MANAGEMENT GUIDELINES FOR ADULTS WITH NEUROFIBROMATOSIS TYPE 2-RELATED SCHWANNOMATOSIS (NF2-SWN)

Tumour Foundation of BC

A GUIDE FOR PHYSICIANS

OVERALL RECOMMENDATION

Referral recommendations are indicated where appropriate

All adults with NF2-related schwannomatosis (formerly known as NF2) should undergo annual assessments by a physician, with increased frequency if complications arise. Managing NF2-SWN is complex and requires a multidisciplinary team approach. Key recommendations include close monitoring of neurological symptoms for changes or progression, regular MRI scans to track existing tumours and detect new ones, and diligent observation of any auditory or visual impairments. Chronic pain should be continuously assessed for effective symptom management, and monitoring for age-related complications is essential to address emerging challenges. Immediate investigation of all symptoms is crucial, as NF2-SWN affects the neurological system through schwannomas, meningiomas, and ependymomas, which can compress the brain, spine, or peripheral nerves.

Hallmark symptoms include hearing dysfunction, imbalance, tinnitus, headaches, pain, visual deficits and peripheral neuropathies. Vigilant monitoring is crucial due to the complexity of NF2-related schwannomatosis, which affects about 1 in 25,000 births and carries a risk of complications.

HEARING IMPAIRMENT

Otolaryngology (ENT) and Audiologist

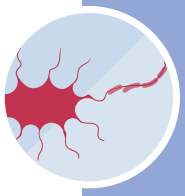
Hearing impairment is often the hallmark feature in NF2-SWN. Bilateral progressive hearing loss results from the development of vestibular schwannomas affecting the vestibulocochlear nerve. Symptoms may initially start with tinnitus or noticeable unilateral hearing impairment, as the tumours advance, progressive hearing loss occurs bilaterally.

Be alert and monitor for tinnitus, dizziness, impaired coordination, headache, pressure or fullness in the ear, pain, and numbness or weakness in the face involving the facial nerve.

A sudden sensorineural hearing loss is a red flag that signifies a medical emergency and needs to be assessed and treated promptly.

The patient will require regular hearing evaluations including BAER (brain stem auditory evoked response), and referrals and monitoring by an ENT and Audiologist. BAER Auditory evaluations can detect changes before hearing is impaired and before these may be visualized by an MRI (National Center for Biotechnology Information, n.d.). Additionally, Pure-tone audiometry (PTA) thresholds and speech discrimination scores (SDS) may be used in examining a patient's auditory function.

The patient may need an evaluation and assistance to access resources such as assistive technologies, hearing aids, an auditory brain implant or a cochlear implant.

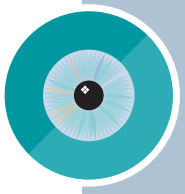


NEUROLOGICAL ISSUES

Neurologist, Neurosurgeon or Neurofibromatosis Clinic Specialists

Assess and monitor the patient for the onset of any new or worsening neurological symptoms or deficits. Meningiomas of the peripheral nervous system affect 80% of people with NF2-SWN over the course of their lifetime. Be alert for signs and symptoms such as new or worsening headaches, seizures, blurry vision, weakness, facial weakness or paralysis, numbness, pain, impaired hearing, tinnitus, balance issues, cognitive changes, or any other neurological deficits. Schwannomas along spinal nerves can lead to weakness, impaired sensation, impaired motor skills, and bowel or bladder dysfunction. In addition, peripheral neuropathy, drop foot, and muscle wasting can develop. Rarely, hydrocephalus can result from cerebrospinal fluid obstruction.

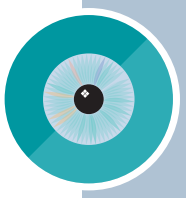
Recommended neurological evaluations include a yearly neurological examination and a yearly MRI of the central nervous system to be conducted until the fourth decade of life (National Center for Biotechnology Information, n.d.).



VISION IMPAIRMENT & EYE ISSUES

Ophthalmologist

Visual impairment arises in approximately one-third of individuals living with NF2-SWN, with the formation of cataracts or other eye disorders often causing vision problems. Eye problems may also occur due to schwannomas developing on the cranial nerves interfering with eye movements, difficulty with blinking, resulting in clouding, double vision, and loss of adequate sensation in the eye. The patient may also develop an epiretinal membrane or retinal



hematoma that can result in vision impairment. Oculoplastic surgery may be required given the importance of maintaining useful vision on a background of progressive hearing loss. Comprehensive eye care management is critical in this patient population.

The patient requires an annual complete ophthalmology examination and a referral to other specialists as needed.

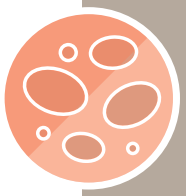
PAIN ISSUES

Pain clinic, Neurologist

Pain issues can arise in individuals with NF2-SWN, the severity varies depending on the growth of schwannomas, particularly the tumours affecting sensory functions. The patient can experience headaches, facial pain, nerve pain, back pain, radiating pain and secondary pain issues to joints and muscles.

Peripheral neuropathy may develop leading to symptoms of pins and needles, burning pain, and muscle weakness.

