Brain-stem glioma growth patterns

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Brain-stem gliomas account for 10% to 25% of intracranial childhood neoplasms. In most cases, the natural history of the disease is a steady progression to death, with a median survival period of 4 to 15 months. The overall 5-year actuarial survival rate in most series is 30%. Matson viewed these tumors as uniformly malignant because their location made them inoperable. Recently, however, several authors have identified subgroups that manifest different biological behavior, are potentially resectable, and have a more favorable long-term prognosis. A better understanding of the heterogeneity of the disease has led to better survival rates in some categories of patients.

Magnetic resonance (MR) imaging has made a major contribution to the diagnosis and treatment of brain-stem gliomas. Whereas in the past these neoplasms were lumped together and simply referred to as "brain-stem gliomas," it has become evident that they are in fact a heterogeneous collection of neoplasms that must be described according to clinical presentation, location, and growth pattern. We have been impressed that the great majority of these neoplasms may be classified as diffuse, focal, cervicomедullary, or dorsal exophytic according to "stereotyped" growth patterns that are obvious on MR imaging. It is the purpose of this report to describe these growth patterns, the mechanisms that are responsible for the MR imaging appearance, and the relationship to surgical selection.

Materials and Methods

Between 1984 and 1990, 88 patients underwent radical excision of brain-stem tumors (Table 1). Forty-four tumors were classified as cervicomедullary, 12 as focal medullary, 12 as dorsal exophytic, and 20 as diffuse. The clinical course and histopathology were correlated with preoperative MR imaging studies and, on this basis, the different growth patterns of benign and malignant neoplasms were identified.

Results

Cervicomедullary Lesions

Of the 44 lesions classified as cervicomедullary, there were 32 low-grade astrocytomas, seven gangliogliomas, four anaplastic astrocytomas, and one ependymoma (Table 1). All of these neoplasms manifested stereotypical growth patterns. While the caudal part of the tumor was identical to an intramedullary spinal cord neoplasm, rostral tumor extension was limited at the junction of the medulla and the uppermost cervical cord. The result was a posteriorly directed expansion that was manifested as a bulge at the level of the obex (Fig. 1 left). Ultimately, some tumors ruptured into the fourth ventricle (Fig. 1 right).

Focal Medullary and Dorsal Exophytic Tumors

A focal tumor was defined as being limited to the medulla without evidence on MR imaging of rostral...
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TABLE 1

<table>
<thead>
<tr>
<th>Tumor Location &amp; Histology</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>cervicomedullary</td>
<td>44</td>
</tr>
<tr>
<td>low-grade astrocytoma</td>
<td>32</td>
</tr>
<tr>
<td>anaplastic astrocytoma</td>
<td>4</td>
</tr>
<tr>
<td>ganglioglioma</td>
<td>7</td>
</tr>
<tr>
<td>ependymoma</td>
<td>1</td>
</tr>
<tr>
<td>focal medullary &amp; dorsal exophytic</td>
<td>24</td>
</tr>
<tr>
<td>low-grade astrocytoma</td>
<td>16</td>
</tr>
<tr>
<td>anaplastic astrocytoma</td>
<td>6</td>
</tr>
<tr>
<td>ganglioglioma</td>
<td>2</td>
</tr>
<tr>
<td>diffuse anaplastic astrocytoma</td>
<td>20</td>
</tr>
<tr>
<td>total cases</td>
<td>88</td>
</tr>
</tbody>
</table>

extension to the pons or of caudal extension to the cervical spinal cord. A dorsal exophytic tumor was defined as a primary medullary tumor that grows posteriorly into the fourth ventricle. These tumors are lumped together because they seem to represent different stages of an identical disease. There were 16 low-grade astrocytomas, six anaplastic astrocytomas (four focal and two dorsal exophytic), and two gangliogliomas (Table 1).

All of these medullary gliomas manifested restricted growth both rostrally and caudally. In the smallest tumors, there was focal swelling of the medulla, with rostral displacement of the pons and caudal displacement of the upper cervical cord. There was no radiological evidence suggesting invasion of either the pons or the cervical cord. The larger tumors expanded posteriorly toward the floor of the fourth ventricle (Fig. 2).

Diffuse Tumors

All 20 diffuse tumors were anaplastic astrocytomas (Table 1). The radiological signature of the diffuse tumors was extension into the contiguous region. High-grade cervical lesions exhibited unhindered axial growth both caudally and rostrally (Fig. 3 left). Instead of expanding posteriorly toward the obex, these lesions grew along the medullary axis, remaining well intraxial as the disease progressed. High-grade medullary tumors grew axially, invading the pons and/or the cervical cord (Fig. 3 right).

Discussion

Neuroradiological Studies

The poor resolution of the radiological techniques available in the 1960's, such as pneumoencephalography and angiography, forced neurosurgeons to lump patients with brain-stem lesions into one group. At that time, the only indication for operative exploration was an atypically benign course that suggested the possibility of misdiagnosis. Computerized tomography (CT) did not have the expected impact on the preoperative eval-

Fig. 1. Magnetic resonance images of cervicomedullary lesions. Left: Image of a ganglioglioma showing posteriorly directed growth and rostral displacement at the cervicomedullary junction (small arrows) above the foramen magnum (large arrow). Right: Image of a low-grade astrocytoma demonstrating tumor expansion in the upper cervical cord and through the obex area (arrows), with rupture into the fourth ventricle.

Fig. 2. Magnetic resonance images of a focal medullary tumor. Left: Preoperative image of the astrocytoma grade II showing displacement of the pontomedullary barrier upward and of the cervicomedullary barrier downward (arrows). Right: Postoperative image demonstrating the resection cavity (arrows) which is confined to the medulla.

