All About Craniopharyngioma

Some Background

Almost 20% of all childhood cancers start in the central nervous system (CNS), which consists of the brain, the spinal cord, and the surrounding fluid (cerebrospinal fluid, or CSF), lining tissues (meninges) and bone (cranium and vertebrae).

There are many different types of pediatric CNS tumors, all of which have long, rather complicated names. The tumor type is generally determined by two things: 1) where in the CNS the tumor starts, or the location, and 2) how the tumor looks under a microscope, also known as the histology. Primary brain tumors are tumors that arise in the brain, while primary spinal tumors grow in the spinal cord. However, some brain tumors can spread to involve parts of the spine, and vice versa. On rare occasion, certain types of tumors can even spread to areas outside of the CNS, such as distant bones or bone marrow.

Ultimately, every cancer treatment plan is individualized for that patient and takes into account not only the stage and the clinical data, but also the goals and desires of the patient and his or her family.

What is a craniopharyngioma?

Before proceeding any further, it is worthwhile to properly define and clarify some important concepts that are relevant to the subject of brain tumors.

The word tumor itself refers to an abnormal growth or mass of cells, also referred to in general terms as a "cancer".

Tumors can be either "benign" or "malignant. In simple terms, "benign" tumor cells usually do not have features associated with invasion or spread (metastasis) to other locations. In contrast, "malignant" tumors have cells that can invade and spread if not treated.

Even when a tumor is benign in terms of how its cells look under a microscope, it can still cause problems for the patient. Although benign tumors may not spread far beyond where they started, they can continue to grow and thus can still cause trouble from local expansion, particularly in an otherwise small, enclosed space like the brain. Pressure and obstruction from a growing mass can lead to severe neurological deficits.

Craniopharyngioma is a benign brain tumor that accounts for about 3-9% of all pediatric CNS tumors. This tumor results from abnormal overgrowth of a part of the brain called Rathke's pouch, located near the pituitary gland. It typically consists of a combination of calcium deposits mixed with cysts, or pockets, of fluid. The fluid characteristically contains protein, lipid (fat) and cholesterol pieces, giving it a so-called "crankcase oil" texture. Craniopharyngiomas do NOT represent cancers, and craniopharyngioma does not spread to other parts of the central nervous system or body; however, craniopharyngiomas develop in a part of the brain where their growth can cause problems with hormone secretion (from compression of the pituitary gland), or vision (from compression of the nerves responsible for sight).

Who gets this tumor, and how?

Craniopharyngiomas can occur in both children and adults, with a peak in incidence at 9 to 14 years of age. There are approximately 120 cases diagnosed each year in the United States in patients under the age of 19 years old. In fact, more than 50% of all patients with craniopharyngioma are under the age of 18 years. There is no clear association of the tumor with a particular gender or race. It is not really known what causes craniopharyngiomas, but they do not appear to "run in families" or to be directly inherited from the parents.
What are the signs of a craniopharyngioma?

The most common symptoms of this tumor are visual changes, most often loss of peripheral vision in one eye (visual field cuts) or blurriness. This is because of the proximity of craniopharyngiomas to the visual nerve pathways in the brain. Similarly, craniopharyngiomas are also close to the pituitary gland, and thus children can present with hormonal, or endocrine, problems. This is because the pituitary gland controls various important hormone systems, including those vital for body growth, sexual organ maturation, and thyroid gland function. Up to half of children can even develop notable personality changes or cognitive deficits. Finally, general signs like nausea, vomiting and headache may occur due to increased and excessive pressure in the brain from the tumor.

Please note that the symptoms mentioned here do not necessarily or automatically mean a child has a brain tumor, but further medical evaluation is required to rule out the possibility of a brain tumor such as craniopharyngioma.

How is a craniopharyngioma diagnosed?

Typically, the diagnosis is made based on a radiology study such as magnetic resonance imaging (MRI) scan of the brain with gadolinium contrast-enhancement. A craniopharyngioma has a very characteristic appearance on MRI scan: a well-defined mass with a combination of solid and cystic parts. Importantly, this is a tumor that occurs in the suprasellar region, a part of the brain also containing the optic chiasm (contains nerves for vision) and hypothalamus (regulates release of growth, thyroid, and stress hormones, among others).

