ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

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Ocular Findings in Spina Bifida

Spina Bifida'da Oküler Bulgular

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ABSTRACT Objective: To investigate the various ocular findings associated with spina bifida. **Material and Methods:** This study is a retrospective study which included 122 patients (56 female patients and 66 male patients) with spina bifida who were referred to Ophthalmology Department for ophthalmologic evaluation between 2015 and 2017. All patients had shunt replacement surgery by Neurosurgery Department before the ophthalmic examinations. **Results:** Results of the Hirschberg and cover tests showed that 49 (40.5%) patients had strabismus and 72 (59.5%) patients did not have strabismus. The mean spherical equivalent refraction was +1±2.01 D in the right eyes and+1.12±1.97 D in the left eyes. The mean astigmatism was-1.04±0.92 D in the right eyes and-1.08±0.95 D in the left eyes. Hypermetropia was common (80%) among the patients with esotropia in the left eye, myopia was common (75%) among the patients with exotropia in the left eye. There was a statistically significant relationship between the spherical equivalent refraction of the left eye and strabismus type (X^2=5.695; p=0.045). Funduscopic examination detected unilateral optic atrophy in three (2.5%) patients, bilateral optic atrophy in six (4.9%) patients, and bilateral papilledema in three (2.5%) patients. Strabismus was more common in patients with fundus abnormalities (n=8, 66.7%). **Conclusions:** Ocular findings such as strabismus and refractory error are very common in patients with spina bifida. Therefore, these patients should be followed up closely after birth for abnormal ocular findings by a team of ophthalmologists and neurosurgeons.

Keywords: Spina bifida; neural tube defect; strabismus; refractive error

ÖZET Amaç: Spina bifidalı hastalarda görülen çeşitli oftalmik bulguların sıklığını değerlendirmek **Gereç ve Yöntemler:** Bu çalışma 2015-2017 yılları arasında oftalmolojik muayene amaçlı Oftalmoloji Departmanı'na refere edilmiş 122 hastayı (56 kadın, 66 erkek) içeren retrospektif bir çalışmadır. Tüm hastalar oftalmolojik muayene öncesi Beyin ve Sinir Cerrahisi Departmanı tarafından şant replasmanı uygulanmış hastalardır. **Bulgular:** Hirschberg ve kapama testinde 49 (40.5%) hastada kayma saptanmış, 72 (%59,5) hastada kayma saptanmamıştır. Ortalama sferik ekivalan sağ gözlerde +1±2,01 D, sol gözlerde+1,12±1,97 D olarak saptanmıştır. Ortalama astigmatizma sağ gözlerde -1,04±0,92 D, sol gözlerde -1,08±0,95 D olarak bulunmuştur. Sol gözlerde ezotropyası olan hastalarda hipermetropi (%80) oranı yüksekti, ekzotropyası olan hastalarda ise miyopi (%75) oranı yüksekti. Sol gözlerde sferik ekivalan refraksiyonu ve kayma tipi arasındaki ilişki istatistiksel olarak anlamlıydı (X^2=5,695; p=0,045). Fundus incelemesinde 3 hastada (%2,5) tek taraflı optik atrofi, 6 (%4,9) hastada çift taraflı optik atrofi, 3 (%2,5) hastada çift taraflı papilödem saptanmıştır. Anormal fundus bulgusu olan hastalarda olmayanlara göre kayma daha sıktı (n=8, %66,7). **Sonuç:** Kayma, refraktif bozukluklar gibi göz bulguları spina bifidalı hastalarda oldukça sık görülmektedir. Bu hastalar anormal göz bulguları açısından doğumdan itibaren oftalmologlar ile beyin ve sinir cerrahlarından oluşan bir ekip tarafından yakından takip edilmelidir.

Anahtar Kelimeler: Spina bifida; nöral tüp defekti; şaşılık; refraksiyon kusuru

Spina bifida is a congenital disorder caused by the incomplete fusion of the embryonic neural tube during spinal cord development. This central nervous system anomaly is associated with considerable morbidity and mortality.[1,2] Spina bifida is the most common congenital defect

affecting the central nervous system and the most complex congenital defect compatible with life.[3] The incidence of spina bifida varies among countries and geographic regions, with the mean incidence being 4.7 per 10,000 live births worldwide.[4] Babies with spina bifida may develop various ophthalmic findings such as primary optic atrophy; papilledema with secondary optic atrophy; extraocular muscle palsies; and damage in the optic nerve, optic pathways, and visual cortex.[5]

The present study determined the frequency of various ophthalmic complications in patients with spina bifida and highlighted the need to follow-up these patients after birth by a team of neurosurgeons and ophthalmologists to improve the quality of life of them.

