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The prevalence of anisometropia aniso-astigmatism and amblyopia in neurofibromatosis type 1

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PURPOSE. *The purpose of this study was to document the prevalence of anisometropia, aniso-astigmatism, and anisometropic amblyopia in patients with neurofibromatosis-1 (NF1) and to compare it with that in age- and sex-matched controls.*

METHODS. *Fifty patients with NF1 and 150 age- and sex-matched controls were examined in this study. Cycloplegic autorefraction was attempted on all patients <16 years old and without cycloplegia on patients >16 years old. Anisometropia was defined as absolute interocular difference of spherical equivalent more than or equal to 1 D. Aniso-astigmatism was defined as interocular difference of refractive astigmatism of more than or equal to 1 D. Amblyopia was defined as two-line decrease in Snellen acuity between the two eyes.*

RESULTS. *The overall prevalence of anisometropia, aniso-astigmatism, and amblyopia in patients with NF1 was 16%, 20%, and 10%, respectively, and they were all significantly higher than in the controls. The amblyopia was either moderate or severe in nature and all affected patients had significant astigmatism (>2.5 D) in the amblyopic eye.*

CONCLUSIONS. *NF1 is a risk factor for anisometropia, aniso-astigmatism, and aniso-astigmatic amblyopia and screening patients with NF1 for refractive errors before age 3 will help to detect patients at risk of amblyopia and give them proper treatment. (Eur J Ophthalmol 2009; 19: 470-4)*

KEY WORDS. *Neurofibromatosis type 1, Anisometropia, Aniso-astigmatism, Amblyopia*

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INTRODUCTION

Neurofibromatosis type 1 (NF1), first described by von Recklinghausen, is one of the most common inherited disorders, occurring in about 1 in 3000 births (1). NF1 is now defined as a neurocristopathy, a disorder involving aberrant proliferation of multiple tissues derived from neural-crest cells (2).

The ocular manifestations of NF1 include iris Lisch nodules, glaucoma, optic nerve gliomas, eyelid neurofibromas, and prominent cranial nerves (3). Amblyopia due to underlying organic ocular pathologies such as optic nerve gliomas or retinal vascular occlusive disease was previously described in patients with NF1 (4, 5).

The purpose of this study was to document the prevalence of anisometropia, aniso-astigmatism, and amblyopia secondary to refractive errors in patients with NF1 and to compare with that in age- and sex-matched controls.

METHODS

Fifty patients with NF1 without any ocular or orbital pathologies other than Lisch nodules were included in the study (two patients with optic nerve glioma and one patient with eyelid neurofibroma were excluded). History of prematurity was also an exclusion criterion. Informed con-

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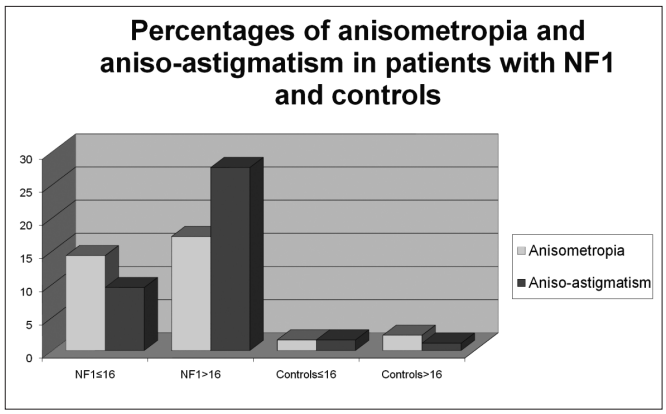

Fig. 1 - *Percentages of anisometropia and aniso-astigmatism in patients with NF1 and controls. NF1 ≤16 = patients with neurofibromatosis type 1 younger than or equal to 16 years of age; NF1 >16 = patients with neurofibromatosis type 1 older than 16 years of age; Controls ≤16 = controls younger than or equal to 16 years of age; Controls >16 = controls older than 16 years of age.*

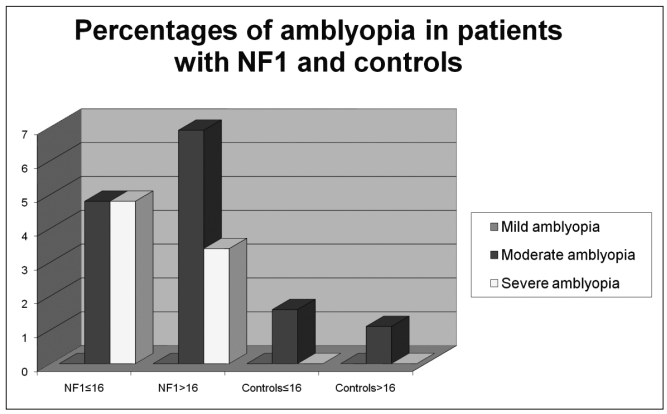

Fig. 2 - *Percentages of amblyopia in patients with NF1 and controls. NF1 ≤16 = patients with neurofibromatosis type 1 younger than or equal to 16 years of age; NF1 >16 = patients with neurofibromatosis type 1 older than 16 years of age; Controls ≤16 = controls younger than or equal to 16 years of age; Controls >16 = controls older than 16 years of age.*

