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A Review: Neurofibromatosis & Its Treatment

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Abstract

This review gives the information about what are the causes, symptoms and treatment of neurofibromatosis or Neurofibromatosis is a genetic nervous system disorder that causes tumors to grow around nerves. Neurofibromatosis causes tumor to grow on nerves and gives rise to many other abnormalities like skin changes and bone deformities. The tumor begins in the cells that make up the myelin sheath, which is a thin membrane that envelops and protects nerve fibers. The type of the tumor depends on its position in the body and the kind of cells involved Neurofibromas is one of the most common tumors that develops in the tissue surrounding the peripheral nerves. The tumor is non-cancerous, but can become cancerous over time. This genetic disorder occurs in both sexes and in all races and ethnic groups.

Keywords: Neurofibromatosis, Schwnnomatosis, Tumors

1. Introduction

The neurofibromatoses are genetic disorders that cause tumors to grow in the nervous system. The tumors begin in the supporting cells that make up the nerves and the myelin sheath--the thin membrane that envelops and protects the nerves. These disorders cause tumors to grow on nerves and produce other abnormalities such as skin changes and bone deformities. Although many affected persons inherit the disorder, between 30 and 50 percent of new cases arise spontaneously through mutation (change) in an individual's genes. Once this change has taken place, the mutant gene can be passed on to succeeding generations. It classified as neurofibromatosis type 1 (NF1), neurofibromatosis type 2 (NF2), and schwannomatosis, a type that was once considered to be a variation of NF2. NF1 is the more common type of the neurofibromatoses. Symptoms of NF1, which may be evident at birth and nearly always by the time the child is 10 years old, may include light brown spots on the skin ("cafe-au-lait" spots), two or more growths on the iris of the eye, a tumor on the optic nerve, a larger than normal head circumference, and abnormal development of the spine, a skull bone, or the tibia. NF2 is less common and is characterized by slow-growing tumors on the eighth cranial nerves. The tumors cause pressure damage to neighboring nerves. To determine whether an individual has NF2, a physician looks for eighth nerve tumors, cataracts at an early age or changes in the retina that may affect vision, other nervous system tumors and similar signs and symptoms in a parent, sibling, or child. The distinctive feature of schwannomatosis is the development of multiple schwannomas

(tumors made up of certain cells) everywhere in the body except on the vestibular branch of the 8th cranial nerve. The dominant symptom is pain, which develops as a schwannoma enlarges or compresses nerves or adjacent tissue. Some people may develop numbness, tingling, or weakness in the fingers and toes.

Neurofibromatosis: Neurofibromatosis (NF) represents a genetic disorder of the nervous system, primarily affecting the development and growth of neural cell tissues. As a result of this disorder, tumors can grow on nerves. Such tumors result in skin changes and bone deformities. The neurofibromatosis consists of three clinical types:

1. Neurofibromatosis Type 1 (NF1)
2. Neurofibromatosis Type 2 (NF2)
3. Schwannomatosis

1. Neurofibromatosis: Type 1 (NF1)

NF1 is the most common type of the neurofibromatosis that occurs normally during adolescence. NF1 was known as peripheral neurofibromatosis or von Recklinghausen's neurofibromatosis, as some of its symptoms like skin spots and tumors seemed to be restricted only to the outer nerves or peripheral nervous system of the affected person. But later the name was changed, as central nervous system tumors are known to occur in NF1. The benign tumor may originate on the skin (cutaneous), under the skin (subcutaneous) and in the connective nerve tissue (neurofibromas).

Signs and symptoms of NF1

a. Curvature of the spine (scoliosis)
b. More than five light brown skin spots about 5 millimeters in diameter in patients under the age of puberty or more than 15 millimeters in adults.
c. Freckling in the armpit and groin areas.
d. Benign growths on the iris of the eye known as lisch nodules or iris hematomas.
e. Tumor on the optic nerve called optic gliomma.
f. Enlargement and deformity of the bones that may cause chronic pain.
g. Hearing loss and learning disabilities.