Fig. 3. Magnetic resonance images of diffuse anaplastic brain-stem gliomas. Left: Image demonstrating unhindered growth from the cervical cord to the upper medulla (arrows). Right: Image showing a diffuse lesion unhindered in its growth by anatomical barriers.
uation of brain-stem tumors due to problems caused by bone artifacts when the posterior fossa is imaged. Attempts to predict tumor grade through the use of growth patterns demonstrated on CT were largely unsuccessful. Evaluation of patterns on contrast-enhanced CT has been little better; the relatively poor resolution permits only a positive correlation between the extent of brain-stem involvement and the length of survival.

Despite these radiological limitations, several authors have maintained over the course of the last 10 years that brain-stem gliomas should not be considered as a single entity. They supported this belief by pointing out that certain categories of lesion were associated with a better prognosis. Hoffman, et al., described dorsally exophytic tumors as being one of these groups, and Epstein and McCleary found that cervicomedullary lesions formed another. However, the reason that these subgroups of brain-stem tumors offered a better prognosis has remained enigmatic.

It has been found that MR imaging signal heterogeneity and patterns of gadolinium enhancement are extremely variable and correlate poorly with histological grade. However, MR imaging is the first radiological modality to provide a detailed anatomical characterization of brain-stem tumors, particularly of their growth patterns. This method has been instrumental in understanding the better survival rates of patients with dorsally exophytic, focal, and cervicomedullary lesions.

Anatomical Considerations

Implicit in the radiological observations is the presence of anatomical barriers at the cervicomedullary and pontomedullary levels. These barriers are relatively impermeable to expanding low-grade lesions but fall rapidly in the face of malignant tumors. That tumor growth within the central nervous system may be affected by surrounding structures is not a new concept. In 1938, Scherer pointed out that the architecture of gliomas is frequently influenced by existing anatomical structures. He stated that fiber tracts and pial borders direct the growth of lesions with low malignant potential. Growth of a benign lesion is much more readily governed by the matrix of surrounding tissue than is the diffusely infiltrating expansion of a high-grade glioma.

Spinal Cord Tumor Growth. The spinal cord may be viewed simplistically as a cylindrical structure banked circumferentially by pia. Scherer believed that pia influenced glioma growth. Other than crossing spinothalamic fibers, there are no transversely oriented anatomical structures that can affect growth at the spinal level. Intra-axial spinal tumors, therefore, tend to expand longitudinally and cylindrically in the cord. This pattern is uniform and irrespective of histological grade.

Brain-Stem Tumor Growth. Conversely, growth patterns are diversified at the brain-stem level. There are three major anatomical differences in the internal organization of the brain stem and the spinal cord. First, the brain-stem cylinder is banked anteriorly and laterally by pia, but its dorsal aspect is lined with a softer barrier, the ependyma of the fourth ventricle.

Fig. 4. Illustrations of growth patterns of cervicomedullary lesions. A: Caudal growth is cylindrical, as for spinal cord tumors (arrow). B: Rostral growth is directed toward the obex (arrow) as a result of hindrance from pial elements and decussating fibers. Note the rostral displacement of the barrier.

Floor. Second, two main groups of transversely placed secondary structures exist within the brain stem: the cervicomedullary and pontomedullary zones of decussations. In accordance with the hypothesis proposed by Scherer, these structures would act as barriers to tumor growth. Finally, the brain stem has projections not seen in the spinal cord, namely the cerebellar peduncles. Consequently, the growth of intra-axial brain-stem lesions is not necessarily longitudinal, as it is in the spinal cord.

Cervicomedullary Junction. At the cervicomedullary junction, anatomical barriers include the pyramidal decussation crossing from side to side, the internal arcuate fibers and medial lemniscus, and the efferent fibers from the inferior olivary complex that stream from a ventromedial position toward the inferior cerebellar peduncle located posterolaterally. Some of these barriers are probably more significant than others, but in combination they could hinder axial growth in accordance with the principles of Scherer and act in conjunction with the enveloping pia to direct the overall growth of a benign astrocytoma.

A tumor originating within the upper cervical cord and below the cervicomedullary barrier (cervicomedullary tumor) is limited in growth by the circumferential pia of the upper cord and the crossing fibers of the low medulla. These barriers tend to direct tumor growth toward the obex, where there is less resistance to expansion (Fig. 4). Magnetic resonance imaging shows that most low-grade cervicomedullary tumors bulge at the obex (Fig. 1). The cervicomedullary barrier may be pushed rostrally to a significant degree but it is not penetrated. Ultimately, the lesion may rupture into the fourth ventricle at the level of the obex, which represents the weak point in the barrier.

Pontomedullary Junction. At the pontomedullary junction, anatomical structures similar to those at the cervicomedullary junction also direct tumor growth. Transverse fibers (pontocerebellar tracts) travel from
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Fig. 5. Illustrations of growth patterns of benign medullary tumors. A: A focal medullary tumor displaces axially oriented fibers as it grows (arrows). B: A larger focal medullary tumor tends to grow subependymally (arrow) since its axial growth is limited by barriers. C: Subependymal lesion becomes dorsally exophytic (arrow) because of the limited resistance to growth offered by the ependyma.

The growth patterns of brain-stem gliomas are influenced by several factors. High-grade lesions may be contained by a given barrier in the early stages of the disease, only to overcome it later. This situation prevailed in the six anaplastic lesions in the focal tumor group and the four anaplastic lesions in the cervicomedullary tumor group. Clinical correlates such as the duration of the illness, the evolution of the disease, and the severity of neurological deficits must be considered in conjunction with the MR imaging evaluations in assessing the histological grade of a brain-stem lesion, and ultimately in establishing the therapeutic plan.

References

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