Neurofibromatosis

An ideal model for multidisciplinary care

Caitlin VanDeCappelle (Meds 2014)

Faculty Reviewer: Dr Sharan Goobie, MSc, MD, FRCPC (Department of Genetics)

ABSTRACT

Neurofibromatosis type 1 (NF1) is an inherited tumor predisposition syndrome with multiple manifestations in children and adults. Due to the multisystemic nature of this syndrome there are multidisciplinary NF1 clinics in many major centres in the United States; however, this is not yet the trend in Canada. Our study seeks to gain understanding of the current state of health surveillance in children with NF1 in Southwestern Ontario, which medical disciplines are involved in their care and parental interest in a future multidisciplinary clinic at London Health Sciences Centre (LHSC).

Methods: 50 parents or guardians of pediatric NF1 patients completed a 39-question telephone interview pertaining to diagnosis, aspects of yearly screening and willingness to attend a multidisciplinary clinic. Responses were then compared to the current screening guidelines for the pediatric NF1 population as suggested by the American Academy of Pediatrics.

Results: Only 56% of patients receive an annual neurological exam, while over 87% are having yearly blood pressure screens. 40% of patients cite their medical geneticist as the main coordinator of their care, while 12% cite no coordination of care. 48% of families travel more than 50 km to LHSC, with the majority visiting >3 times per year. 96% of participants are interested in participating in a multidisciplinary clinic.

Conclusions: The results obtained from this study support the development of a multidisciplinary NF1 clinic at LHSC.

INTRODUCTION

Neurofibromatosis 1 (NF1) is an autosomal dominant condition with a birth incidence of 1 in 2500 to 3300.¹ It affects all racial groups and genders equally, and can affect neurological, cognitive, social and physical development. The NF1 gene, located on chromosome 17q11.2, functions as a tumour suppressor gene. Clinical criteria exist for establishing a diagnosis of NF1, and therefore genetic testing is not often required.⁴ Mutations in the NF1 gene result in features such as neurofibromas, multiple café au lait spots (hyperpigmented macules), skinfold freckling, iris Lisch nodules and optic gliomas.² Neurofibromas are heterogenous benign peripheral nerve sheath tumours, which most often appear as discrete subcutaneous or cutaneous growths. Some individuals may only have mild skin lesions, whereas others may develop disfiguring tumours and life-threatening complications. Complications of NF1 can include optic gliomas, spinal nerve tumors, hypertension, scoliosis and oth-

er bone abnormalities. There is also a 5 to 10% increased risk for malignant peripheral nerve sheath tumors. Other serious complications can include brain tumors, seizures, rhabdomyosarcomas and pheochromocytomas.¹ Along with physical manifestations, NF1 is also associated with an increased prevalence of cognitive impairment. Prevalence of learning disabilities among children with NF1 has been estimated to range from 25 to 61%.³

The current mainstay of management for NF1 is age-specific monitoring of disease manifestation and patient education.⁴ Health surveillance guidelines proposed by the American Academy of Pediatrics suggest an annual physical exam including blood pressure monitoring, skin examination, screening for scoliosis and a full neurological assessment.⁵ An annual ophthalmologic exam in childhood (less frequently in older children and adults) is recommended to screen for optic glioma.⁵ Other studies and investigations, such as MRI imaging, are currently only recommended on the basis of clinical signs and symptoms, i.e. suspected intracranial or internal tumours.⁵

Care for NF1 patients typically involve various specialists and support services. Multidisciplinary NF clinics have been established in various locations within the United States to provide a setting in which a diagnosis and follow up of patients with NF1 can be coordinated. At the Neurofibromatosis Clinic of the Children's Hospital Medical Center in Cincinnati, Ohio, patients are referred for diagnosis, genetic counseling and various medical and surgical consultations. Patients are then followed annually where history is updated and full exam is completed, and family members at risk for NF also undergo full skin examination and slit-lamp examination of the irides. Current literature suggests that close collaboration such as this will facilitate a uniform approach to the diagnosis and management of NF1 and its complications.⁴

Our study seeks to gain more understanding of follow up management of our NF1 patient population at LHSC — which disciplines are involved, who is coordinating such care, the extent to which guidelines are being followed without such clinic involvement — and to define necessary services as identified by our patients in order to improve the current management and surveillance of our NF1 patients and their families.

METHODS

Parents of 122 children (under age 18) who were seen in the department of genetics at LHSC for a possible diagnosis of NF1 were invited to participate in a telephone questionnaire. To be included in this study, families must have a child under 18 years, a diagnosis (confirmed by genetic test or clinically) of NF1 and a previous visit

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with the department of genetics at LHSC. The questionnaire consisted of 39 questions related to their children’s features of NF1, the types of health care professionals involved in their care, aspects of their child’s yearly medical screening and their willingness to attend a multidisciplinary NF1 clinic. The study was approved by the research ethics board at UWO (REB#102904).