2. Neurofibromatosis: Type 2 (NF2)

NF2 is less common type of neurofibromatosis which is characterized by bilateral tumors on the eighth cranial nerve. The tumor mainly occurs on the vestibular nerve (another branch of the eighth cranial nerve near the auditory nerve). It causes damage to the neighboring nerves and vital structures such as cranial nerves and the brainstem which can be life-threatening. It is also known as bilateral acoustic neurofibromatosis or central neurofibromatosis.

Signs and symptoms of NF2

a. Hearing loss
b. Ringing in the ears
c. Headache
d. Facial pain or weakness
e. Feeling unsteady and off balance
f. Cataract at an early age
g. Glioma and meningioma

3. Schwnnomatosis:

Schwannomatosis is a rare form of neurofibromatosis only recently recognized. It rarely affects people before their 20s or 30s. Schwannomatosis causes painful tumors called schwannomas to develop on cranial, spinal and peripheral nerves, but not on the nerve that carries sound and balance information from the inner ear to the brain (the eighth cranial nerve).

Aetiology:

Neurofibromatosis is an autosomal dominant genetic disorder, that is, an affected person has 50% chance of passing it on with each pregnancy. It can be the result of a mutation in the genetic material of the sperm or egg at conception in families having no previous history of neurofibromatosis. Nearly 50% of the cases are inherited and rest are due to spontaneous genetic mutation. NF1 and NF2 are linked to mutations in separate genes. The NF1 gene has been traced to chromosome 17 and the NF2 gene is located on chromosome 22. These findings are important, as it may help during a blood test or other genetic tests to know if a relative has NF.

Diagnosis and treatment of neurofibromatosis:

Diagnosis involves several baseline studies like hearing and vision screening tests, psychological testing to evaluate possible learning disorders, electroencephalogram (EEG), X-rays of the bones and head CT (computed tomography) or MRI (magnetic resonance imaging). Annual eye examinations are important in early detection of optic nerve lesions. Skeletal involvement, including scoliosis, hemi hypertrophy, or long-bone modeling defects, should be documented. Blood pressure should be checked at each visit and hypertension treated promptly if detected. Hypertension workup should include evaluation for pheochromocytoma (i.e., measurement of urinary catecholamine’s and metanephrines) and testing for renal artery stenosis. Percutaneous transluminal renal artery

angioplasty may, in some cases, effectively treat renal artery stenosis secondary to fibro muscular dysplasia. Symptoms of spinal cord neurofibromas may be subtle and slowly progressive; prompt identification and early surgical intervention allow for optimal outcome.

Treatment:

The treatment for NF1 includes removal of the neurofibromas for cosmetic purposes, getting intervention for children with learning disabilities and treating the complications like seizures, scoliosis, speech impairment, high blood pressure, optic nerve tumors and early or delayed onset of puberty. It's rare that neurofibromas become cancerous, but for such occurrences, surgery, chemotherapy or radiation treatment can be done. There is no specific treatment for NF, but genetic counseling and early detection of treatable conditions or complications can benefit people. The asymptomatic patient needs to be re-examined yearly and a symptomatic patient can be benefited from surgical treatment of tumors. Recent advances in laser technology have permitted nonsurgical removal of small, cutaneous neurofibromas. Although laser treatment has been used for various cutaneous, hyper pigmented lesions (e.g., port-wine stains, tattoos), it has not yet proven successful in permanent removal of café-au-lait spots.

Drugs:

Farnesyl transferases used in combination with lovastatin have shown synergistic effects in growth inhibition of MPNST cell lines in vitro. Sorafenib also appears to inhibit MPNST cell growth in vitro. A rapamycin complex 1 inhibitor (RAD001) demonstrated decreased tumor cell growth when used alone, and, when used in combination with erlotinib (an epidermal growth factor receptor tyrosine kinase inhibitor), showed even further growth inhibition and tumor cell apoptosis. Hyaluronan oligomers, another promising agent, has shown efficacy in slowing growth of MPNSTs in animal models. These small molecules, when used in combination with a traditional chemotherapy agent (doxorubicin), substantially inhibit tumor growth.

2. Conclusion

By minimising the risk factors we can overcome development of disease in future. Both surgical and medical treatment is necessary for the complete management of patients of neurofibromatosis.

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