MATERIAL AND METHODS

Ethics committee approval was obtained from İstanbul Bilim University Clinical Researchs Ethics Committee (ethics committee approval number: 44140529/ 2018-2475) prior to the study and the study was conducted according to the tenets of the Declaration of Helsinki. This study included 122 patients (56 female patients and 66 male patients) with spina bifida who were referred to Ophthalmology Department for ophthalmologic evaluation between 2015 and 2017. All patients were performed shunt replacement surgery by Neurosurgery Department before the ophthalmic examinations. The examination findings of the patients were obtained by retrospectively examining the files.

Strabismus and ocular motility were evaluated using cover-uncover, prism cover, and Hirschberg tests. The degree of strabismus was determined by evaluating corneal light reflex by using a penlight (Hirschberg method) or by performing the prism cover test, if possible. If present, inferior oblique overaction (IOOA) was graded on levoversion (for the left IO) and on dextroversion (for the right IO) on a scale from "0" to "+4." The lens, vitreous, and fundus were evaluated by performing ocular examination by using an indirect ophthalmoscope, if possible with biomicroscopy. If examination could not be performed by indirect ophthalmoscopy or biomicroscopy we examined the patient in the operating room under general anesthesia. During examination nystagmus was noted if present. The direction of nystagmus was defined by the direction of its quick phase. Moreover, the presence or absence of papilledema and optic atrophy was recorded during funduscopic examination.

Cycloplegic refraction was performed by using a pediatric autorefractometer (spot vision screener; Welch Allyn, USA) in patients younger than 3 years and by using an autorefractometer (KR-8900; Topcon, the Netherlands) in patients older than 3 years. Patients who could not be evaluated using these methods were examined by performing skiascopy. Cycloplegia was induced using two drops of topical cyclopentolate (0.5% concentration for children younger than 1 year and 1% concentration for children older than 1 year), which were administered at a 5-minute interval.

Autorefraction measurements of sphere and cylinder were converted into spherical equivalent refraction (SER), where SER = Sphere+(Cylinder/2). For children younger than 2 years, significant refractive error was defined as a spherical equivalent of-5.00 diopters (D) or more for myopia, +4.00 D or more for hyperopia, and 1.0 D or more for astigmatism. For children aged between 2 and 4 years, significant refractive error was defined as a spherical equivalent of-3.00 D or more for myopia,+2.00 D or more for hyperopia, and 1.0 D or more for astigmatism. For children aged between 5 and 18 years, significant refractive error was defined as a spherical equivalent of -0.75 D or more for myopia, +2.00 D or more for hyperopia, and 1.0 D or more for astigmatism.[6,7]

STATISTICAL ANALYSIS

All statistical analyses were performed using SPSS statistical software (SPSS for Windows, version 24.0; SPSS, Inc., Chicago, IL, USA). Data were analyzed using descriptive statistical methods (frequencies, percentages, means, and standard deviations). Qualitative data were compared using Pearson chi-square and Fisher exact tests. Independent samples *t*-test was used to compare quan-

titative variables between groups. All analyses were performed with a 95% confidence interval, and $p < 0.05$ was considered statistically significant.

RESULTS

The mean age of the patients was 63±59.9 months (range, 2-319 months). Of the 122 patients included in the study, 66 (54.1%) were male and 56 (45.9%) were female.

There was significant refractive error in 70 (%66) of 106 patients. Results of the Hirschberg and cover tests showed that 49 (40.5%) patients had strabismus and 72 (59.5%) patients did not have strabismus. Of the patients with strabismus, 42 (85.7%) had esotropia, 6 (12.2%) had exotropia. 6 patients had esotropia in their right eyes, 9 patients had esotropia in their left eyes and 27 patients had alternan esotropia. Four patients had alternan exotropia, 1 patient had exotropya in his right eye and 1 patient had exotropya in his left eye. All patients had constant exotropia. One (2%) patient had hypertropia because of the fourth cranial nerve palsy. When the patients were examined for ocular motility, 1 patient was detected to have restriction in abduction in his left eye and 1 patient had restriction in abduction in both eyes due to sixth cranial nerve palsy. Moreover, 1 (0.8%) patient had grade 1+ IOOA in her left eye. The degree of tropia was 0-15 degrees in 37 (78.7%) patients, 15-30 degrees in 9 (19.1%) patients, and 30-45 degrees in 1 (2.1%) patient. Moreover, nine (7.4%) patients had nystagmus, and five (4.1%) patients had nystagmus along with strabismus (Table 1).

