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ARMED FORCES INSTITUTE OF PATHOLOGY

ATLAS OF TUMOR PATHOLOGY

Section X—Fascicles 35 and 37

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James W. Kernohan
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TUMORS OF THE CENTRAL NERVOUS SYSTEM

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INTRODUCTION

Tumors of the central nervous system have never received the attention given to neoplasms in other parts of the body. This may be due to lack of general understanding of this group of tumors, to a somewhat cumbersome nomenclature which has been attached to them, or to the fact that they have been considered rather rare. This fascicle discusses all neoplasms arising within the skull and spinal canal from the brain and spinal cord, meninges, nerve roots, blood vessels and extradural tissues in the spinal canal. Tumors of the pineal body, originally announced as a separate fascicle, are included with the central nervous system. The pituitary gland tumors are ordinarily considered with tumors of the central nervous system, as they impinge on neighboring structures and produce neurologic phenomena and pathologic changes of interest to the neuropathologist; in this Atlas, however, they are discussed separately in Fascicle 36.

Primary tumors involving the central nervous system, once considered rare, are now recognized as occurring with considerable frequency. In recent years about 9 percent of all neoplasms removed surgically at the Mayo Clinic were located in the central nervous system or its coverings—the meninges. During the same period the incidence of carcinomas of the stomach and rectum was about 10 percent, carcinomas of the colon about 9.5 percent, and carcinomas of the female breast almost 10 percent. In the group of neoplasms of the central nervous system available for study in our laboratory, about 80 percent were located in the cranial cavity and about 20 percent were located in the spinal canal, emphasizing the fact that tumors of even the spinal cord are not rare.

The classification of central nervous system tumors used in this fascicle is based on the cell type from which the tumor was derived, insofar as this has been possible, since evidence indicates that neoplasms arise from pre-existing cells by a process of dedifferentiation (see Kernohan, Mabon, Svien, and Adson). The gliomas, derived from the neuroglia, the specific supporting nervous tissue, are the most interesting, most complicated, and at the same time most controversial of the central nervous system tumors. There is a very limited variety of cells in the adult nervous system, and there should be a limited variety of

gliomas. If we consider microglia to be a modification of the reticuloendothelial system and thus not of ectodermal origin, there are only three types of glial cells in the nervous system. The three types of glial cells of the central nervous system are astrocytes, oligodendroglia, and ependyma. Primary neoplasms of nerve cells are rare and will be discussed separately as neuroastrocytomas. We should thus have three types of neoplasms arising from these three types of cells but with varying degrees of dedifferentiation or various stages of anaplasia. However, the nomenclature of brain tumors is not nearly as simple as this suggestion implies.

In most series of brain tumors, especially in the glioma group of tumors, there are a number which are unclassified and perhaps are unclassifiable. The size of this group varies from one series to the next and to a large extent depends on the criteria set up by each investigator and how rigidly the criteria are adhered to. In brain tumors obtained as the result of surgical exploration, not infrequently very small specimens are removed for biopsy from deep-seated inaccessible tumors, and these small fragments are inadequate for accurate diagnosis and classification. We have a fair number of such cases and we have been in the habit of indexing them as "glioma—type (?)." Some such designation seems to us to be adequate, although there are many ways by which they could be designated such as "unclassified glioma," "unclassified tumor" if the lesion cannot be identified as a glioma, and so forth. There is another, relatively small group in which diagnosis cannot be reached; we have put it in the category of "unclassifiable" glioma or tumor. Adequate amounts of tissue are available, which we repeatedly re-examine. In the light of increased experience we have been able to reduce the number of these tumors still more, and expect that in time this puzzling group can be included into known categories.

Some tumors of the central nervous system have a predilection for certain areas of the brain. For example, meningiomas are located most commonly in the parasagittal area or on the anterior part of the base of the skull such as the sphenoid ridge, olfactory groove, or around the sella turcica. They are uncommon in the occipital lobes or in the posterior fossa. These same tumors are common in the thoracic segments of the spinal cord but rare in the lumbosacral portions. Cerebral neurilemomas are found almost exclusively on the eighth cranial nerve root and only with great rarity on other cranial nerve roots except in cases of von Recklinghausen's disease. Medulloblastomas occur in the midline of the cerebellum of children and occasionally in the same location in young adults.

