

Neurofibromatosis, type 2

Also known as: bilateral acoustic neurofibromas (BANF), central neurofibromatosis

Clinical Characteristics

Neurofibromatosis, type 2 (NF2) is characterized by neurofibromas, which are schwannomas (tumors of the myelin sheaths) on nerves of the central nervous system. These tumors are especially prevalent in the inner ear. Other growths, including meningiomas, and (rarely) ependyomas and astrocytomas, could potentially develop as well. The tumors are not malignant, but are numerous. They cause problems such as tinnitus, hearing loss, balance difficulties, and decreased vision.

Neurofibromatosis, type II and Hearing Loss

The development of a vestibular schwannoma (also called an acoustic neuroma) on the eighth cranial nerve can cause unilateral hearing loss, bilateral hearing loss, or tinnitus. The hearing loss is generally progressive, and may eventually result in complete deafness.

Natural History

Neurofibromatosis 2 is a completely separate diagnosis from Neurofibromatosis 1 (also known as von Recklinghausen's Disease). The clinical description, natural history, genetics, and management of these two conditions are entirely different.

NF2 is diagnosed in both males and females, and in all ethnicities. It is estimated that between 1 in 25,000 and 1 in 40,000 are affected by the disorder.

Onset of NF2 is usually between 18 and 24 years of age, though manifestations have appeared in a child as young as 2. The most important predictor of disease severity appears to be age of onset. Almost all affected individuals develop bilateral vestibular schwannomas by the time they are 30 years old. The first presenting symptom is most often unilateral hearing loss, followed by focal weakness, tinnitus, bilateral hearing loss, and balance problems. There is variable expressivity in regards to the number and location of tumors. Skin tumors are seen in about 70%. At least two-thirds of patients develop spinal tumors, usually schwannomas. About half develop meningiomas, usually in the cranium. Some degree of vision impairment in one or both eyes is common. Cataracts are the most common problem to develop. A recently described symptom is mononeuropathy in childhood, and progressive polyneuropathy in adulthood.

Most people with NF2 have the condition due to a single mutation in a gene. Larger chromosomal deletions, however, could result in mental retardation and multiple congenital anomalies. These are not "common" characteristics of NF2, but can occur under certain circumstances. Although survival time continually improves with earlier diagnosis and better treatment, the location and sheer number of tumors result in a

shortened life span. Death occurs an average of 15 years after the diagnosis has been made, making the average age of death 36 years.

Genetics

The gene *NF2*, on chromosome 22, is the only known gene associated with NF2. It encodes for a protein called merlin, or schwannomin, which acts as a tumor-suppressor. NF2 is **autosomal dominant**. This means that an affected individual has a 50% chance with each pregnancy of having an affected child, and a 50% chance of having an unaffected child. About half of individuals with NF2 inherit the disorder from a parent, while the other half has a new mutation. 25-30% of those with a new mutation are mosaics, meaning the mutation is found in only some of their cells.

Management

The diagnosis of NF2 is made clinically. Genetic testing is available for confirmation of diagnosis, predictive genetic testing for family members at risk, and prenatal diagnosis and/or preimplantation genetic diagnosis once a mutation has been identified in an affected family member. Molecular genetic testing will reveal a mutation in *NF2* in about 70% of individuals with NF2 and a family history. Mutations are identified about 60% of the time in those with no family history.

Management is typically achieved through a specialty center. Professionals associated with treatment at such a center will likely include a neurosurgeon, otolaryngologist, neurologist, geneticist, audiologist, and ophthalmologist.

Following diagnosis, an initial evaluation should include a head MRI, a careful examination of the skin, an ophthalmologic evaluation, and a hearing evaluation which should include a BAER.

Surgery remains the primary treatment for tumors. Smaller tumors can often be removed completely, while larger tumors may require debulking or decompression in order to preserve nerve function. Whenever surgery is being considered, it must first be considered as to whether the tumor is truly causing impairment and if a surgical procedure would be more harmful than beneficial.

Regular evaluation and consultation with an audiologist is warranted. Hearing aids are often helpful in the early stages of the condition, and cochlear implantation may be an option for those without significant nerve damage. Regular eye examinations are recommended. A yearly neurologic evaluation and brain MRI is recommended.

For those “at risk” family members in whom a mutation has been identified but symptoms have not yet begun to appear, an annual MRI and hearing evaluation is recommended. At-risk children (in which a mutation may or may not have been identified) should begin screening by MRI around 10 to 12 years. A scheduled appointment with a geneticist and/or genetic counselor is also recommended for both affected and “at risk” family members.

Resources for Families

Statewide Genetics Program

Phone: 608-267-7148

Fax: 608-267-3824

Email: meyeram@dhfs.state.wi.us

Wisconsin First Step Hotline

Phone: 1-800-642-7837 voice/TTY

Website: www.mch-hotlines.org

Wisconsin Office for Deaf and Hard of Hearing

Phone: 1-608-266-3118 voice/TTY

Website: www.dhfs.state.wi.us/sensory

Regional Children and Youth with Special Health Care Needs Centers

Centers in Green Bay, Wausau, Milwaukee, Madison, and Chippewa Falls

Website: http://dfhs.wisconsin.gov/DPH_BFCH/cshcn/index.HTM

WI Chapter of Families for Hands & Voices

Phone: (920) 437-7370

Website: www.handsandvoices.org

Parent-to-Parent of Wisconsin

Phone: 1-888-266-0028

Email: rmathea@shsmh.org

Family Village online resource

Library Card Catalog of Disorders

www.familyvillage.wisc.edu

NF2 Crew: Neurofibromatosis II Support

www.nf2crew.org

National Organization for Rare Disorders (NORD)

www.rarediseases.org