TEXAS NEUROFIBROMATOSIS FOUNDATION®

DID YOU KNOW IN AMERICA, EVERY HOUR THREE BABIES ARE BORN WITH NEUROFIBROMATOSIS?

Facts about Neurofibromatosis (NF) and Schwannomatosis (SWN)

- NF is the most common neurological disorder caused by a single gene.
- NF involves the uncontrolled growth of tumors along the nerves anywhere in the body, internal and external, and at any time through an individual's life.
- NF1 affects 1 out of every 3,000 people
- NF2-related SWN affects 1 in every 25,000 people
- Other SWN disorders affect 1 in 40,000 people

DIAGNOSTIC CRITERIA FOR NF1

If a patient meets two or more of the following manifestations:

- Six or more light brown spots on the skin (often called "café-au-lait" macules), measuring more than 5 millimeters in diameter in pre-pubertal children or more than 15 millimeters across in post-pubertal individuals.
- Two or more neurofibromas tumors of any type, or one plexiform neurofibroma (a neurofibroma that involves many nerves).
- Freckling in the axillary (armpit) or the groin.
- Two or more Lisch nodules or two or more choroidal abnormalities.
- A tumor on the optic visual pathway (called an optic pathway glioma).
- A distinctive osseous lesion such as sphenoid dysplasia; anterolateral bowing of the tibia (tibial dysplasia); or pseudarthrosis of a long bone.
- Apathogenic NF1 gene variant
- A parent with NF1 by the above criteria.

TEXAS NEUROFIBROMATOSIS FOUNDATION®

DIAGNOSTIC CRITERIA FOR *NF2*-related SWN

If a patient has one of the following:

- Bilateral vestibular schwannomas (VS)
- An identical NF2 pathogenic variant in at least two anatomically distinct NF2-related tumors (schwannoma, meningioma, and/or ependymoma)
- Either two major or one major and two minor criteria present as follows:

Major Criteria

- Unilateral vestibular schwannoma
- First-degree relative other that a Sibling with NF2-relatd SWN
- Two or more meningiomas (a single meningioma qualifies as a minor criterion)
- NF2 pathogenic variant* in an unaffected tissue such as blood

* When the variant is present at significantly less than 50%, the diagnosis is mosaic NF2-related SWN

Minor Criteria

Can count more than one of a type (e.g., two schwannomas=two minor criteria)

- Ependymoma; schwannoma (note: if the major criterion is unilateral vs, at least one schwannoma must be dermal in location)

Can count only one

- Juvenile subcapsular or cortical cataract; retinal hamartoma; epiretinal membrane in a person aged less than 40 years; meningioma (note: multiple meningiomas qualify as a major criterion; meningioma cannot be used as both major and a minor criteria)

TEXAS NEUROFIBROMATOSIS FOUNDATION®

DIAGNOSTIC CRITERIA FOR MOSAIC SWN

Mosaicism is confirmed for *LZTR1*-related, *SMARCB1*-related, or *NF2*-related SWN by either of the following:

- Clearly less than 50% pathogenic variant allele fraction (VAF) in blood or saliva

OR

- Pathogenic variant not detected in blood or saliva but shared pathogenic variant in two or more anatomically unrelated tumors.

DIAGNOSTIC CRITERIA FOR *SMARCB1*-Related SWN

A diagnosis can be made when a patient **meets one of the following criteria**:

- At least one pathologically confirmed schwannoma or hybrid nerve sheath tumor AND a *SMARCB1* pathogenic variant in an unaffected tissue such as blood or saliva
- A common *SMARCB1* Pathogenic variant in two anatomically distinct schwannomas or hybrid nerve sheath tumors
  Note: diagnosis requires surgical specimen to confirm tumor histology

DIAGNOSTIC CRITERIA FOR *LZTR1*- Related SWN

A diagnosis can be made when a patient **meets one of the following criteria**:

