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Caring for children with neurofibromatosis type 1

BY JANICE SAMPSON, DNP, RN, CNE; HEATHER L. THOMPSON, PhD, CCC-SLP; AND DENISE M. WALL PARILO, PhD, RN

Abstract: This article discusses the variable physical manifestations of neurofibromatosis type 1 among children in terms of presentation, disease severity, and prognosis, and addresses appropriate nursing interventions and patient teaching.

Keywords: attention-deficit hyperactivity disorder, café-au-lait macules, genetic disorder, Lisch nodules, neurofibroma, neurofibromatosis type 1, plexiform neurofibroma, selumetinib

INDIVIDUALIZED CARE for children and families is at the core of improved outcomes in any healthcare arena. The unpredictable course of the genetic neurocutaneous disorder neurofibromatosis type 1 (NF1), which typically manifests during infancy or childhood and progresses throughout life, demands astute nursing assessment skills and comprehensive, ongoing interdisciplinary cooperation.[1] Nurses play a key role by using a personalized approach to facilitate the coordination of care. This article discusses the variable physical manifestations of NF1 among children in terms of presentation, disease severity, and prognosis, and addresses appropriate nursing interventions and patient teaching.

About NF1

NF1 is a genetic disorder affecting the epidermal, skeletal, and central nervous systems. It is characterized by multiple benign nerve sheath tumors (neurofibromas) and areas of abnormal skin color (see *Key terminology*). Neurofibromas usually develop in the skin but can appear anywhere in the body, and they tend to increase in size and number as the patient ages.[2]

According to the National Organization for Rare Disorders, most children with NF1 have normal intelligence, but about half experience learning disabilities. Many also exhibit attention-deficit hyperactivity disorder (ADHD).[2,3]

A surprisingly common autosomal dominant genetic disorder, NF1 has an incidence of about 1 in 2,700 births.[4] The disorder is caused by a mutation of the NF1 gene on chromosome 17q11.2. This gene regulates production of neurofibromin, a protein expressed in many tissues throughout the body, including the brain, kidney, spleen, and thymus. Neurofibromin is thought to act as a tumor suppressor.[5,6] Approximately half of all cases of NF1 are new gene mutations and about half of patients have a family history of the

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disorder.[2,7] NF1 affects both genders and all racial and ethnic groups.[8]

Signs and symptoms usually appear in infancy or early childhood (see *Common signs of NF1*).[1] A clinical diagnosis of NF1 is made when patients exhibit two or more hallmark characteristics in specific areas, according to guidelines from the National Institutes of Health Consensus Development Conference:[9]

- six or more café-au-lait macules (coffee-colored hyperpigmented lesions) of 5 mm or greater in diameter in children and 15 mm or greater in adolescents after puberty
- two or more neurofibromas or one plexiform neurofibroma (tumors that involve multiple branches of nerves that can occur internally or externally)
- an optic glioma (tumor of the optic nerve)
- two or more Lisch nodules, also known as iris hamartomas (small pigmented tumors of the iris)
- a distinctive bony lesion, such as sphenoid dysplasia or thinning of the long bone cortex with or without pseudoarthrosis
- freckling in the axillary or inguinal regions
- a first-degree relative (parent, sibling, or child) with NF1 meeting the above clinical criteria.

While the diagnosis of NF1 is generally based on the clinical criteria, in some unconfirmed cases, genetic testing is completed through the analysis of DNA or mRNA from a blood sample or tissue biopsy.[10]

Patients suspected of having NF1 should receive a timely evaluation by a knowledgeable team of specialists engaged in interprofessional practice and transdisciplinary care, such as a neurologist, dermatologist, ophthalmologist, orthopedist, psychologist, and speech-language pathologist. Radiographs and other imaging studies should be obtained as needed. An interdisciplinary team or clinic at a major hospital or university treatment center is an excellent resource for initial assessment and follow-up evaluation.

Following the identification of tumors or other physical manifestations, patients should be referred for surgical intervention if indicated for painful or disfiguring tumors, radiation, or chemotherapy following current best practices. For patients seeking support in reproductive health or prenatal counseling, a genetic counselor can help the family make informed decisions.