Questionnaire responses were then compared to the current screening guidelines for the pediatric NF1 population as suggested by the American Academy of Pediatrics. Proportions of patients whose NF1 medical screening met current guidelines were calculated. Trends in deficits of patient care were identified. Types of medical specialties involved in the NF1 patients’ care were assessed. This information was used to assess potential components of a multidisciplinary NF1 clinic. Overall interest in a multidisciplinary NF1 clinic was determined using the proportion of positive responses (compared to negative responses) to a yes/no question. Given the small patient sample, formal statistical analysis was not required.

RESULTS

Of 122 families sent a letter of participation, 52 families were successfully contacted for a telephone interview. Two families from this group did not meet survey requirements as they did not have confirmed diagnoses of NF1. Mean age for diagnosis was 4 years (range 2 months to 13 years), where mean current age was 11 (range 1-17 years). Table 1 shows the distribution of features of participants in the study. These percentages are fairly consistent with the general trends in the NF1 literature.

Table 1: Reported Clinical Characteristics of Children With NF1 in Study Group

FEATURE	NUMBER (%) (n = 50)
6 or more café au lait spots	49 (100%)
Inguinal/axillary freckling	46 (92%)
Learning delay	25 (50%)
Parent/sibling/child with NF1	20 (40%)
2 or more cutaneous neurofibromas	17 (34%)
Macrocephaly	17 (34%)
ADHD	14 (28%)
2 or more Lisch nodules	14 (28%)
Optic gliomas	10 (20%)
Brain tumour	7 (14%)
Scoliosis	6 (12%)
Bone deformity (other than scoliosis)	5 (10%)
Seizures	4 (8%)
Early puberty	4 (8%)
Autism	3 (6%)
Plexiform neurofibroma	2 (4%)
High blood pressure	2 (4%)
Other tumour	2 (4%)
Late puberty	1 (2%)

Table 2 shows that 40% of study participants believe their medical geneticist to be the main coordinator of their care, while 24% listed their pediatrician and 6% their family doctor. 12% of respondents felt that no healthcare professional was their main coordinator.

Table 2: Healthcare Professional Acting as Main Coordinator of Care

HEALTHCARE PROFESSIONAL	NUMBER (%) (n = 50)
Medical Geneticist	20 (40%)
Pediatrician	12 (24%)
None	6 (12%)
Family doctor	3 (6%)
Dermatologist	2 (4%)
Neurosurgeon	2 (4%)
Neurologist	1 (2%)
Oncologist	1 (2%)
Other	3 (6%) Mother, Plastic surgeon

Table 3 shows the percentage of participants adhering to the recommendations of a yearly skin, eye, neurological and blood pressure exam. Only 56% of participants are receiving a yearly neurological exam, while over 87% of participants are getting their blood pressure check each year. Note that 2 participants were not included as their current guardians were unaware of their most recent screenings.

Table 3: Reported Adherence to Annual Examinations

EXAM	NUMBER (%) (n = 48)
BP check	42 (87.5%)
Eye exam	41 (85.4%)
Skin exam	31 (64.6%)
Neurological exam	27 (56.3%)

Table 4 shows the number of visits to LHSC made per year for NF1-related reasons. The majority of respondents make the trip 3 to 4 times each year for NF1-related appointments. Notably, 48% of study participants travel further than 50 km to the LHSC Children’s Hospital for each visit.

Table 4: Reported Number of Visits to LHSC per Year

NUMBER OF VISITS	NUMBER (%) (n = 50)
0	1 (2%)
1-2	9 (18%)
3-4	28 (56%)
5-10	9 (18%)
> 10	3 (6%)

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DISCUSSION

The American Academy of Pediatrics recommends that pediatric patients with NF1 receive blood pressure monitoring and neurological, eye and skin examinations annually.⁷ As per our results, between 22 and 44% of our NF1 pediatric population are not meeting all of the surveillance recommendations. Particular deficits appear to be with the neurological and skin examinations, which are also the examinations that take more time during an office visit. This may be due to lack of clear physician roles, time constraints and lack of physician awareness of guidelines.

While medical geneticists and pediatricians were frequently named as the primary coordinators for our patients, this may be a recruitment bias as the list of participants was generated from those referred to medical genetics for a possible diagnosis of NF. Many other health care professionals were also listed as having a role in the care of these patients (Table 2). Based on these results and the comments from parents during the interviews, we propose that a multidisciplinary NF1 clinic should involve a medical geneticist, pediatrician, oncologist, neurologist, ophthalmologist, neurosurgeon, developmental pediatrician and social worker.

Of the families surveyed, 96% were interested in attending a multidisciplinary NF clinic. Benefits reported by families included convenience, less time away from school or work, social connection to others with NF and improved communication between specialists. As approximately half of our patients live more than 50 km away from LHSC, many families felt that a one-stop visit to see all the healthcare professionals involved in their child's care would be beneficial. Furthermore, this may ensure that guidelines are more frequently met, as patients would receive all screenings at one visit.

This study supports the development of a multidisciplinary NF1 clinic at LHSC and a clinic proposal has been developed. This clinic has the potential to improve the medical management of children with NF1, decrease the travel burden on parents who may need to come to London for multiple different specialist appointments related to their child's diagnosis and provide the opportunity for education and research related to this condition.

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