Certain tumors tend to be more frequent at different ages. Tumors found in the young are different in frequency and type from those encountered in the nervous system of the adult, and both differ from those found in old people.

In children most brain tumors are found in the cerebellum, and in this age group the most common tumor is a cystic astrocytoma; the second in order of frequency is a medulloblastoma, followed by ependymomas of the fourth ventricle. In the aged the most common tumor is a highly malignant astrocytoma (glioblastoma multiforme), found almost exclusively in the cerebrum.

Symptoms

Brain tumors produce symptoms of two types: first, those due to the fact that the brain is enclosed in a rigid box, the skull, and consequently the growth of the tumor produces general symptoms due to a marked increase in the intracranial pressure; second, symptoms due to the local effect of the tumor on the special function of the part of the brain in which it is growing or on which it impinges. Symptoms of the first group are of no help in localizing the lesion for surgical attack, since tumors in almost any part of the brain may produce these general symptoms. Symptoms of the second group are important because of their localizing value, but they may be and often are complicated by the superimposition of the symptoms due to generalized increased pressure. This generalized increased pressure may be the result of the size of the neoplasm itself, but more commonly it is due to associated edema of the brain tissue around and even at a considerable distance from the tumor. Edema of the brain does not of necessity indicate the type or degree of malignancy of the tumor, but marked edema is usually more pronounced in rapidly growing, highly malignant neoplasms than in other tumors. Nor is edema of the brain specific for primary brain tumors, since it frequently accompanies metastatic tumors, abscesses, trauma, and so forth.

Edema of the Brain

This reaction of the brain (fig. 1) to tumor, injury, and inflammation is sometimes referred to as "brain swelling" and sometimes as "brain edema." Many workers differentiate "brain swelling" associated with tumors from "brain edema" such as is found in uremia, but we have been unable to observe any of the differences reported by others, and consider the two types of edema the same thing. This edema may be purely a local reaction in the neighborhood of the tumor. Sometimes it involves one lobe (fig. 20); at other times it extends to several lobes or even to one whole hemisphere. Occasionally, but rarely, it spreads to the opposite hemisphere of the cerebrum. The cerebellum is rarely involved.

The causes of the edema are not known, but when it is present there are marked accentuations of the symptoms produced by the primary lesion. The involvement of neighboring tissues and functioning areas adds new signs or symptoms and makes the localization of the lesion more difficult or even impossible. At times the edema changes the course of the symptoms produced by the lesion in a dramatic and very critical manner.

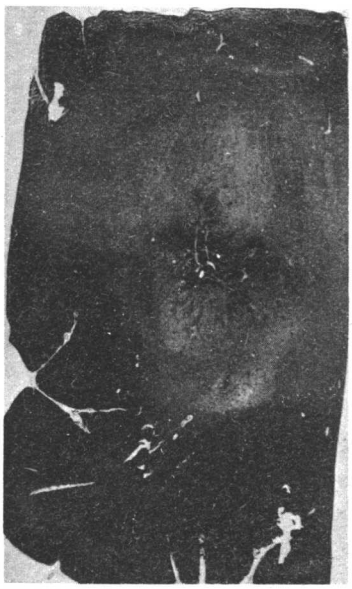

Fig. 1

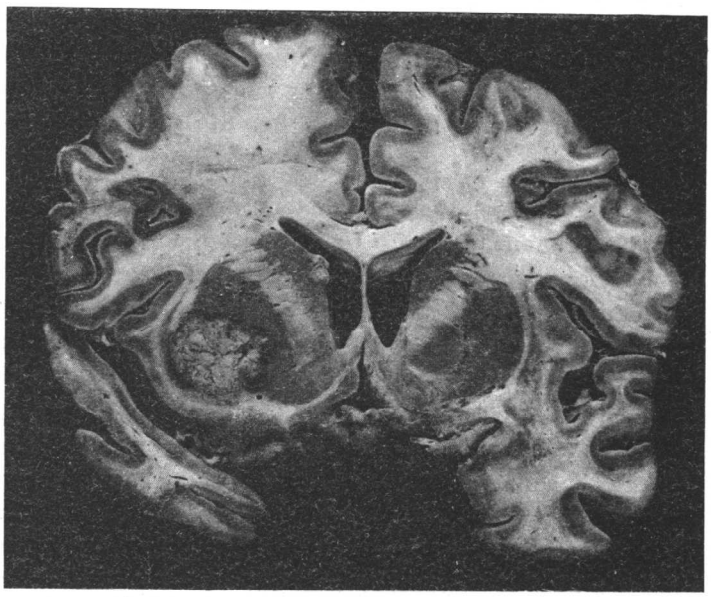

Fig. 2

Figure 1. Brain edema in the neighborhood of an astrocytoma in the left frontal lobe. A. F. I. P. Acc. No. 219007–27.

