

PLEXIFORM NEUROFIBROMAS IN NEUROFIBROMATOSIS TYPE 1

This resource is for individuals with neurofibromatosis type 1 (NF1) who are suspected or confirmed to have a plexiform neurofibroma. This resource is to be used as general information only and is not considered medical advice. Please consult with your NF care provider for additional information.

To begin to understand plexiform neurofibromas, some background knowledge is needed.



WHAT ARE TUMORS?

A tumor, also referred to as a neoplasm, is an abnormal growth or mass of tissue. Tumors vary in size, can appear anywhere in the body, and may or may not pose a health threat. Tumors are often classified as either benign or malignant.

A **benign tumor** is a mass that lacks the ability to invade neighboring tissue or spread to other areas of the body. Benign tumors typically have a slower growth rate than malignant tumors. When removed completely, it is possible that they do not grow back. These types of tumors are often not serious. However, sometimes they press against nerves, blood vessels or other neighboring structures which cause pain or other symptoms.

A **malignant tumor** is a cancerous type of growth. Malignant tumors can grow and spread to other areas of the body such as the lungs, liver, bones or brain. This is called metastasis and is potentially life-threatening.

Benign and malignant tumors can sometimes be differentiated by imaging, such as MRI (magnetic resonance imaging) or CT (computed tomography), with or without PET (positron emission tomography). These imaging studies are used to look at location, size and other characteristics of the growth. A biopsy (sampling of tumor cells) and examination under a microscope with specialized techniques is also used to determine different tumor types.

WHAT IS A NEUROFIBROMA?

Neurofibromas are growths made up of normal nerve tissue with additional types of cells including mast cells, connective tissue cells, and blood vessels. Mast cells are inflammatory cells that release a substance called histamine which is thought to be the reason that neurofibromas are sometimes itchy.

Not everyone with a neurofibroma has NF1, but these types of tumors are commonly seen in this condition.

WHAT ARE THE DIFFERENT TYPES OF NEUROFIBROMAS?

There are different ways to classify neurofibromas. For simplicity, they can be categorized into two types; cutaneous neurofibromas and plexiform neurofibromas.

Cutaneous Neurofibromas

Cutaneous neurofibromas are the most common type of neurofibroma. These are benign tumors that develop along a nerve on or under the skin. They may look like small lumps, bumps, or nodules. Cutaneous neurofibromas may develop at any time of life, but also seem to increase in number during times of hormone changes, such as during puberty or, for women, during pregnancy. Typically, adults with NF1 will develop more tumors as they age. Cutaneous neurofibromas usually have well defined borders. They do not typically cause any medical problems but can be a cosmetic concern for some individuals.

Cutaneous neurofibromas usually do not require any treatments. However, they can typically be removed by surgery or other procedures if they cause discomfort or are bothersome in some way. There are pros and cons to surgical interventions which should be discussed with an NF specialist. There is no way to determine when, where, or how many neurofibromas will develop over the lifetime, as it varies greatly from person to person. Some people with NF1 may have only a few neurofibromas while others may develop many.



Cutaneous neurofibromas are benign tumors and are not at risk of becoming malignant.



Plexiform Neurofibromas

Plexiform neurofibromas are another type of benign tumor that grow along nerves. Approximately 30-50% of individuals with NF1 have a plexiform neurofibroma.

Unlike cutaneous neurofibromas that typically grow as small nodules, plexiform neurofibromas are often larger, diffuse growths with less well-defined borders. They can appear anywhere inside or outside of the body. They may be relatively small or they may involve larger portions of the body. Plexiform neurofibromas often feel like a bunch of cords or knots beneath the skin and may have a variation in texture or darker pigmentation on top of the skin. Plexiform neurofibromas also differ from cutaneous neurofibromas because they are generally thought to be present at birth and usually grow intermittently during childhood.

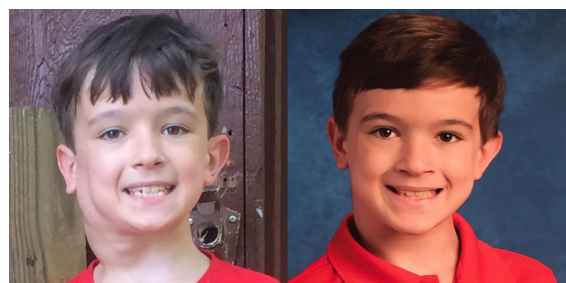


Plexiform Neurofibroma Treatment Options

Until recently, surgery has been the main treatment option for plexiforms.