TABLE 1: All patients had horizontal nystagmus General distribution of patients.

		n	%
Gender	Female	56	45.9
	Male	66	54.1
	Total	122	100
Significant refractive error	Yes	70	66.0
	No	36	34.0
	Total	106	100
Strabismus	Yes	49	40.5
	No	72	59.5
	Total	121	100
Strabismus type	Esotropia	42	85.7
	Exotropia	6	12.2
	Hypertropia	1	2.0
	Total	49	100
Inferior oblique overaction	Yes	1	0.8
	No	121	99.2
	Total	122	100
Degree of strabismus	0-15 degrees	37	78.7
	15-30 degrees	9	19.1
	30-45 degrees	1	2.1
	Total	47	100
Fundus abnormalities	Unilateraloptic atrophy	3	2.5
	Bilateral optic atrophy	6	4.9
	Bilateral papilledema	3	2.5
	None	110	90.2
	Total	122	100
Nystagmus	Yes	9	7.4
	No	113	92.6
	Total	122	100

The mean SER was+1±2.01 D in the right eyes and+1.12±1.97 D in the left eyes. The mean astigmatism was -1.04±0.92 D in the right eyes and -1.08±0.95 D in the left eyes. In all, 70 (66%) patients showed no significant refractive error. According to the SER of the right eyes, 76 (62.3%) patients had hypermetropia and 30 (24.6%) patients had myopia. According to the SER of the left eyes, 83 (68%) patients had hypermetropia and 20 (18%) patients had myopia. Spherical equivalent refraction of 0-2 years patients was +1.68±1.83 D in the right eyes and+2.0±1.41 D in the left eyes. Astigmatism value of 0-2 years patients was -1.14±0.98 D in the right eyes and -1.0±1.41 D in the left eyes. Spherical equivalent refraction of 2-4 years patients were+1.25±0.35 D in the right eyes and +1.25±0.35 D in the left eyes. Astigmatism value of 2-4 years patients was -2.125±0.53 D in the right eyes and -1.25±1.41 D in the left eyes. Spherical equivalent refraction of ≥5 years patients were +4.87±2.29 D in the right eyes and +3.75±1.06 D in the left eyes. Astigmatism value of ≥5 years patients was -2.75±2.12 D in the right eyes and -2.25±0.88 D in the left eyes (Table 2).

Funduscopic examination detected unilateral optic atrophy in three (2.5%) patients, bilateral optic atrophy in six (4.9%) patients, and bilateral papilledema in three (2.5%) patients (Table 1). Strabismus was more common in patients with fundus abnormalities (n=8, 66.7%) according to the patients

TABLE 2: Refractive errors according to age groups.

	SER (right eyes)	Astigmatism (right eyes)	SER (left eyes)	Astigmatism (left eyes)
0-2 years (n=31)	+1.68 ±1.83 D	-1.14 ± 0.98 D	+2.0 ± 1.41 D	-1.0 ± 1.41 D
2-4 years (n=37)	+ 1.25 ± 0.35 D	-2.125 ± 0.53 D	+1.25 ± 0.35 D	-1.25 ± 1.41 D
≥5 years (n=54)	+4.87 ± 2.29 D	-2.75 ± 2.12 D	+3.75 ± 1.06 D	-2.25 ± 0.88 D

with no fundus abnormality. However, the relationship between fundus abnormalities and strabismus was not statistically significant (X^2= 3.786; p= 0.052). Among the patients with fundus abnormalities, five (11.9%) had esotropia, two (33.3%) had exotropia, and one had hypertropia. Because only one patient had hypertropia, this patient was excluded from the analysis for evaluating the relationship between strabismus type and fundoscopic abnormalities. Esotropia was more common in patients with fundus abnormalities (71.4%); however, this result was not statistically significant (X^2= 1.935; p= 0.206). Among the patients with fundus abnormalities, 1 (8.3%) had nystagmus and 11 (91.7%) did not have nystagmus. Moreover, no significant relationship was observed between nystagmus and fundus abnormalities (X^2= 0.018; p= 0.619)