Key terminology

Articulation and phonology deficits	Deficits in articulation (affecting single sounds) or phonology (affecting sounds from an entire class), which can result in decreased intelligibility.[25]
Dermal neurofibroma	A benign peripheral nerve sheath tumor. Due to the variability of NF1, individuals can present with one or thousands of this tumor type.[37]
Moyamoya	The most frequently occurring form of vasculopathy in children with NF1, affecting 2.3% to 6% of patients.[17]
Tibial dysplasia	A unilateral and variable bowing of the tibia that can progress to fracture; affects young children with NF1.[11]
Plexiform neurofibroma	A benign tumor that involves multiple peripheral nerve branches; present in approximately 50% of children with NF1.[38]
Pseudoarthrosis	A deficit of the long bones affecting approximately 5% of patients with NF1.[11]
Resonance impairments	Resonance disorders leading to a nasal-sounding voice quality.[25]
Speech disorders	Speech impairment leading to a harsh, breathy, or hoarse vocal quality.[25]

Disease progression

The range, severity, and rate of progression of NF1 signs and symptoms are unpredictable and can vary with age. Gutmann and colleagues report that infants with NF1 exhibit café-au-lait macules.[10] Early in a child's development, orbital or tibial dysplasia may also be observed. Tibial bowing and pseudarthrosis can contribute to mobility impairment, requiring significant medical follow-up and possibly orthopedic intervention for long bone dysplasia or scoliosis.[11-13]

Preschool children may present with an optic glioma that can impact vision.[10] Plexiform, dermal, and paraspinal neurofibromas can emerge in childhood and adolescence. In adolescents with NF1, sexual development may be early (precocious puberty) or delayed.[2,10]

Tumor progression in NF1 is of considerable concern due to its variability and propensity to affect different body regions, which can contribute to significant pain and decreased quality of life.[14] Dermal neurofibromas may cause pruritus but are not usually painful. However, plexiform tumors can be painful if they protrude into proximal structures. The impact of NF1 depends largely on tumor location, the effect on adjacent tissues, and related complications.[7]

Patients can also experience signs and symptoms beyond those required for a clinical diagnosis of NF1. For example, children with NF1 may present with cardiac anomalies or hypertension.[15,16] An elevated risk of cerebral vasculopathy,

which can result in a stroke, has also been described as a possible complication in NF1.[16,17] Brain malformations, paraspinal neurofibromas, brainstem gliomas, and seizures may occur, requiring careful monitoring and surveillance.[10,15] Neurofibromas become malignant in an estimated 8% to 13% of patients.[18]

Impairments in gross and fine motor functioning have also been reported.[19] Delays in motor functioning may impact a child's ability to independently complete activities of daily living such as tying shoelaces or writing.[20] Assessments performed early in development can increase the probability that children with NF1 will have access to appropriate services. Early intervention may improve short-term and long-term outcomes.

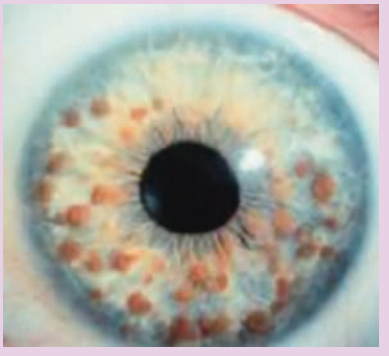
Treatment options

Due to emerging research, medications for the treatment of patients with clinical manifestations of NF1 are constantly changing and tailored to each patient's unique condition. Many patients take medications to manage ADHD, seizures, and/or pain. Patients with bone dysplasia may be prescribed vitamin D if a deficiency is identified.[10]

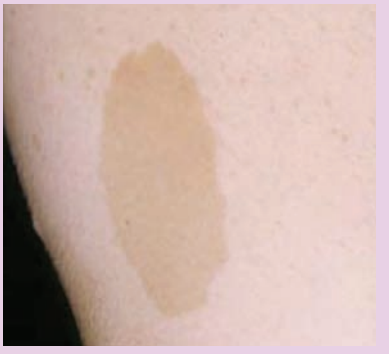
While the current focus of pharmacologic treatment is symptom management (for example, managing ADHD with stimulants), clinical trials are currently underway to evaluate the efficacy of oral selective mitogen-activated protein kinase inhibitors, including the investigational drug selumetinib.[21,22] In at least one clinical trial, selumetinib has been shown to shrink large plexiform tumors in children.[23] However, further research is needed to evaluate the efficacy of this and other pharmacologic options.

Not only do nurses need to remain up to date on these clinical trials and current research findings, but they also need to be engaged as interdisciplinary team members carrying out research in NF1. Access to current information provided via nurses who are involved directly in research can provide NF1 patients and their families with encouragement and hope for improved outcomes.