Unexplained pain requires prompt medical investigation to rule out or detect possible malignancy.



SKIN ISSUES

Dermatologist

Cutaneous fibromas and lesions such as café au lait spots are less common in patients with NF2-SWN than in patients with NF type 1. When present, patients need a dermatological evaluation to assess any changes or progression of the cutaneous lesions. When schwannomas occur in the skin, they appear as bumps under the skin or on the skin's surface.

MOBILITY ISSUES

Physiotherapist or Occupational Therapist, Neurologist

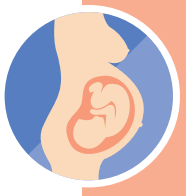
Mobility and balance are frequently encountered challenges requiring management in NF2-SWN. Vestibular schwannomas in NF2-SWN patients commonly result in hearing impairment and balance issues. It is crucial to assess and optimize the patient's mobility, gait, and musculoskeletal function. Addressing the root cause of mobility challenges, prioritizing patient safety and maximizing functional abilities is essential.

PSYCHOLOGICAL ISSUES

Psychologist, Psychiatrist, Counsellor, Tumour Foundation of BC

Living with a chronic genetic disorder such as NF2-SWN can lead to significant stress and anxiety. The daily health challenges and the uncertainty associated with a rare condition often contribute to feelings of depression and distress in patients. It is crucial to provide support through counseling and referrals to mental health services.

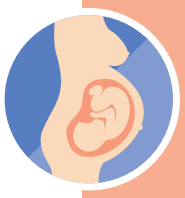
When assessing your patient, carefully consider emotional, mood, and psychological changes they may be experiencing. If needed, refer the patient to a psychiatrist or psychologist for further evaluation and support. Additionally, connecting them with the Tumour Foundation of BC can be beneficial. The organization can help the patient access a supportive community, educational resources on neurofibromatosis, participation in events, and opportunities to connect with others facing similar challenges with NF.



PREGNANCY AND GENETIC COUNSELLING

Geneticist, BC Provincial Medical Genetics Program, NF specialist

NF2-SWN is inherited in an autosomal dominant manner with approximately 50% of individuals having an affected parent. The severity of the condition varies and cannot always be accurately predicted in families. Referring your patient to genetic testing and counseling will allow the patient to explore the implications of and options for starting a family, and it will provide clarity on the patient's specific gene mutation. Although it is unclear whether schwannomas increase in size during pregnancy, hormonal fluctuations may affect



any existing meningiomas, and therefore the risk of possible intracranial pressure in pregnancy is an important issue to address.

Furthermore, genetic testing data is valuable information that could be used to determine eligibility for potential future novel treatments or clinical trials.

To explore the Provincial Medical Genetics Program and initiate a referral, visit: ***http://www.bcwomens.ca/our-services/medical-genetics***

TUMOURS

NF2 specialist, Neurosurgeon, ENT surgeon, Plastic surgeon, Orthopedic Surgeon, Oncologist

Patients with NF2-SWN are affected by various tumours of the nervous system. Examine the patient thoroughly for new or worsening tumours anywhere on and inside the body. Symptomology can alert you to order further investigations such as MRI imaging.

Types of tumours that may occur in NF2-SWN:

SCHWANNOMAS

Schwannomas are the most common type of tumours seen in individuals with NF2-SWN. These benign tumours develop from Schwann cells, which are responsible for producing the myelin sheath that covers nerves. The most common site for these growths in NF2-SWN is the vestibulocochlear nerve. They can also emerge along any nerve of the body, including the cranial nerves, peripheral nerves, and spinal nerves.

VESTIBULAR SCHWANNOMAS

Bilateral Vestibular schwannomas are the hallmark of NF2-SWN and are associated with significant challenges associated with hearing loss, tinnitus, balance issues, deafness, facial nerve weakness, and possible brainstem compression. These tumours involving the cochlear and vestibular nerves need ongoing monitoring with MRI imaging. Treatment and management are complex and require a multidisciplinary team approach, ideally led by an NF specialized team.

NON-VESTIBULAR SCHWANNOMAS

Non-Vestibular schwannomas can occur along the spinal nerves, cranial nerves, and the peripheral nerves. Please monitor your patient for symptoms of weakness, numbness, tingling and pain. MRI scans are necessary to track these tumours.

MENINGIOMAS

Meningiomas are prevalent in NF2-SWN, with around 80% of patients developing these tumours. While some individuals may be asymptomatic, many experience symptoms such as headaches, seizures, blurred vision, weakness, and numbness. Regular MRI scans are essential for monitoring and management.

EPENDYMOMAS

Ependymomas are benign tumours found within the spinal cord. About 20% of individuals with NF2-SWN are affected. While many patients may not show symptoms, others may experience pain, sensory disturbances, and weakness. MRI scans are crucial for monitoring the progression and severity of ependymomas.

MULTIDISCIPLINARY COLLABORATION AND EXISTING TREATMENT OPTIONS

Managing the care of patients with NF2-SWN requires a coordinated effort among specialists including neurologists, neurosurgeons, otolaryngologists, audiologists, ophthalmologists, oncologists, neuro-oncologists, geneticists and rehabilitation specialists such as physiotherapists. Neurofibromatosis clinics, when available, provide the most comprehensive specialized care for this condition.