Among the patients with esotropia in the right eye, 8 (21.6%) were myopic and 29 (78.4%) were hypermetropic. Among the patients with exotropia in the right eye, three (75%) were myopic and one (25%) was hypermetropic. No statistically significant relationship was observed between the spherical equivalent refraction of the right eye and strabismus type (X^2 =5.239; p=0.052). However, hypermetropia was common (78.4%) in patients with esotropia and myopia was common (75%) in patients with exotropia. In contrast, among the patients with esotropia in the left eye, 7 (20%) were myopic and 28 (80%) were hypermetropic. Among the patients with exotropia in the left eye, three (75%) were myopic and one (25%) was hypermetropic. Moreover, a statistically significant relationship was observed between the spherical equivalent refraction of the left eye and strabismus type (X^2=5.695; p=0.045). In addition, hypermetropia was common (80%) among the patients with esotropia in the left eye and myopia was common (75%) among the patients with exotropia in the left eye. 92.30% of the patients in the 0-2 years were esotropia and 7.69% were exotropia. 78.94% of the patients in the 2-4 years were esotropia and 15.78% were exotropia. 88.23% of the patients in the ≥5 years years were esotropia and 11.76% were exotropia (Table 3).

TABLE 3: Strabismus types according to age groups.

	Esotropia (%)	Exotropia (%)
0-2 years (n=13)	92.30	7.69
2-4 years (n=19)	78.94	15.78
≥5 years (n=17)	88.23	11.76

DISCUSSION

Because spina bifida is the most common complex congenital defect compatible with life, early diagnosis and treatment of complications related to this disorder are of utmost importance.[3] Spina bifida may be accompanied by various ophthalmologic abnormalities. Therefore, ophthalmologists and neurosurgeons should work together to manage ophthalmologic abnormalities that may arise in patients with spina bifida.[5]

Strabismus is frequently observed in patients with spina bifida, with esotropia (convergent strabismus) being the most common strabismus type.[5] Previous studies have attributed the high prevalence of esotropia in patients with spina bifida to abducens nerve palsy caused by the recurrent episodes of elevated intracranial pressure and hydrocephalus.[8,9]

Pinello et al. found that 44% (26/59) patients with spina bifida were squint, with convergent squint being the most common type (80%).[10] Anderson et al. detected strabismus in 42 out of 112 (39%) patients with spina bifida. Moreover, most of these patients had esotropia (n=26) and few of

these patients (n=14) had exotropia.[11] Similarly, another study reported that 73% patients with strabismus had esotropia.[12] When compared healthy children and children with spina bifida; in a study by Ünsal et al. in 76 healthy children over 4 years of age, esotropia was found in 2.6% and exotropia in 1.3%.[13] Cumurcu et al. found that with cerebral palsy (CP) cases in our country; strabismus was detected in 15 (32.6%) of the children with CP and in 9 of the children in the control of the group (18%).[14] In the present study, 40.5% (n=49) patients had strabismus, of which 85.7% (n=42) had esotropia, which is consistent with the literature.

Anderson et al. detected nystagmus in 26% (n=29) of the patients, of which 23 also had strabismus.[11] Cumurcu et al. reported nystagmus in 10 (21.7%) children with CP and 3 (6%) of the control group.[14] In the present study, nine (7.4%) patients had nystagmus and five (4.1%) patients had nystagmus along with strabismus. The small number of the patients with nystagmus in the present study may be due to including all patients with spina bifida irrespective of its type, i.e., spina bifida occulta and spina bifida aperta.

Saunders et al. reported a study which includes 59 preterm infants. They found an association between the infants with abnormal cranial ultrasound in the neonatal period and early hyperopia.[15] Ozturk et al. found hyperopia in 70% of their patients with neurological diseases.[16] Likewise, Cumurcu et al. found a high rate of hypermetropia in patients with CP.[14] Hypermetropia was common among the patients included in the present study (hypermetropia of the right eye in 62.3% patients and of the left eye in 68% patients), which is consistent with the studies of Saunders et al. and Ozturk et al.[15,16]

The limitation of our study is that there were missing data on the refraction values of children < 5 years. Therefore, refractive errors in 0-2 years and 2-4 years groups seem to be lower than those in 5 years and older.

Optic atrophy is common in patients with spina bifida and hydrocephalus.[17] Caines et al. detected optic atrophy in 2 out of 22 patients.[12] Funduscopic examination performed in the present study detected unilateral optic atrophy in three (2.5%) patients and bilateral optic atrophy in six (4.9%) patients.

Gaston et al. detected papilledema in 6 out of 55 patients.[8] In the present study, bilateral papilledema was detected in three (2.5%) patients. The low rate of papilledema in the present study may be because all the patients included in the study were diagnosed with spina bifida previously and were treated by performing shunt placement.