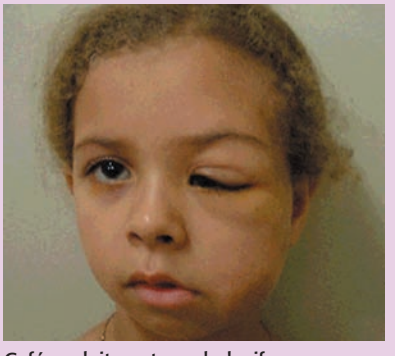
Common signs of NF1



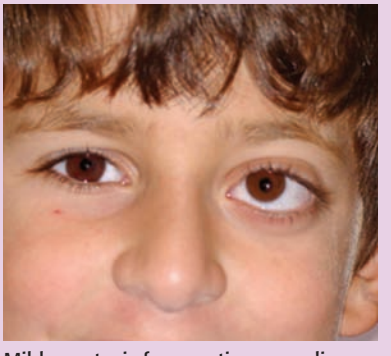
Lisch nodules of the iris



Café-au-lait spot



Café-au-lait spots and plexiform neurofibromas of the upper eyelid



Mild proptosis from optic nerve glioma

Sources: (top left) Diab M, Staheli LT. *Practice of Pediatric Orthopedics.* 3rd ed. Philadelphia, PA: Wolters Kluwer; 2015.; (bottom left) Courtesy of Dr. Claudia Pabon Bejarano, Escola Paulista de Medicina, UNIFESP, São Paulo, Brazil.; (top and bottom right) Nelson LB, Olitsky SE. *Harley's Pediatric Ophthalmology.* 6th edition. Philadelphia, PA: Wolters Kluwer; 2013.

Addressing developmental issues

Children with NF1 should be assessed for learning disabilities, ADHD, and speech or language impairments.[3,24-26] Communication problems can also manifest as deficits in articulation and phonology, impairments in voice (such as a hoarse vocal quality) or resonance (such as hypernasality), or delays in receptive and/or expressive language.[25]

Behavioral concerns that may impede normal development include deficits in visuospatial ability and social competence.[27] Learning difficulties may be compounded by frequent absences from school for medical appointments or hospitalization.

Parents and caregivers of children with NF1 require information to guide lifetime care planning. Synthesizing results of previous investigations, Gutmann and colleagues concluded that individuals with NF1 have a lifespan that is 8 to 21 years shorter than those in the general population.[10] For family planning, couples in which one partner has

NF1 may consider genetic testing to identify the presence of NF1 in an embryo, but such tests have been shown to be effective only 80% of the time with the possibility of false positives.[28]

Nurses caring for pediatric NF1 patients should respect parental perspectives and encourage parents to participate in the child's care to help decrease parental anxiety. Family education and emotional support are tools that empower each member of the family to cope more effectively, leading to improved patient outcomes and anticipatory guidance.[29]

Interdisciplinary teamwork

Nurses play a key role on the NF1 interdisciplinary team from the time of diagnosis through the course of the patient's health journey. Due to the prevalence of NF1 and its disease process, nurses may see these children in almost any setting. For example, nurses may provide services to children identified in the neonatal ICU or during a routine visit for a well-child exam. In these areas, nurses must utilize their assessment skills to help identify children who exhibit symptoms of NF1 such as café-au-lait macules.

Nurses must utilize their assessment skills to help identify children who exhibit symptoms of NF1, such as café-au-lait macules.

In addition, nurses may work with children in specialty clinics (such as medical genetics, neurology, dermatology, gastrointestinal, cardiology, or endocrinology clinics) who are being treated for a specific complication of NF1. In these specialty clinics, the nursing focus is symptom management, prevention of complications, family-centered care, and education. For example, regular BP monitoring will alert the nurse to the potential for hypertension. Collaborating with pharmacists, the nurse can help patients and parents prevent adverse drug reactions and assist with follow-up.

In the home healthcare setting, nurses must establish a plan of care tailored for the child's unique medical needs. In an acute care setting, children may need care for a range of admission diagnoses, from influenza to tumor management, to pre- and postoperative care (see *Caring for hospitalized patients*).

Besides supporting families at the time of diagnosis, nurses must continue to perform comprehensive assessments to initiate and continue an individualized plan of care as the child develops. Assessments in a clinical setting should include neurologic, orthopedic, dermatologic, renal, and cardiovascular system workups. Nurses should complete assessments with a focus on the presenting diagnosis and stay especially alert for neurologic signs and symptoms, such as cognitive deficits and seizure activity. School nurses may assist children with medications prescribed to manage various disorders or symptoms, such as ADHD, seizures, or pain.