As mentioned earlier, craniopharyngioma is a benign tumor and thus is not expected to spread from the brain to the spine, cerebrospinal fluid (CSF), or other sites outside the CNS. Thus, no additional scans are required unless indicated by symptoms or physical exam findings.

How is craniopharyngioma treated?

Although craniopharyngiomas are benign tumors that have relatively good long-term outcome, the optimal management of them is a very controversial issue in pediatric neuro-oncology. One major explanation for this is the inherent conflict between wanting to "cure" the patient and wanting to minimize the long-term morbidity, or negative side effects. Physicians are understandably hesitant to recommend and pursue the most aggressive treatment, if it risks leaving the child with worse neurologic problems than the underlying tumor itself. Recent publications from St. Jude’s Children’s Hospital highlight these concerns. Of 55 patients treated, almost all remained alive at the time of analysis; however, long term side effects included hormone deficiencies, shunt dependence, and seizures. Due to the potential for long term problems, it is very beneficial for children with craniopharyngiomas to be followed with multidisciplinary care to minimize the late complications. Additionally, treatment recommendations should be provided by a multidisciplinary team that includes a neurosurgeon, a radiation oncologist, and a pediatric neuro-oncologist.

Although no clear consensus has been reached in the medical community on the best therapeutic regimen for craniopharyngioma, presented below are some general management principles. It is important to remember, however, that each patient's case should be approached individually, and the treatment plan designed accordingly.

Surgery

Surgery is typically the initial and major component of therapy, although the "right" or "best" extent of surgery is a matter of much debate. Some believe that the main goal should be gross total resection of the tumor, or in other words, complete surgical removal of all visible tumor. It is technically possible to perform a total resection in about 70-90% of cases. The success rate of total resection alone also ranges from 70-90%, (meaning the tumor comes back in about 10-30% of patients), which is quite good. So if total tumor resection is achieved based on both what the surgeon describes and what the post-surgical MRI scan shows, then careful observation after surgery is reasonable. Any additional treatment could be used only if and when indicated (ie: if the tumor comes back in the future). A new treatment approach is the use of sinonasal approach which is when the surgeon accesses the brain through the nose. Some patients are still best treated with craniotomy (an incision into the skull).

A complete surgery with no other required treatment is an optimal situation, but bear in mind that the rates of serious surgical complications following complete tumor resection are high: 50-90% risk of damage to the hypothalamus, 1-12% risk of brain hemorrhage during the surgery, and even a small risk of death. Not surprisingly, the skill and experience of the surgeon plays
an important role in the outcome, both in terms of better tumor control and fewer surgical complications. Surgery may be best performed by a pediatric neurosurgeon with experience operating on patients with craniopharyngioma.

However, even in the best of surgical hands, there are many cases in which the craniopharyngioma may press against or be adhered to various critical brain structures (optic chiasm, hypothalamus, blood vessels), thereby making total resection essentially impossible. Instead, the surgeon removes as much as tumor as is safely possible.

This has led to several important questions: If only part of the tumor is removed, can the patient be "watched" with no further treatment safely? Should a partial resection be followed with radiation therapy to eradicate, or "mop up", the remaining tumor cells? Could this approach achieve equally good results as a total resection (if it had been possible), while decreasing the possible long-term side effects of a big surgery? In fact, knowing that the naked eye at the time of surgery cannot possibly see individual, microscopic tumor cells that might be left behind, should gross total resection alone EVER be done? Instead, should partial surgery and postoperative radiation for residual tumor be the goal for all patients, thus minimizing surgical risk and maximizing microscopic tumor control.

*(Please note: the term "partial" is be used synonymously with "incomplete" or "subtotal", all of which describe any surgery that is less than a total resection.)*

Studies have tried to answer these questions, and found that craniopharyngioma patients treated with partial resection and radiation have 10-year and 20-year progression-free-survival rates as high as 70-90%. In other words, these patients are living without signs of growing or returning tumor as long as 10 and 20 years after treatment. Notice that this is comparable to the rates mentioned earlier for complete surgery alone, but with much lower rates of problems like hypothalamus damage or brain hemorrhage.