Surgery plays a crucial role in addressing symptomatic tumours in NF2-SWN. Small, asymptomatic vestibular schwannomas are typically monitored with MRI, while larger, symptomatic ones often require surgical intervention to alleviate symptoms and prevent complications. Additionally, meningiomas are generally treated through surgery, while for spinal cord ependymomas, which are usually low-grade, surgery is considered only if symptoms emerge. Ongoing clinical monitoring remains important in guiding treatment decisions.

Radiation therapy can be used to manage and control the growth of some tumours associated with NF2-SWN, especially in cases where surgery is not an option. This therapy carries a risk of damage to surrounding tissues and the potential for malignant transformation. It is therefore imperative for the patient to be referred to specialists such as neurosurgeons, neuro-oncologists, ENT specialists and oncologists to explore the risks versus benefits, and to create an individualized treatment plan.

Cochlear implants, which are surgically inserted, bypass damaged parts of the cochlea and directly stimulate the auditory nerve, therefore providing a sense of sound and improved hearing. Patients with NF2-SWN that are most likely to benefit from these implants typically have had a vestibular schwannoma tumour resection but still have a functional cochlear nerve remaining (Children's Tumor Foundation). These devices can greatly improve the patient's quality of life in daily interactions, facilitating an improved ability to communicate. Coordination with oncologists

and neurotologists is crucial, in addition to evaluating the potential surgical risk for the patient.

Bevacizumab (Avastin), a monoclonal antibody targeting VEGF, has shown promise in some studies for reducing tumours, particularly vestibular tumours, and improving hearing in NF2 patients (Zhu, Y., and G. Bratslavsky, editors. Neurofibromatosis Type 2. NCBI Bookshelf, National Center for Biotechnology Information, 2019, ***https://www.ncbi.nlm.nih.gov/books/NBK470350/)***. An important consideration for clinicians exploring the use of Bevacizumab is its limited availability in Canada; therefore, its use as a treatment option is evaluated on a case-by-case basis.

Clinical trials are underway for NF2-SWN, with recent research investigating the potential of gene therapy and immunotherapies in its management. For information on new and ongoing clinical trials, please visit ***https://clinicaltrials.gov***

The complexity of NF2-SWN treatment and management necessitates a collaborative approach to ensure that patients receive optimal, holistic care and to improve their prognosis and disease management. The Tumour Foundation of BC remains dedicated to supporting patients, their families, and clinicians in navigating this challenging disorder.

FOR FURTHER INFORMATION:

TUMOUR FOUNDATION OF BC

tumourfoundation.ca
Info@tumourfoundation.ca
Toll Free: 1-800-385-2263

Charitable No. 13104 1352 RR 0001

Tumour Foundation of BC

REFERENCES

1 Children's Tumor Foundation. (2024). *Diagnosed with NF2* brochure. Retrieved June 24, 2024, from ***https://www.ctf.org/wp-content/uploads/2023/12/CTF-Diagnosed-with-NF2-Brochure-2024_v2.pdf***

2 Louis, D. N., Perry, A., Reifenberger, G., von Deimling, A., Figarella-Branger, D., Cavenee, W. K., ... & Ellison, D. W. (2016). The *2016 World Health Organization classification of tumors of the central nervous system: A summary*. Neuro-Oncology, 18(5), 624-642. ***https://doi.org/10.1093/neuonc/now250***

3 *Merck Manual Professional Version*. (n.d.). Vestibular schwannoma. In Inner ear disorders. Retrieved June 24, 2024, from ***https://www.merckmanuals.com/en-ca/professional/ear,-nose,-and-throat-disorders/inner-ear-disorders/vestibular-schwannoma***

4 National Center for Biotechnology Information. (n.d.). *Neurofibromatosis 2 (NF2)*. In Pagon, R. A., Adam, M. P., Ardinger, H. H., et al. (Eds.), GeneReviews® [Internet]. University of Washington, Seattle. Retrieved June 24, 2024, from ***https://www.ncbi.nlm.nih.gov/books/NBK1201/#nf2.Management***

5 National Institute of Neurological Disorders and Stroke. (n.d.). *Neurofibromatosis fact sheet*. Retrieved June 24, 2024, from ***https://www.ninds.nih.gov/health-information/disorders/neurofibromatosis#:~:text=Other%20symptoms%20of%20SWN%20a,or%20loss%20of%20muscle%20function***

6 NHS. (n.d.). *Neurofibromatosis type 2 (NF2) - Symptoms*. Retrieved June 24, 2024, from ***https://www.nhs.uk/conditions/neurofibromatosis-type-2/symptoms/#:~:text=Many%20people%20with%20NF2%20will,changes%20%E2%80%93%20particularly%20in%20your%20feet***

7 Tiwari, R., & Singh, A. K. (2022). *Neurofibromatosis type 2*. National Center for Biotechnology Information. ***https://www.ncbi.nlm.nih.gov/books/NBK470350/***

We are grateful to Nerve Tumours UK and NF2 BioSolutions for their editing assistance.