Figure 2. Metastatic carcinoma from left main bronchus to left lenticular nucleus. Note the discrete, sharply demarcated, unencapsulated tumor nodule. There is a second, smaller metastasis to left caudate nucleus. A. F. I. P. Acc. No. 219007–1.

GROSS. The gross changes are flattening and broadening of the convolutions, narrowing of the sulci, and diminution or practical disappearance of the fluid from the subarachnoid space over the hemispheres.

MICROSCOPIC. Perret and Kernohan found that the microscopic changes involve all the elements of the cerebrum. There are a loosening of the ground substance, separation of the nerve fibers and myelin sheaths, distention of the spaces around the blood vessels and nerve cells, and swelling and clasmatodendrosis of the astrocytes and their transformation into gemästete glia. These swollen astrocytes have abundant acidophilic cytoplasm and short heavy processes; there may be one, two, three or more nuclei, and the cell bodies may be very large. There is swelling of the oligodendroglia. In the cerebral cortex and basal nuclei both chromatolysis and pyknosis of the nerve cells may be seen, and satellitosis by the oligodendroglia around the degenerating nerve cells is often very prominent. The satellitosis is occasionally so active that mitotic figures of the satellite cells (the oligodendroglia) may be seen. It is usually very difficult to distinguish betweeen brain edema around a tumor or an abscess and changes in an infarct of the brain in its earlier stages. We have rarely seen scavenger cells (gitterzellen) in any of the numerous sections of the brain edema which we have studied, and usually find these scavenger cells in brain infarcts after the seventh day and sometimes as early as the fifth day. The phenomenon of brain edema is more prominent in the white than in the gray matter, but no part of the cerebrum is immune to these changes.

Special Stains

In the development of our present understanding of tumors of the central nervous system special histologic technics were employed and were highly valuable. These technics are still important, more especially as a research tool. However, almost without exception, diagnosis of all brain tumors can be accurately made with the hematoxylin and eosin or other simple routine stains. Impregnation methods and other special stains can be used and at times should be used but mainly to confirm the diagnosis made on routinely stained sections. Special technics are sometimes necessary when we are studying a complicated or unusual tumor, especially the glioma group. However, in routine work, special histologic technics are not essential.

Malignancy of Central Nervous System Tumors

The malignancy of a brain tumor depends on the rapidity of its growth and its location in relation to vital centers. Some of the slowest growing neoplasms of the body and some of the body's most highly malignant tumors can be found in the cerebrospinal axis. An unexplained peculiarity of primary central nervous system tumors is the extreme rarity of metastasis outside of the central nervous system, even in tumors derived from nonspecific tissues. The only

example in our collection is a hemangiosarcoma of the frontal lobe (reported by Abbott and Love), which ultimately metastasized to the lungs.

Local extension of gliomas into the subarachnoid space is the commonest mode of spread. These local extensions are the result of the tumors breaking directly through the pia mater or else invading the perivascular spaces of cortical blood vessels and extending along them into the subarachnoid space. In the majority of instances in which tumors extend into the subarachnoid space in this way, the meningeal involvements remain localized.

Metastatic Brain Tumors

Reported instances of metastatic tumors to the central nervous system vary exceedingly, depending to a large extent on the source of the material, whether it is obtained at operation or at necropsy. The majority of brain and cord tumors in our laboratory are from the neurosurgical service, although some are from our necropsy service, and as a result the numbers of our metastic tumors are relatively small in comparison to the numbers of primary tumors. Figures from various sources show an incidence of metastatic tumors ranging from less than 3 to almost 40 percent of all tumors found in the central nervous system.