sent was obtained from all the patients and the study was approved by the Göztepe Training and Research Hospital ethics committee. Visual acuity was tested by Snellen chart at 6 meters. Patients ≤16 years old and patients below 30 years of age with manifest hypermetropia were assigned to cycloplegic autorefraction (with cyclopentolate) and patients >16 years old were assigned to autorefraction without cycloplegia (VISION 2020 E-Resource, for eye care management worldwide). Slit-lamp biomicroscopy and dilated fundus examinations were also performed. A total of 150 age- and sex-matched controls were obtained by screening primary and high school students and also randomly selected healthy subjects living in the district.

Anisometropia was defined as absolute interocular difference of spherical equivalent (SE, sphere +1/2 cylinder) more than or equal to 1 D (6). Aniso-astigmatism was defined as interocular difference of refractive astigmatism of more than or equal to 1 D (7). Amblyopia was defined as two-line decrease in acuity between the two eyes (mild amblyopia). Four- to five-line decrease in acuity was considered moderate amblyopia and a decrease of six lines or more was considered severe amblyopia (8). Myopia was defined as an SE refraction of at least 0.50 D, hyperopia as an SE refraction of at least 2 D in pediatric patients and 1 D in adults, and astigmatism as a cylinder of at least 1 D.

Chi-square and Fisher exact chi-square tests were used for the statistical analyses. $p<0.05$ Was considered significant.

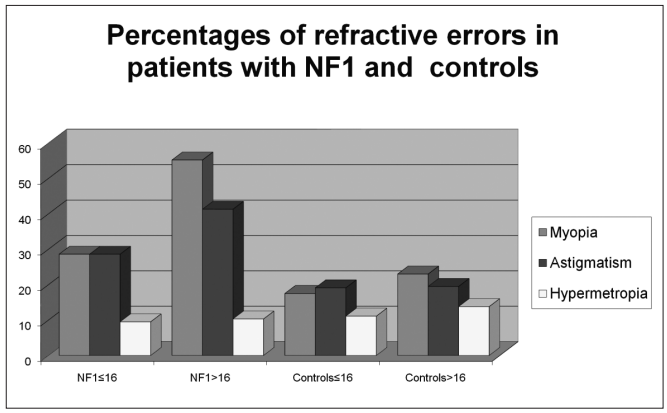

Fig. 3 - *Percentages of refractive errors in patients with NF1 and controls. NF1 ≤16 = patients with neurofibromatosis type 1 younger than or equal to 16 years of age; NF1 >16 = patients with neurofibromatosis type 1 older than 16 years of age; Controls ≤16 = controls younger than or equal to 16 years of age; Controls >16 = controls older than 16 years of age.*

RESULTS

There were 21 patients ≤ 16 years of age with a mean age of 11.71±3.38 and 29 patients >16 years with a mean age of 30.07±10.52. The male/female ratio was 8/13 in patients ≤ 16 and 10/19 in patients >16. The control group with subjects ≤ 16 (n=63) had a mean age of 11.67±3.14 and a male to female ratio of 24/39, whereas the controls >16 (n=87) had a mean age of 30.14 ±10.42 and a male to female ratio of 30/57. There were no statistically significant differences

between the patients with NF1 and the controls with regard to age and male to female ratios (p>0.05).

The prevalence of anisometropia was 14.3% in patients with NF1 ≤ 16, 17.2% in patients with NF1 >16, and 16% overall (all significantly higher than in the controls, p=0.047, p=0.006, and p=0.0001, respectively, Tab. I and Fig. 1). The prevalence of aniso-astigmatism was 9.5% in patients with NF1 ≤ 16, which was not significantly higher than in the controls (p=0.153), 27.6% in patients with NF1 >16, and 20% overall, which were both significantly higher than in the controls (p=0.0001 both).

The prevalence of amblyopia was 9.5% in patients with NF1 ≤ 16 (one moderate, one severe amblyopia) and 1.6% in controls (p=0.153) (Tab. I and Fig. 2). The prevalence of amblyopia was 10.3% in patients with NF1 >16 (two moderate and one severe) and it was significantly higher than controls (p=0.048). The overall prevalence of amblyopia in the patients with NF1 was 10% and it was also significantly higher than in the controls (p=0.004). All of the amblyopic patients with NF1 also had significant aniso-astigmatism (>2.5 D).

Data about the prevalence of astigmatism, myopia, and hypermetropia in the patients with NF1 and controls is summarized in Table II and Figure 3. The prevalence of myopia and astigmatism was significantly higher than in the controls in both patients with NF1 >16 and overall (p=0.001), and there was no difference between the prevalence of hypermetropia in both NF1 groups and the controls. Although myopia and astigmatism were more frequent in the patients with NF1 >16 compared to NF1 ≤ 16 patients, there was no significant difference in the prevalence of myopia, astigmatism, and hypermetropia between the two NF1 groups.