As they grow and develop, children with NF1 need regular ophthalmologic screening and growth assessments. Other indicated screening tests depend on specific signs and symptoms. For example, MRI of the brain is indicated for children who experience seizure activity and for those with accelerated

Caring for hospitalized patients

During hospitalization, patients with NF1 may require care following surgery for tumor removal and/or require attention for comorbidities such as moyamoya, a rare, progressive cerebrovascular disorder caused by arterial occlusion in the basal ganglia.[33] Performing a detailed neurologic assessment is a priority to determine baseline functioning.

If a patient with NF1 is hospitalized for a comorbid condition, nurses need to assess for signs and symptoms of complications associated with NF1. For example, headache is a very significant finding that requires follow-up. While many patients experience headaches, a headache in a child with NF1 is urgent because it can indicate an underlying life-threatening condition such as vasculopathy, hypertension, or a space-occupying brain lesion.[34] These disorders can cause seizure activity, stroke, or cardiopulmonary arrest.

Nurses also play an essential role in pain management. Children with NF1 may experience pain secondary to their disease process and/or to a surgical or orthopedic procedure. The use of age-appropriate pain intensity assessment tools to determine the level of pain is the first step in pain management.[35] The assessed level of pain intensity guides the decision for pain medication. Nonpharmacologic interventions such as distraction (for example, with music, toys, or electronic devices, depending on the child's age) have also been shown to decrease anxiety and pain.[36]

Resources

Children's Tumor Foundation
www.ctf.org

Genetics Home Reference: Neurofibromatosis type 1
https://ghr.nlm.nih.gov/condition/neurofibromatosis-type-1

National Organization for Rare Diseases: Neurofibromatosis 1
https://rarediseases.org/rare-diseases/neurofibromatosis-type-1-nf1

Neurofibromatosis California
www.nfcalifornia.org

Neurofibromatosis Midwest
www.NFmidwest.org

head growth to monitor for hydrocephalus. Those with severe hypertension should be regularly assessed for renal artery stenosis and other complications.

As care for children with NF1 is provided in various settings, nurses are encouraged to seek out opportunities for interdisciplinary education to promote optimal patient care.[30]

Screening for speech and language deficits

Because children with NF1 are at risk for speech and language impairments, they should also undergo speech, language, and hearing screenings early in their development and receive a referral for a speech-language assessment as soon as possible following identification of speech or language deficits. Currently, research into the effectiveness of speech-language interventions for these children is sparse. However, a computer-based literacy training program demonstrated benefits with school-age patients in at least one recent study.[31] These results suggest promise for the utility of interventions in speech, language, and reading.

School nurses should work closely with classroom teachers to provide collaborative care so the child with NF1 can participate in the regular academic curriculum to the greatest extent possible. Recognition of family history and the home environment should always be considered as possible contributing factors of any outliers in a child's academic performance. Other environmental factors can also play a role in how well children with NF1 will progress.

Although many children with NF1 exhibit cognitive functioning that is below the normal range, others perform well academically as a direct result of the support they receive at home and from other resources. Nevertheless, nurses and caregivers should recognize that children may struggle in school as the demands of the educational curriculum increase from the elementary grades to high school. Continuous monitoring and reassessment of school performance is imperative for academic success.

Patient support

To ensure continuity of care, nurses can collaborate with other members of the multidisciplinary team and monitor referrals made to healthcare providers to ensure that patients, families, and caregivers receive what is requested. During routine clinic visits, nurses can administer questionnaires and quality-of-life measures to assess changes over time. Quality-of-life questionnaires have been developed specifically for people with NF1.[14,32]

A diagnosis of NF1 begins a patient's lifelong journey of interactions with members of the healthcare system. Through numerous medical appointments, patients and families of children with NF1 need to connect with others experiencing this disease process. An excellent and comprehensive resource is the Children's Tumor Foundation, which is a national nonprofit organization with a major emphasis on funding research and improving the care and support of patients with NF1 and their caregivers (see *Resources*). Regional organizations provide opportunities for patients with NF1 and their families to make connections with healthcare providers and find additional support in their communities. ■

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Janice Sampson is an associate professor in the School of Nursing, California State University in Sacramento, Calif. Also at California State University in Sacramento, Heather Thompson is an assistant professor in the Department of Communication Sciences and Disorders, and Denise Wall Parilo is a professor in the School of Nursing.

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