Another way of analyzing data on metastatic tumors in the brain is to consider the source of the tumors. Kiefer recently reviewed 100 metastatic brain tumors in our laboratory and found that more than one third originated in the lungs, slightly less than one fourth arose in various segments of the gastrointestinal tract, while about one tenth originated in the breasts and a similar number took origin in the kidneys. He found that less than one tenth were melanomas; yet it has been estimated that half of all melanomas metastasize to the central nervous system. Kiefer also found that metastases were derived from many other sources but that in no instance were the metastases from any one organ more than three percent. The route by which the cancer cells entered the nervous system was predominantly by way of the arterial blood stream. He also found that metastases in the brain were multiple in about 70 percent of cases and that neither side was involved more often than the other. Metastases were found in the cerebrum in 92 percent of cases, in the cerebellum in 44 percent, and in the brain stem in 8 percent, so that in this series of cases, metastases were located fairly uniformly throughout the central nervous system.

When metastases are present they are usually sharply circumscribed without any capsule (fig. 2). At times they may be difficult to discover because they resemble the surrounding brain in color and consistency. Metastatic carcinomas in the brain, as a rule, are identical with the original tumor from which they arose. Occasionally carcinomas metastasize only to the meninges, where the carcinoma may become widespread and produce the condition of meningeal carcinomatosis.

Spinal Cord Tumors

The same types of tumors (fig. 3) are found in the spinal cord as in the brain, but the frequency and distribution of various types differ. In the spinal cord, as compared with the brain, meningiomas are relatively increased, gliomas are only half as frequent, and neurilemomas become an important tumor at all levels. In the series of cord tumors reported by Woltman, Kernohan, Adson, and Craig, 47 of the 70 cases of sarcomas were extramedullary hemangioendotheliomas. The increased amount of fat and blood vessels in the extradural space of the spinal canal and the greater number of nerve roots ensheathed in dura but traversing that space explain the relatively greater number of vascular tumors and neurilemomas here. The 16 lymphosarcomas found by Kloos are unexpected and unexplained, as lymphoid tissue is not normally found in this location.

Ependymomas are the most common type of glioma in the spinal cord, astrocytomas are less frequent, while oligodendrogliomas are very rare. Approximately one half of all the gliomas of the spinal cord arise from the conus medullaris and filum terminale. The conus medullaris is the tapering lower end of the spinal cord which contains an ependymal-lined cavity—the ventriculus terminalis—and it continues downward as the filum terminale—the rudimentary terminal filament of the spinal cord. The filum terminale contains many ependymal cells forming small canals or scattered islands of cells. These excessive collections of cells explain adequately the predominance of ependymomas in this region, but do not explain why gliomas are more common here than elsewhere in the spinal cord. Ependymomas of the conus medullaris and filum terminale are somewhat different from those found in the brain and the remainder of the cord in that many of them are of papillary type with excessive myxomatous degeneration of the stroma, giving these tumors a unique and characteristic appearance.

Syringomyelia was present in 10 of 16 cases of spinal cord tumors in which necropsy was performed. The reason for this high association of these two conditions is not at once apparent, but the syringomyelia seemed to antedate the neoplasm. The cavitation was associated with one hemangioendothelioma and three types of gliomas.

Study of a series of our cases of spinal cord tumors reported by Woltman, Kernohan, Adson, and Craig brought out a surprising and so far unexplained relationship between the duration of symptoms and location of the tumor in the spinal canal. The average preoperative duration of symptoms in intramedullary tumors, which grow in a small compact structure, was five years, while tumors growing between the spinal cord and dura and in the extradural space, where there is adequate room for expansion and growth, produced symptoms requiring medical advice and surgical relief in an average length of time of almost three and of two and one half years respectively.

