THE PROBLEM OF THE GLIOBLASTOMAS*

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THE YEARS 1918 and 1926 are two important dates in the development of neurological surgery. Therefore, in studying the problem of the glioblastomas, we must first consider what conditions we faced prior to 1918 and then again what influenced this problem after 1926.

In 1918 ventriculography was discovered. Prior to that date, those few of us who were attempting to do neurological surgery were occupied primarily with detailed neurological studies to enable us to arrive at a diagnosis of brain tumor, and then we carried these examinations still further trying to localize the lesion. When we had finally exhausted all our methods of study, which at that time consisted solely of the history and neurological examination, we had the further problem, no mean one at that time, of convincing our neurological or medical colleagues that an operation should be undertaken; and then, finally, we had the problem of the operation itself. It is difficult for neurosurgeons today to realize what we were up against. For example, the first dozen patients with brain tumor I saw in 1911 were all blind. I wondered whether I would ever see one before he was blind. In those days, we never dared to make a positive diagnosis of tumor unless the patient had a full-blown choked disc. The only exception to this rule was if we were fortunate enough to have a patient with typical Jacksonian convulsions. I do not remember just when I operated upon the first patient with tumor who had no choked disc, but it was after 1918. Though we made most careful neurological examinations, many of the symptoms and signs elicited we were unable to interpret correctly. For example, paresis of one sixth nerve caused us no end of difficulty and mental juggling trying to fit it into a clinical picture. We did not appreciate that bilateral sixth nerve paralysis was a very different matter. While unilateral sixth nerve paresis was a general sign of increased intracranial pressure due, as Cushing pointed out in 1911, to pressure on the nerve by a branch of the basilar artery, bilateral sixth nerve paralysis was due to a pontine lesion where the two sixth nerve nuclei lie close together. It took some of us some time to realize what a great difference existed between paresis and paralysis of these nerves and how seriously this might affect the diagnosis and prognosis in a given case.

The significance of visual fields was by no means clear, and the sign of a partial or complete homonymous hemianopsia we didn’t learn to interpret until after 1911, when Adolph Meyer and Archambault described the visual

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pathway traversing the temporal lobe. It was only then that the importance of very careful study of the visual fields was appreciated. Even nystagmus and ataxia caused us difficulty, and I recall vividly exploring a patient’s cerebellum twice because of these signs, and only at a third attempt, because of some other signs that had developed, did I finally remove a large frontal meningioma. Frontal and cerebellar lesions were not infrequently confused and v. Monakow advanced the theory of diachisis to explain such occurrences. These are but a few of the diagnostic pitfalls we encountered.

Then came the operative procedure. Though this is still a formidable affair, in those days it was far more so, for we lacked many of the aids we have today. Blood transfusion was just beginning to be used, but it was unusual to have more than one pint ready, and of course that was long before the days of blood banks. Matching of blood was not well developed and citrated blood had not been heard of. So we had to use either direct transfusion by the Crile method or Kimpton tubes, waxed cylinders in which the blood was collected and then introduced into the patient. The control of hemorrhage was an ever-present problem. Wax to control bleeding from the bone and silver clips to control bleeding from the brain vessels we did have. Bits of muscle were also used as a hemostatic, taken either from the patient himself or from another being operated upon at the time, or by using pigeon’s breast, as was practised by de Martel. The value of giving the patients fluid during the operation to counteract the fluid loss was not known or appreciated, and the control of increased pressure by tapping the ventricles had not become a routine procedure. In fact, I recall a meeting held here in Philadelphia in 1922 at which there was a lengthy discussion on the wisdom of doing a ventricular puncture in the course of an operation, and there were those who strongly opposed it.

Then it happened innumerable times that the patient was operated upon but the tumor was not found. No neurosurgeon today can fully appreciate the chagrin and mortification of being obliged to acknowledge that—time and time again.

When we did remove the tumor, the pathologist told us it was a glioma.

In 1918 Dandy made his epoch-making discovery of ventriculography. This was not immediately accepted, but as soon as it was, it transformed the matter of localization completely. It soon became almost a disgrace not to locate a tumor at operation, and negative explorations were far less frequent. After ventriculography came into general use, the incidence of locating a tumor jumped from about 55 per cent to over 97 per cent, but there still were tumors that we did not expose because we did not have facilities to incise the cortex freely, and therefore hesitated to incise it with impunity as we do today.

The pathologist still reported gliomas, but from this time on we removed tumors much more frequently and came to realize that though the pathologist reported all the tumors as gliomas there were different types. Some were cystic, some were well encapsulated, some contained calcium and
threw a shadow on the x-ray plate. The patients with the cystic, the calcified, and the well encapsulated tumors had a much better prognosis, and, even if the tumor had not been completely removed, had a longer survival period. We found that by combining a decompression with the operative removal, we were able to make many of these patients comfortable and get a certain number back to work, and we continued to follow this policy from 1918 to 1926. Then in 1926, Cushing and Bailey published their valuable monograph in which, by making use of the special stains of Cajal and Hortega, they were able to differentiate and classify the various tumors of the glioma group. They found that in the cystic tumors certain cells predominated and these they called astrocytes and the tumors astrocytomas. Another type of cell was found in the calcified tumors which they called oligodendroglialomas. In still another type that proved to be radio-sensitive, they identified medulloblasts and called the tumor medulloblastoma. Still another tumor was recognized that was rapidly growing and had a very short history, and this was called a glioblastoma.

