CHAPTER 11

Tumors Originating in the Brain – Medulloblastomas, PNETs and Ependymomas

Foolishly, I waited 7 months before I joined this (or any) group. By that time, my son had radiation, chemo, and a recurrence of his medulloblastoma while on treatment. Because of advice from a person on this group, we decided to travel to St. Jude’s for Maurice’s second surgery. You will not find more comprehensive knowledge about childhood brain tumor care than on a listserv such as this one. Definitely not from an oncologist! I wish you and all the rest of us the best.

Mitch, Father of a son with medulloblastoma.
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• metastases
• ependymoma
• M stage
• therapy options
• PNET
• staging
• tumor grade
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• MRI, MR-Spect and PET scans
• myxopapillary ependymoma
• tumor markers
• obstructive hydrocephalus
The most important fact I can share with you about PNETs is that we have one good chance to treat them – the first treatment. Our success with re-treatment, after they recur, is much less effective. That is why everything that you can have going for you must be used in the beginning. This tumor is not nice and it will not wait. (See also Chapter 22: Children-Special Considerations.)

**MEDULLOBLASTOMAS AND PRIMITIVE NEUROECTODERMAL TUMORS (ALSO CALLED PNETS) GENERAL QUESTIONS**

**WHAT IS A PNET?**

PNETs are a family of brain tumors that typically occur in younger children and also are diagnosed in the 18 to 40-year-old group. Most grow in the back part of the brain (cerebellum) and are called *medulloblastomas*. About 20 percent start in the upper brain and are called *supratentorial PNETs* (SPNET)s.¹ No one used the term PNET until 1973, when a group of pathologists devised a new category for tumors they could not classify by their system at that time. It is generally accepted that despite the similar appearance under the microscope, medulloblastoma in the cerebellum and SPNET in the upper hemispheres respond differently to treatment.

**WHAT ARE SYMPTOMS OF A PNET?**

Typical symptoms of medulloblastoma in older children and adults include headaches, vomiting, double vision, clumsiness or wobbliness (ataxia), or weakness of a leg or arm. For SPNETs, a seizure can be the first symptom. In infants, the symptoms are less obvious. A baby may be fussy, vomiting off and on for weeks, or register a large head size during routine checks with the pediatrician. Average time from symptoms to diagnosis in our study of more than 400 children was 90 days, with some as long as 18 months.

**HOW ARE PNETS CLASSIFIED OR STAGED? IS THE TYPE IMPORTANT?**

PNETs are usually described by their location. Typical medulloblastomas (infratentorial PNETs) start out at the top-center of the cerebellum in the fourth
ventricle; a minority grows within the cerebellum. (See Chapter 2 for basic anatomy.) SPNETs begin in the upper brain and can invade the ventricles. Over the last 20 years, we have learned that not all PNETs are created equal. Some grow slowly and can be completely removed. Others invade locally or spread and lodge along the spinal cord. The invasive ones wrap around the pons (the middle portion of the brain stem), sometimes extending up to the midbrain (the upper portion of the brain stem) or downward to the medulla (the bottom portion of the brain stem).

Under a microscope, PNETs appear different from astrocytomas (Chapter 10); they look more like (immature) fetal cells to the neuropathologist. By definition, all are malignant; none are low grade.

### Table 11-1 Tumor (T) and Metastasis (M) Stage for PNETs

<table>
<thead>
<tr>
<th>T-stage</th>
<th>Description</th>
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<tbody>
<tr>
<td>T-1</td>
<td>Tumor &lt; 3 cm in diameter and limited to the classic midline position in the vermis, the roof of the 4th ventricle, and less frequently to the cerebellar hemispheres.</td>
</tr>
<tr>
<td>T-2</td>
<td>Tumor &gt; 3 cm and invading one adjacent structure or partially filling 4th ventricle.</td>
</tr>
<tr>
<td>T-3a</td>
<td>Tumor further invading two adjacent structures or completely filling the 4th ventricle with extension into the aqueduct of Sylvius, foramen of Magendie, or foramen of Luschka, thus producing marked internal hydrocephalus.</td>
</tr>
<tr>
<td>T3b</td>
<td>Tumor arising from floor of 4th ventricle and filling 4th ventricle.</td>
</tr>
<tr>
<td>T-4</td>
<td>Tumor spread through Aqueduct of Sylvius to involve 3rd ventricle, midbrain, or down into upper cervical cord.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>M-stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M-0</td>
<td>No gross subarachnoid or blood-borne metastasis</td>
</tr>
<tr>
<td>M-1</td>
<td>Microscopic tumor cells found in cerebrospinal fluid</td>
</tr>
<tr>
<td>M-2</td>
<td>Gross nodular seeding in cerebellum, cerebral subarachnoid space or in 3rd or 4th ventricles</td>
</tr>
<tr>
<td>M-3</td>
<td>Gross nodular seeding in spinal subarachnoid space</td>
</tr>
<tr>
<td>M-4</td>
<td>Spread outside the nervous system into bone marrow, bones, liver, or lungs (Extra-neuraxis metastasis)</td>
</tr>
</tbody>
</table>

The most common staging system is called the M-stage. (M stands for “metastasis.”).

It is absolutely critical to know the M-stage before any treatment begins, as the choice and intensity of therapy depends upon it. T-stage is a measurement.
of size and extension but is not as important as M stage, which measures how far the tumor has spread.³ (See Table 11-1 and Chapter 22: Children – Special Considerations.)

**ARE THERE FACTORS THAT HELP PREDICT LONGER OR SHORTER SURVIVAL?**

Studies by our group and others over the last 10 years have indicated that while tumor spread at diagnosis (M-stage) is most important in tailoring therapy, it is not the only factor. I have heard some physicians say, “You have a 40 percent chance of being cured, because you have widespread tumor.” You are one specific and unique case; the doctor is merely stating his understanding of PNETS for all patients. In actuality, for the individual the odds are either 100 percent or 0 percent with nothing in between. If it works for you, it is 100 percent.

**DIAGNOSIS**

**DOES THE LOCATION OF MY PNET MAKE A DIFFERENCE?**

Yes it does.

- Tumors in the upper brain (SPNETs) may not be quite as responsive to the same therapies as the medulloblastoma (infratentorial PNET).
- SPNETs metastasize less frequently (10 percent) compared with medulloblastomas (35 percent).
- Most clinical trials place SPNETs in a higher risk category, requiring therapy that is more intensive.
- A tumor that has not spread will be easier to remove than one that has invaded wider areas.

**WHAT TESTS ARE NEEDED FOR THE INITIAL EVALUATION OF A PNET?**

Throughout North America and Europe, the brain MRI is the “gold standard” for diagnosis and treatment decisions with typical PNETs. A CT scan may show the tumor, but details that allow the neurosurgeon to plan a maximal resection usually are better appreciated on the MRI. For an explanation of the MRI and CT, see