- At least one pathologically confirmed schwannoma or hybrid nerve sheath tumor and *LZTR1* pathogenic variant in an unaffected tissue such as blood or saliva
- A common *LZTR1* pathogenic variant in two anatomically distinct schwannomas or hybrid nerve sheath tumors
  Note: diagnosis requires surgical specimen to confirm tumor histology

TEXAS NEUROFIBROMATOSIS FOUNDATION®

DIAGNOSTIC CRITERIA FOR 22q- Related SWN

A diagnosis of 22q-related SWN can be made when an individual does not meet criteria for *NF2*-related SWN*, SMARCB1*-related SWN, or *LTZR1*-related SWN **and has both of the following molecular features:**

- Loss of heterozygosity (LOH) of the same chromosome 22q markers in two anatomically distinct schwannomas or hybrid nerve sheath tumors AND
- A different NF2 pathogenic variant in each tumor which cannot be detected in unaffected tissue
- Note: diagnosis requires at least two surgical specimens

DIAGNOSTIC CRITERIA FOR SWN NOS (not otherwise specified) and SWN NEC (not elsewhere classified)

A diagnosis of schwannomatosis-NOS can be made if both of the following criteria are met, and genetic testing was not performed or is not available:

- Presence of two or more lesions on appropriate imaging consistent with non-intradermal schwannomas, and
- Pathologic confirmation of at least one schwannoma or hybrid nerve sheath tumor

A diagnosis of schwannomatosis-NEC can be made if both of the above criteria are met and genetic testing does not reveal a pathogenic variant in known schwannomatosis -related genes.

TEXAS NEUROFIBROMATOSIS FOUNDATION®

WHAT EVERY PEDIATRICIAN SHOULD KNOW ABOUT NF

NF TYPE 1:

- Very common autosomal dominant disorder. Many diagnostic signs may not develop until adolescence thus delaying clinical diagnosis. DNA testing is available if needed.
- **All children should have MRI brain or pediatric ophthalmology exam by 18 months to rule out optic glioma.**
- Neurofibromas of skin are rarely a cancer risk.
- Risk of brain tumor and other cancers is higher in NF-1 than the general population.
- Short stature is seen in 15% of patients with NF-1. Precocious puberty is more frequent in NF-1 and can be due to tumor of the optic chiasm/hypothalamus.
- Over 40% of children with NF-1 have ADD or ADHD.
- Over 40% of children with NF-1 have dyslexia or other language-based learning disability.
- Scoliosis requires orthopedic or NF clinic investigation for specific complications of NF-1.
- Curvature of tibia or other long bone requires x-ray to rule out pseudoarthrosis and pathologic fracture.
- **Complaints of persistent and severe pain related to a mass must be evaluated for possible transformation of benign neurofibroma to malignant peripheral nerve sheath tumor (highly malignant sarcoma)-lifetime risk in NF-1 is about 10%.**
- NF 1 is an autosomal dominant disorder but affected parents may show a distinctly different clinical expression than their children.

NF2-related Schwannomatosis:

- NF2 is a rare autosomal dominant, but **childhood onset NF2 may progress more rapidly than the pattern seen in their parent**. DNA testing is available.
- Audiology and pediatric ophthalmology screening should be conducted yearly beginning at age 3 years.
- Screening MRI of brain and spine should be considered by age 6 years or sooner if symptoms of spinal cord compression are noted (ex: toe walking, pathologic enuresis, etc.).
- Early evaluation in an NF clinic is advised.
- Patients (children, adolescents, or adults) reporting hearing deficits, vertigo or dizziness should be evaluated and monitored.

Schwannomatosis:

- Autosomal dominant disorder, clinically like NF2 but without intracranial tumors.
- Hallmark is relentless **neuropathic pain** and occasional patchy distribution muscle atrophy.
- Treatment of pain is symptomatic medical management; occasionally nerve sheath tumors require resection. Limited risk of malignancy.
- Genetic analysis is REQUIRED for the diagnosis of a specific type of schwannomatosis

Texas Neurofibromatosis Foundation®

P: 972.739.6086 | 877.515.TXNF | F: 972.739.6087

www.texasnf.org | www.facebook/texasnf