

Neurofibromatosis Type 1 and Neurofibromas

Definition

Neurofibromas are benign nerve sheath tumors. They arise from the supportive tissue within peripheral nerves. As these tumors grow, they displaced and compress important nerve fascicles within the nerve. This causes pain, weakness, and numbness. Although neurofibromas are frequently solitary and occur at random, they can also occur in multiple locations in patients with neurofibromatosis.

Neurofibromatosis

Neurofibromatosis type 1 ([NF1](#)) affects 1/3500 people. It is either inherited with an autosomal dominant pattern, or occurs in 30-50% of patients from spontaneous de novo mutation without a family history of the disease. NF1 patients have multiple cutaneous neurofibroma, solitary neurofibromas on peripheral nerves, or very large and frequently proximal tumors termed plexiform neurofibromas. 3-5% of plexiform neurofibromas may dedifferentiate into a malignant peripheral nerve sheath tumor. Patients with NF-1 are at increased risk for specific malignant diseases, including neurogenic sarcomas, astrocytomas, optic netrve gliomas, pheochromocytomas, embryonal rhabdomyosarcomas and chronic myeloid leukemias of childhood. Patients with NF1 have a 1000 to 10000 fold greater risk of developing a malignancy with 30% ultimately dying from some form of cancer (vs 25% of the general population).

The diagnostic criteria for NF-1 include two or more of the following:

- Six or more café au lait macules over 5mm in greatest diameter in prepubertal individuals and over 15mm in greatest diameter in postpubertal individuals
- Two or more neurofibromas of any type, or one plexiform neurofibroma
- Axillary or inguinal freckling
- Optic glioma
- Two or more lisch nodules (iris hamrtomas of melanotic origin)
- A distinctive osseous lesion, such as sphenoid dysplasia or thinning of the long bone cortex with or without pseudoarthrosis
- A first degree relative (parent, sibling, or offspring) with NF-1 by the above criteria

Diagnosis

Because neurofibromas can occur in any nerve in the body, symptoms are variable. In general, neurofibromas can be asymptomatic, cause progressive pain, weakness, tingling, and numbness, or present as a mass in the neck or extremities. Tapping on the neurofibroma often causes

electrical pain to shoot down the extremity (i.e., Hoffman-Tinel's sign). Although one can suspect the diagnosis of neurofibroma on history and examination, it is confirmed with MRI, with and without contrast. It is usually not possible to differentiate a schwannoma from a solitary neurofibroma preoperatively. Definitive diagnosis is obtained after the tumor is removed. In general, needle biopsy is not recommended.

Treatment Options

Small, asymptomatic neurofibromas, especially in older patients, may be observed on serial MRIs. If weakness, numbness, or pain is present, then microsurgery to remove these lesions is recommended. Although radiosurgery may be an option for solitary neurofibromas in the head or spine, for the extremities this is not an option. In general, neurofibromas in patients with neurofibromatosis are only removed when they become symptomatic or if they are significantly growing in size.

Surgery

This is the mainstay of solitary neurofibroma treatment. The nerve is exposed under general anesthesia. Using a microscope and intraoperative electrophysiological monitoring, the tumor is carefully removed from the nearby functional nerve fascicles. The tumor usually involves a few nerve fascicles that may or may not have been made non-functional by the tumor—these fibers are removed with the tumor. If intraoperative electrical testing reveals that these fascicles are functional, a nerve graft may be indicated. This is a decision made during the surgery. Nevertheless, all other remaining nerve fascicles are preserved, thereby maintaining their function. Surgery is efficacious in resolving pain, weakness, and numbness in the majority (80-90%) of patients.

Complications

Besides the normal risks of surgery, including reactions to anesthesia and infection, patients who undergo neurofibroma removal are at risk for paralysis (5%), numbness (5%), and worsened pain (5%). The risks depend on the function of the parent nerve. To minimize these risks, the majority of functional nerve fascicles need to be preserved. If the tumor originates from a motor nerve, or significant sensory nerve, an en bloc nerve resection should not be performed; instead a fascicle sparing approach should be utilized.

Outcomes

Patients with neurofibromas usually have an excellent prognosis with or without surgical resection. Aside from the risks of numbness, weakness, and neuropathic pain, with complete tumor removal the chance of recurrence may be approximately 2-4%. Recurrence depends on the extent of resection and whether surgical margins were tumor free based on histopathology and intraoperative examination of the parent nerve.