Malignant Peripheral Nerve Sheath Tumor (MPNST) in Neurofibromatosis Type 1 (NF1)

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What is an MPNST?

MPNST stands for "Malignant Peripheral Nerve Sheath Tumor." MPNST can be called other names such as neurogenic sarcomas, malignant schwannomas or neurofibrosarcomas. They are aggressive tumors and are one of a type of cancer known as sarcomas which can arise anywhere in the body. MPNST can occur in patients with or without NF1. In patients with NF1, the risk of developing an MPNST during their lifetime is 8 to 13%, meaning about one in ten people with NF1 may get an MPNST at some point in their lives. We don't know which patients with NF1 will get an MPNST, but people who have already had one MPNST may be at higher risk for developing another one. Patients with a specific type of NF1 genetic mutation called a "microdeletion" and those with a large number of the benign (not cancer) plexiform neurofibroma tumors may also be at higher risk.

What causes MPNST and what are the symptoms?

In people with NF1, most MPNST develop within an already existing benign (not cancer) tumor known as a plexiform neurofibroma. Plexiform neurofibromas arise from nerves in the body and can become very large in size and cause a variety of clinical problems such as pain or weakness. We don't know what causes a plexiform neurofibroma to become an MPNST, but we do know that some things, like a history of radiation exposure, can increase the risk of transformation. The most common symptom patients experience when they have developed an MPNST is pain in the area of the tumor. This pain can be completely new or may be a worsening of the usual pain associated with a known plexiform neurofibroma. In someone with NF1, new pain, worsening of existing pain and especially pain that wakes one up from sleep, should *never* be ignored! People with a developing MPNST may also notice that a visible tumor is growing more quickly than it had before.

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How are MPNST diagnosed?

If you or someone you know think you may have an MPNST, you should see a doctor as soon as possible. The doctor will likely order some imaging tests to look at the area of concern, such as an MRI (magnetic resonance imaging) and/or a PET (positron emission tomography) scan. The MRI will let you and your doctor see how large the tumor is and where it is located. A PET scan shows your doctor how "active" the tumor is which can help tell the difference between a slow growing plexiform neurofibromas and a fast-growing MPNST. In most cases, the only way to definitively diagnose an MPNST is by getting a sample of it (called a biopsy) and looking at it under the microscope. Even then, it can sometimes be difficult to

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diagnose an MPNST, so it is important that your doctor is familiar with NF1. If there is a question about the diagnosis, it is always ok to ask for a second opinion!

How is an MPNST treated?

If you are diagnosed with an MPNST, the most important thing is not to panic! Knowledge is power and once you know about the tumor, you and your medical team can work together to figure out the best treatment plan.

First, you should be seen by an oncologist (a doctor specializing in cancer) who has experience with treating these types of tumors. Usually, the first thing your oncologist will do is check to see if the tumor has spread anywhere else in your body to find out the best way to treat you. There are three main ways that MPNST are currently treated: surgery, radiation therapy and chemotherapy. If possible, surgery to remove the whole MPNST is usually the best option. Sometimes radiation treatment before surgery is recommended. The chance for cure is the best if the MPNST can be completely removed by surgery. Even with complete removal of the tumor, in some cases radiation therapy is recommended to maximize the chance that the MPNST does not come back. In addition, some MPNST are too large or too close to important blood vessels or organs to remove safely with surgery. In these cases, radiation and chemotherapy may be used to try to shrink the tumor before surgery. Many patients will receive a combination of all three types of treatment. The best treatment is usually determined by several doctors with specialized expertise.

One question some people have is why radiation therapy is used to treat MPNST when exposure to radiation in the past is a known possible cause for the development of MPNST. The reason for this is that when benign (not cancer) tumors like plexiform neurofibromas are exposed to radiation, this increases the risk of that tumor transforming to the more aggressive (cancer) type tumor. However, once a tumor has already become more aggressive, radiation therapy is a very important part of treatment to keep these tumors from coming back. The doctors who specialize in treating patients with radiation (radiation oncologists) do their best to only give radiation to areas where there is known or suspected cancer and to limit the radiation of healthy tissues or benign tumors as much as possible.

What is the future of MPNST research?

While some patients can be permanently cured by the treatments currently available, some MPNST do not respond to those treatments or the MPNST may come back after some time. There are many researchers studying ways to treat the tumors in these situations, including different types of targeted and immunotherapies. There are often clinical trials for patients with MPNST, and the website www.clinicaltrials.gov is a good resource for finding them.

References:

Kim, A., et al. "Malignant Peripheral Nerve Sheath Tumors State of the Science: Leveraging Clinical and Biological Insights into Effective Therapies." Sarcoma 2017: Article ID 7429697; 10 pages. https://doi.org/10.1155/2017/7429697

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