DISCUSSION

This study documented that anisometropia, aniso-astigmatism, and aniso-astigmatic amblyopia were more common in patients with NF1 than in controls. The amblyopia was either moderate or severe in nature and all affected patients had significant astigmatism (>2.5 D) in the amblyopic eye.

TABLE I - PERCENTAGES OF ANISOMETROPIA, ANISO-ASTIGMATISM, AND AMBLYOPIA IN PATIENTS WITH NF1 AND IN CONTROLS

	NF1 ≤16 (n=21)	NF1 >16 (n=29)	Overall NF1 (n=50)	Controls ≤16 (n=63)	Controls >16 (n=87)	Overall controls (n=150)
Anisometropia	3 (14.3)	5 (17.2)	8 (16)	1 (1.6)	2 (2.3)	3 (2)
Aniso-astigmatism	2 (9.5)	8 (27.6)	10 (20)	1 (1.6)	1 (1.1)	2 (1.3)
Amblyopia	2 (9.5)	3 (10.3)	5 (10)	1 (1.6)	1 (1.1)	2 (1.3)
Mild amblyopia	0	0	0	0	0	0
Moderate amblyopia	1 (4.8)	2 (6.9)	3 (6)	1 (1.6)	1 (1.1)	2 (1.3)
Severe amblyopia	1 (4.8)	1 (3.4)	2 (4)	0	0	0

Values are n (%).
NF1 ≤16 = patients with neurofibromatosis type 1 younger than or equal to 16 years of age; NF1 >16 = patients with neurofibromatosis type 1 older than 16 years of age; Controls ≤16 = controls younger than or equal to 16 years of age; Controls >16 = controls older than 16 years of age.

TABLE II - PERCENTAGES OF REFRACTIVE ERRORS IN PATIENTS WITH NF1 AND CONTROLS

Refractive errors	NF1 ≤16 (n=21)	NF1 >16 (n=29)	Overall NF1 (n=50)	Controls ≤16 (n=63)	Controls >16 (n=87)	Overall controls (n=150)
Myopia	6 (28.6)	16 (55.2)	22 (44)	11 (17.5)	20 (23.0)	31 (20.7)
Astigmatism	6 (28.6)	12 (41.3)	18 (36)	12 (19.1)	17 (19.5)	29 (19.3)
Hypermetropia	2 (9.5)	3 (10.3)	5 (10)	7 (11.1)	12 (13.8)	19 (12.7)

Values are n (%).
NF1 ≤16 = patients with neurofibromatosis type 1 younger than or equal to 16 years of age; NF1 >16 = patients with neurofibromatosis type 1 older than 16 years of age; Controls ≤16 = controls younger than or equal to 16 years of age; Controls >16 = controls older than 16 years of age.

The prevalence of anisometropia and aniso-astigmatism in Australian 6-year-old children was found to be 1.6% and 1%, respectively (7).The prevalence of anisometropic amblyopia varies in different populations: 0.38% in preschool children in America, 0.37% in 18- to 19-year-old men in Singapore, and 1.3% in Australian adults (8-10). Our study showed an overall anisometropic amblyopia in the same order of magnitude (1.3%) in the control group.

Anisometropic amblyopes present at a later age than do children with other types of amblyopia. Only 15% of anisometropic amblyopia was identified before the age of 5 during a 4-year study in Leicestershire (11). The presence of significant astigmatism in the amblyopic eye is a risk for treatment failure of anisometropic amblyopia (12). Optical correction of astigmatism should be provided prior to age 3 to 5 years, to prevent development of amblyopia (13).

Donahue found that amblyopia was rare in anisometropic children before 2 years (14%) but its incidence rose rapidly thereafter and by age 3 65% of children with anisometropia had developed amblyopia. The prevalence of amblyopia increased only slightly after this. The use of screening technology that identifies children with anisometropic refractive error before age 4 and allows for early treatment should reduce the proportion and depth of amblyopia (8).

Overall astigmatism and myopia prevalence were also higher in patients with NF1 when compared to controls. In a study evaluating the frequency of refractive errors in patients with NF1 with a mean age of 8.4 years (range 4 to 12), the prevalence of myopia was estimated as 23.1%, which was significantly more common than in controls (14). Astigmatism in this study was estimated as 19.5% and was the same in the controls. The higher prevalence of myopia and astigmatism (both 28.6% in patients with NF1 ≤16 and 55.2% and 41.3%, respectively, in patients with NF1 >16) in our study were probably due to the higher age of our study groups since both myopia and astigmatism tend to increase with age (15, 16).

A high prevalence of anisometropia and aniso-astigmatism has previously been associated with high maternal age, prematurity, and coronal synostosis (7, 17, 18). This study demonstrated that NF1 is also a risk factor for anisometropia, aniso-astigmatism, and aniso-astigmatic amblyopia and screening patients with NF1 for refractive errors before the age of 3 will help to detect patients at risk of amblyopia and give them proper treatment.

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