

<table>
<thead>
<tr>
<th>Type of Glioma</th>
<th>Cushing</th>
<th>Copenhagen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Astrocytomas</td>
<td>37.1%</td>
<td>43.0%</td>
</tr>
<tr>
<td>Glioblastomas</td>
<td>30.3%</td>
<td>25.9%</td>
</tr>
<tr>
<td>Spongioblastoma polare</td>
<td>4.7%</td>
<td>4.4%</td>
</tr>
<tr>
<td>Ependymomas</td>
<td>3.6%</td>
<td>10.2%</td>
</tr>
<tr>
<td>Astroblastomas</td>
<td>5.1%</td>
<td>2.5%</td>
</tr>
</tbody>
</table>

While the materials differ considerably it is not in the way one would expect if we had included benignant gliomas in our glioblastoma group. Our small percentage of astroblastomas cannot be explained in this way as the microscopical picture is quite different, and the localizations of these tumors differ from those of the glioblastomas. Furthermore, the number of these tumors is too small to affect the issue.
2. The three types of glioblastoma are only the same tumor exhibiting different characteristics at different stages of development. In view of the longer histories in the multi- and magnocellular groups it seems extremely improbable that the angionecrotic type could be the final stage of development of these types, while the opposite is obviously impossible.

3. The three types of glioblastoma are only the same tumor exhibiting different characteristics in different localizations of the brain. This seems improbable as all types have been met with in most regions of the brain, even if the different types largely favor certain localizations.

4. The three types of glioblastoma are only the same tumor exhibiting different characteristics according to the age and different condition of the "host." This is a possibility that must be borne in mind, but we have no foundation at all for this assumption. Still, especially in view of Einarson and Neel's theory, it is a tempting thought and further research, particularly of histological character, seems indicated.

5. The three types of glioblastoma are really three different tumors. In view of the many features common to all three types, we feel that the term "type" covers their differences—both pathologically and clinically the pictures are so similar that we prefer to speak of an angionecrotic, a multicellular and a magnocellular type of glioblastoma multiforme. That the differentiation between these types, however, has not only a scientific, but also a very practical surgical significance is, we feel sure, fairly established.

SUMMARY

In a series of glioblastomas significant differences are found in macroscopical and microscopical pathology, in age of patients at time of admission, in length of histories, in cerebral localization, and especially in postoperative survival time. It is suggested that the group of gliomas named glioblastoma multiforme is composed of three types differing in the above-mentioned aspects. The names glioblastoma angionecroticum, gl. multicellulare and gl. magnocellulare are proposed for these three different types.

REFERENCES

8. Einarson, L., and Neel, A. V. Contribution to the study of diffuse brain sclerosis with a compre-