However, plexiform neurofibromas are often difficult to remove surgically because they are made of extensive nerve and blood vessel tissue that is mixed with normal tissue. When considering treatments for a plexiform neurofibroma, the benefits and risks of surgical intervention should be considered. Because it is often hard to remove all of a plexiform, surgeons often can only take out a portion of the tumor. This is called a debulking procedure. Unfortunately, plexiform neurofibromas may grow back after surgery. How and when they grow back after a surgery varies for every individual.

More recently, medications are being developed to treat plexiforms which can make surgery less necessary in some individuals. There are a group of medications, called MEK inhibitors, that have been shown to reduce the size of plexiform neurofibromas in many individuals with NF1. In spring of 2020, a MEK inhibitor called Koselugo (selumetinib) was approved by the Food and Drug Administration for treatment of symptomatic plexiform neurofibromas in children with NF1 and may be an option for some individuals who cannot have surgery. For more information, go to ctf.org/mek.



Before and after photo showing tumor shrinkage while taking the MEK inhibitor drug Koselugo (selumetinib).

WHAT COMPLICATIONS CAN ARISE FROM A PLEXIFORM NEUROFIBROMA?

Plexiform neurofibroma often do not cause any symptoms but since they may sit next to or surround important organs, they can cause medical complications.

- Because of the presence of mast cells within these types of neurofibromas, they may cause bothersome itching.
- Depending on their size and location, some plexiform neurofibromas can be disfiguring. They may change or distort a person's appearance and this can be upsetting to some individuals.

- Plexiform neurofibromas can be present anywhere inside or outside of the body. They can press on important organs such as those in the breathing or gastrointestinal tracts and cause dysfunction. If they involve the peripheral nerves or spinal cord, they can cause pain, weakness, numbness, tingling or bowel/bladder problems.
- It is not uncommon for plexiform neurofibromas to be slightly painful when bumped or pushed, but plexiforms should not cause severe pain. Anyone who has severe and persistent pain or rapid change in size of a plexiform neurofibroma, should seek medical care immediately.
- Although plexiform neurofibromas are benign, they are at increased risk of becoming malignant or cancerous. When a plexiform neurofibroma becomes cancerous, it is referred to as a malignant peripheral nerve sheath tumor (MPNST).
- MPNSTs are very concerning tumors and may be difficult to manage. Treatments may include surgery, radiation, chemotherapy or a combination of all three. The lifetime risk of an individual developing an MPNST from a plexiform neurofibroma is approximately 8-12%.

WHEN SHOULD YOU BE CONCERNED ABOUT A PLEXIFORM NEUROFIBROMA?

As mentioned above, many plexiform neurofibromas do not cause medical issues. However, due to the risk of developing an MPNST and other potential complications, it is important to be aware of concerns warranting further evaluation.

Signs and symptoms that a plexiform may be changing or becoming malignant are:

- Rapid growth of the plexiform
- Severe or persistent pain in the area of the plexiform
- Change of the plexiform to have a harder texture
- New neurologic symptoms like weakness, numbness, tingling or bowel/bladder problems
- New symptoms that could be coming from an involved organ

Individuals with NF1 should let their doctors know immediately if any of these symptoms develop so appropriate testing can be performed.



How can a plexiform neurofibroma be evaluated by medical professionals?

Medical professionals have several ways to evaluate plexiforms. Following plexiforms over time with these methods is an important part of comprehensive NF1 care.

First, clinicians can perform a thorough physical examination to document the ways in which a plexiform involves the body. Next, they can use an MRI scan of the affected part of the body to better understand the size and extent of the plexiform on the outside as well as the inside of the body. MRIs are usually reserved for plexiforms that involve a more extensive part of the body. Finally, other radiology procedures may be necessary if there is concern for the development of a malignant peripheral nerve sheath tumor. Positron emission tomography (PET scan) uses a radioactive tracer to look at the chemical activity in cells within a plexiform to tell whether a cancer is developing or present.

It is important to seek medical advice from a healthcare provider who is familiar with NF1 and can monitor for concerning symptoms associated with a plexiform neurofibroma. To locate an NF Clinic in your area, go to: [ctf.org/doctor](https://www.ctf.org/doctor).