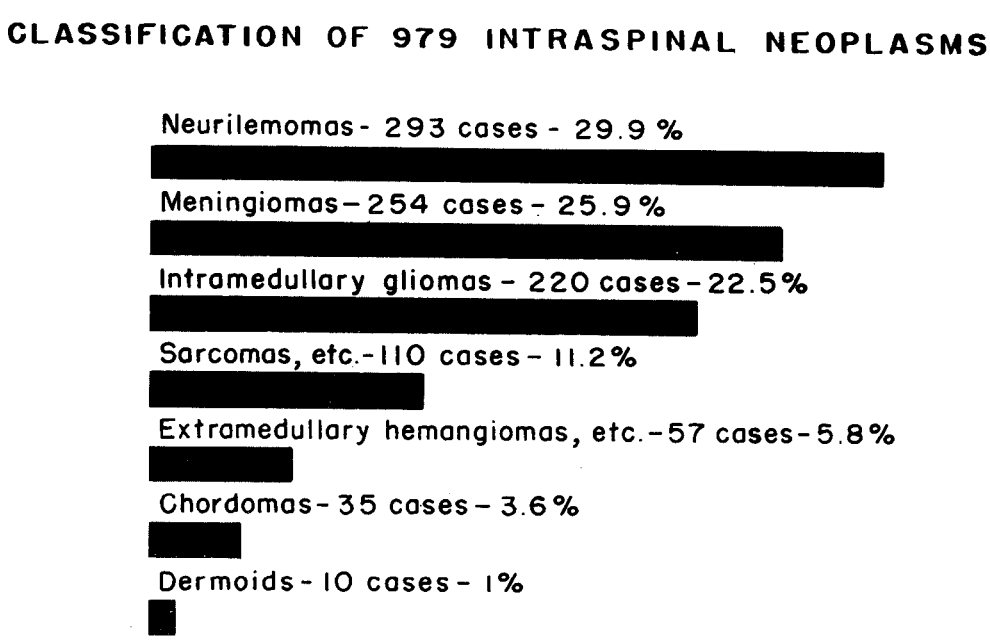

Figure 3. Various types of intraspinal neoplasms with their relative frequencies. A. F. I. P. Acc. No. 219007–127.

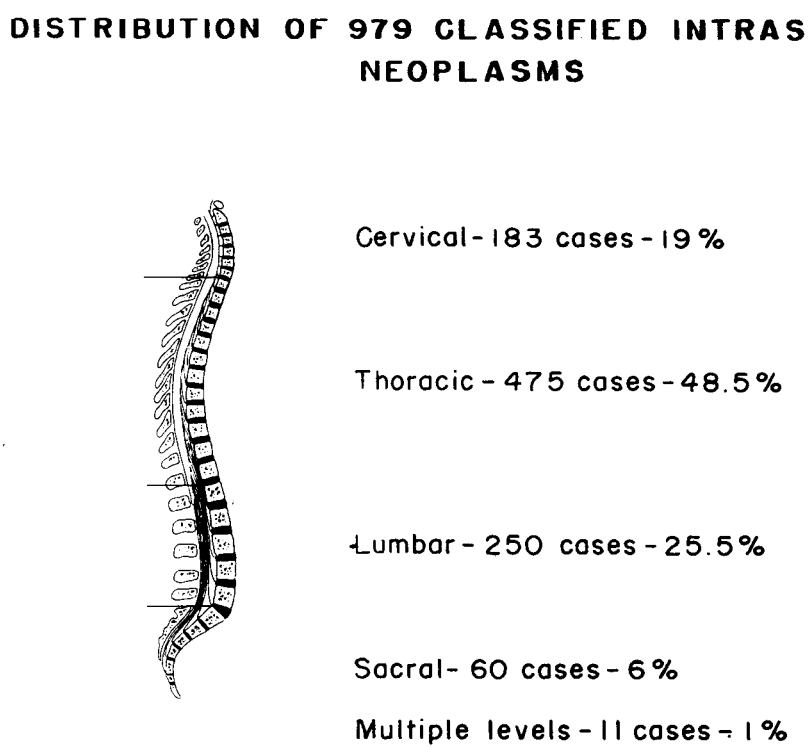

Figure 4. This figure shows the distribution of 979 tumors at the various levels of the spinal cord. A. F. I. P. Acc. No. 219007–2.

Table I

INCIDENCE OF SYRINGOMYELIA IN 16 CASES

Tumor	Syringomyelia	
	Present	Not present
Astrocytomas	1	3
Ependymomas	5	2
Oligodendrogliomas	2	0
Hemangioendotheliomas	2	1
Total	*10	6

* 62.5 percent.

Tumors of the spinal cord have a good prognosis, much better than brain tumors, due chiefly to the fact that most of the tumors of the spinal cord are of low grade malignancy. In our follow-up study of 51 patients with intramedullary tumors reported nineteen years ago, by Kernohan, Woltman, and Adson, we found that an average postoperative survival period of more than seven years was obtained. All patients from whom neurilemomas or meningiomas were removed were cured as far as the neoplasm was concerned. Some patients were suffering from paraplegia as a result of tumor compressing and destroying the spinal cord; the removal of the tumor did not restore the function of the spinal cord in many of these patients, although improvement of their paraplegic symptoms was shown by some.

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