CONCLUSION

Ophthalmic findings such as strabismus and refractory error are very common in patients with spina bifida. Therefore, these patients should be followed up closely after birth for ophthalmic complications by a team of ophthalmologists and neurosurgeons as the risk of amblyopia due to strabismus and refractive errors in patients with spina bifida may be reduced.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Alev Koçkar, Raziye Dönmez Gün;* ***Design:*** *Alev Koçkar, Raziye Dönmez Gün, Elvan Alper Şengül;* ***Control/Supervision:*** *Elvan Alper Şengül, Erdal Yüzbaşıoğlu;* ***Data Collection and/or Processing:*** *Alev Koçkar, Elvan Alper Şengül;* ***Analysis and/or Interpretation:*** *Raziye Dönmez Gün, Alev Koçkar;* ***Literature Review:*** *Raziye Dönmez Gün, Alev Koçkar;* ***Writing the Article:*** *Raziye Dönmez Gün, Alev Koçkar;* ***Critical Review:*** *Elvan Alper Şengül, Erdal Yüzbaşıoğlu;* ***References and Fundıngs:*** *Raziye Dönmez Gün, Alev Koçkar;* ***Materials:*** *Raziye Dönmez Gün, Alev Koçkar.*

REFERENCES

1. Hall JG, Solehdin F. Genetics of neural tube defects. MRDD Res Rev. 1998;4(4):269-81. [Crossref]
2. Olney R, Mulinare J. Epidemiology of neural tube defects. MRDD Res Rev. 1998;4(4):241-6.[Crossref]
3. Liptak GS, El Samra A. Optimizing health care for children with spina bifida. Dev Disabil Res Rev. 2010;16(1):66-75. [Crossref] [PubMed]
4. McDonnell GV, McCann JP. Issues of medical management in adults with spina bifida. Childs Nerv Syst. 2000;16(4):222-7. [Crossref] [PubMed]
5. Harcourt RB. Ophthalmic complications of meningomyelocele and hydrocephalus in childern. Br J Ophthalmol. 1968;52(9):670-6. [Crossref] [PubMed] [PMC]
6. De Becker I, MacPherson HJ, LaRoche GR, Braunstein J, Cottle R, McIntyre LL, et al. Negative predictive value of a population-based preschool screening programme. Ophthalmology. 1992;99(6):998-1003. [Crossref]
7. Bowling B. Kanski's Clinical Ophthalmology: A Systematic Approach. Strabismus. 8th ed. China: Elsevier; 2016. Chapter 18, p.755.
8. Gaston H. Ophthalmic complications of spina bifida and hydrocephalus. Eye (Lond). 1991;5(Pt 3):279-90. [Crossref] [PubMed]
9. Clements DB, Kaushal K. A study of the ocular complications of hydrocephalus and meningomyelocele. Trans Ophthalmol Soc U K. 1970;90:383-90.
10. Pinello L, Bartolin C, Drigo P. [Visual motor and visual defects in spina bifida]. Pediatr Med Chir. 2003;25(6):437-41.
11. Anderson HA, Stuebing KK, Buncic R, Mazow M, Fletcher JM. Factors associated with strabismus in spina bifida myelomeningocele. J Pediatr Ophthalmol Strabismus. 2012;49(5):284-9. [Crossref] [PubMed] [PMC]
12. Caines E, Dahl M, Holmström G. Longterm oculomotor and visual function in spina bifida cystica: a population-based study. Acta Ophthalmol Scand. 2007;85(6):662-6. [Crossref] [PubMed]
13. Ünsal SE, Ün EŞ, Kılınç S. [Prevalence of refractive errors and amblyopia and their correlation with demographic factors in the children over four years of age who underwent their first ophthalmologic examinations]. İzmir Dr. Behçet Uz Çocuk Hast Dergisi. 2013;3(3):181-5. [Crossref]
14. Cumurcu T, Cumurcu HB, Erkorkmaz Ü, Yardım H. [Ocular findings in children with cerebral palsy]. Fırat Tıp Dergisi. 2007;12(1):48-52.
15. Saunders KJ, McCulloch DL, Shepherd AJ, Wilkinson AG. Emmetropisation following preterm birth. Br J Ophthalmol. 2002;86(9):1035-40. [Crossref] [PubMed]
16. Ozturk AT, Berk AT, Yaman A. Ocular disorders in children with spastic subtype of cerebral palsy. Int J Ophthalmol. 2013;6(2):204-10.
17. Rabinowicz M. Visual function in children with hydrocephalus. Trans Ophthalmol Soc UK. 1974;94:353-66.