These glioblastomas were, and still constitute, the most serious problem for the neurological surgeon. There are several fundamental principles that are involved in dealing with them.

First. Are we able to determine prior to operation the pathology of a tumor? The history of a glioblastoma is not characteristic but there are certain features that strongly suggest the diagnosis. If an adult patient has symptoms of increased intracranial pressure rapidly, in a month or two, and if the symptoms and signs indicate that the tumor is in the cerebrum, he is very likely to have a glioblastoma. I say adult because, though this type of tumor does occur in children, it is far less common than in adults, and I emphasize cerebrum as glioblastomas occur far more commonly above the tentorium than below it. In my own series there were 233 cerebral glioblastomas and only 7 cerebellar. Still, on the history alone, we would not be justified in making such a diagnosis. But it is well to remember that glioblastomas do constitute about 45 per cent of all brain tumors. Recently, some roentgenologists claimed to be able to identify a glioblastoma in an angiogram by the vascular pattern.

Second. What is the best method of handling a brain tumor today? There is no question that all benign tumors and well encapsulated tumors should be removed surgically. Even if the tumor is extraordinarily large or if it is located in a somewhat inaccessible place like the lateral ventricle, the third ventricle or the fourth, it should be removed. Some meningiomas undergo malignant degeneration and recur. Some oligodendrogliomas cannot be completely removed and sooner or later begin to grow again. Medulloblastomas, which are very radio-sensitive, may be completely removed at times but more often are incompletely removed and then are controlled with deep x-ray therapy for a number of years before they cause renewed trouble. But all neurosurgeons are agreed that all these tumors should be operated upon and an attempt made to remove them. I have always taken the same
attitude in regard to glioblastomas. Though I have rarely if ever permanently
cured a patient with glioblastoma, I firmly believe these patients should be
given relief, and relief they most certainly can get, sometimes for a number
of years.

I have seen patients who, completely incapacitated temporarily, were
entirely restored to a normal state so that they were able to carry on their
work for a year or more. I recall a physician who had hemiparesis and was
partially aphasic who was restored so that he was able to carry on his
practice for a full year. This does not happen in many cases but sufficiently
often, I believe, to justify the procedure. Then, too, most of the patients
can be kept from becoming blind and be relieved of the excruciating head-
aches from which one with brain tumor suffers if operation is not performed.

By means of electrocoagulation and suction and the use of hemostatics
like fibrin foam or gelfoam, more and more radical removals can be under-
taken. But up to the present time, a permanent cure of a glioblastoma has
rarely if ever been obtained. We therefore are faced with the third important
question, and this involves an ethical as well as a purely medical problem.

Third. If we can determine that we are dealing with a glioblastoma that
cannot be cured, should we do anything for such a patient? A group of
younger neurosurgeons has in the past 5 or 10 years taken the attitude that
if they can positively determine they are dealing with a glioblastoma,
there is no use in operating. Some of them arrive at the diagnosis by a needle
biopsy and others by an angiogram. To my way of thinking, this point of
view cannot be too severely condemned. First of all, these men evidently
do not believe that giving patients temporary relief is worth while, and there-
in are neglecting one of the important functions of a physician. Of course we
would all prefer to operate only on those patients whom we can cure, and
it is distressing to see patients return with a renewal of their symptoms, but
does that give us the right to refuse them temporary help? Then too, neither
a pathological diagnosis nor angiography is absolutely infallible. In the
same way, I am entirely opposed to giving a patient deep x-ray therapy
without first having a pathological diagnosis. I recall a lovely girl some years
ago who had symptoms of a cerebellar tumor. The surgeon was so certain
she had a medulloblastoma that he gave her deep therapy. She improved
temporarily, and this was construed as confirmation of the diagnosis; there-
fore when her symptoms recurred, she was again given a course of x-ray
therapy, but this had no effect. I saw her when she had marked impairment
of vision, advised operation and removed a cholesteatoma. Her vision was
saved and she has been perfectly well since then. This and similar ex-
periences have made me feel very strongly that no patient should ever re-
ceive x-ray therapy until a pathological diagnosis has been made.

Lastly, this point of view, of not operating in these cases, is that of the
defeatist, an attitude that I have never been able to accept. Had medicine
followed this line of reasoning, progress would have been markedly hindered.
Certainly many of you recall the days where there were no cures of carcinoma
of the stomach or the lung. Seventy-five years ago, Billroth wrote with distress of the high mortality he had in doing laparotomies for ovarian tumors but that did not deter him from continuing to try to remove them. Countless other examples could be cited in medicine and surgery where a defeatist attitude would have delayed progress.

The sound method of dealing with the glioblastomas seems to me therefore, until some more effective method of treatment is discovered, to continue to attempt to remove these tumors surgically, always aiming to be radical enough to try to obtain a cure. With this idea in mind, we must make more strenuous efforts and make use of every new device that is offered.

The greatest stumbling block in the cure of glioblastomas has been the difficulty of finding the limits of an infiltrating tumor. The electrosurgical unit and suction have been of inestimable help but they are not enough. A very promising aid lies in the recent discovery by Selverstone and Sweet that a tumor can be impregnated with radio-active phosphorus and then its limits be outlined by the use of a specially constructed Geiger counter.

Certainly we cannot hope to solve the glioblastoma problem by throwing up our hands and saying there is nothing we can do. On the contrary, the solution lies in our constantly pressing on, making more and more strenuous efforts to remove these tumors, and not allowing ourselves to be deterred by any obstacles that lie in our path.