**Radiation Therapy**

A post-operative MRI scan of the brain is usually obtained to look for any leftover tumor. Residual craniopharyngioma can appear as anything from calcified little "flecks", to a more standard-looking cystic-solid mass. Based on what the MRI shows, together with what the surgeon reports he or she was able to do in the operating room, the surgery is classified as a "total" versus "less-than-total" (aka "partial", "subtotal", or "incomplete") resection.

If it is a partial resection, radiation therapy to the tumor site should be considered. This consists of radiation to both solid and cystic components of the tumor, to reduce the risk of local tumor recurrence. If the radiation is delayed and the patient is observed, the likelihood of tumor regrowth is high (70-100% over the next 5 years). Although it is generally recommended that patients who get partial resections should receive the radiation therapy upfront, rather than delaying it until the tumor comes back, there may be certain patients, especially those of very young age, for whom delaying radiotherapy is reasonable. In the postoperative setting, radiation is usually delivered only to the region of the original tumor, including the surgical area and all remaining tumor. Surrounding brain tissue and other critical structures are excluded from the treatment field as much as possible.

Much attention has understandably been paid to the possible long-term complications of radiation therapy to the brain and spine of a growing child. These can include deficits in memory, learning, and social/emotional adjustment, among other things. The development of such side effects depends on many factors, including extent of pre-radiation surgery, amount and location of brain that is treated, age of the child at the time of radiation, and how much radiation dose is given, among others.

However, modern radiotherapy techniques and proper attention to minimizing radiation dose to important brain structures whenever feasible can allow for safe and effective treatment, even in younger children. There have been considerable efforts within the field to decrease the dose of radiation and volume of brain that receives radiation to minimize long term toxicity. While no therapy is without its side effects, radiation therapy can be planned and delivered in such a way as to minimize potential long-term side-effects. Newer methods of delivering radiation therapy, such as stereotactic radiosurgery or proton radiotherapy (see below), are promising options to limit radiation to normal brain tissues. Radiotherapy for craniopharyngioma is best accomplished at a major radiation oncology center where physicians and staff are familiar with pediatric patients and technologically capable of treating childhood cancers.

**Proton Radiotherapy**

Proton radiotherapy is a special kind of radiotherapy that uses protons instead of the usual x-rays. The advantage of proton
radiotherapy is that it can be shaped to a patient's tumor better than x-ray therapy, avoiding treatment of normal structures, and thus potentially decreasing radiation side effects.

A number of small studies at proton facilities around the world have found proton therapy to be safe and effective in treating these tumors, while theoretically limiting the dose of radiation received by normal tissues. This could result in less toxicity and fewer long term complications for these patients. Studies are following patients treated with protons long term to determine how this treatment will affect long term toxicity.

Chemotherapy

There is currently no role for chemotherapy in the treatment of craniopharyngioma. As it is a benign tumor, disease spread to distant locations is not typically expected, and thus systemic (i.e. "body-wide") medication like chemotherapy has not been extensively used. Some have tried to inject chemotherapy directly into craniopharyngioma cysts in order to delay the need for surgery/radiation, but this approach is experimental. Other groups have utilized immune modulators, such as interferons, to reduce tumor size in the setting of recurrence; again, this approach remains experimental.

Current research is studying genetic mutations that may be present in craniopharyngiomas. These mutations are present in many individuals with craniopharyngioma. Targeted therapy may offer a new treatment option to many individuals with this tumor. A medication called vemurafenib is being studied in certain craniopharyngioma tumors, as are many other targeted therapies.

Follow-up Care and Survivorship

It is important to have a plan for who will provide your cancer-focused follow up care (an oncologist, survivorship doctor or primary care doctor). Talk with your oncology team about developing a survivorship care plan. If you would like to find a survivorship doctor to review your history and provide recommendations, you can contact cancer centers in your area to see if they have a survivor's clinic or search for a clinic on OncoLink's survivorship clinic list.