Identical Twins with “Mirror Image” Anisometropia and Esotropia

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SUMMARY
Introduction Identical twins account for 0.2% of the world population and 8% of all twins. A “mirror image” variation can be found in 25% of identical twins. Studies of twins assume a special place in human genetics due to the possibility of comparing genetic and other factors. We present two pairs of identical male twins with mirror-image astigmatism and esotropia.

Case Outline The first was a pair of twelve-year old identical twins with “mirror image” myopic astigmatism. The Twin 1 had myopic astigmatism in the right eye, while the Twin 2 was affected by the left eye myopic astigmatism. The second was a pair of six-year old identical twins with esotropia and hypermetropic astigmatism. The Twin 1 had esotropia in the left eye, while the right eye was affected in the Twin 2. Esotropia was surgically corrected.

Conclusion In this study we pointed to the role of genetic factors in the development of refractive error, as well as the type of strabismus. Refraction anomalies (myopia, hypermetropia and astigmatism) are complex heterogeneous disorders and ideal for genetic investigation. The knowledge of genetic mechanisms involved in refractive error susceptibility may allow treatment to prevent progression or to further examine gene-environment interactions. We hope that this paper will initiate further investigation of refraction anomalies in twins and future multicentre studies, which, to our knowledge, have not been conducted in our country so far.

Keywords: “mirror image” twins; refraction anomalies; esotropia

INTRODUCTION
There are approximately 125 million twins and triplets (roughly 1.9% of world population) and 10 million monozygotic twins (MZ) [1] in the world. Monozygotic twins are always of the same sex, have the same genotype, while personality traits influenced by other, non-genetic factors are less similar. Identical twins account for 0.2% of the world population and 8% of all twins. In the so-called “mirror-image” twins variants there are potential phenotypic differences between the right and left sides of individuals (Spemann, 1920), and they can be found in 25% of identical twins [2, 3]. Studies of twins take a special place in human genetics due to the possibility of comparing genetic and other factors. Twin studies have been described as a perfect natural experiment to study the relative importance of genetic and environmental factors [4]. Refraction anomalies (myopia, hypermetropia and astigmatism) are complex heterogeneous disorders and ideal for genetic investigation [5]. Monozygotic twins with the “mirror-image” refraction anomaly or esotropia are rare. We present two pairs of identical male twins with “mirror-image” astigmatism and esotropia.

CASE REPORT
The patients underwent a complete ophthalmic examination, including visual acuity determination, biomicroscopy, an indirect ophthalmoscopic exam with a 20D condensing lens (Heine 500, Germany), refractometry/keratometry (computerized refractometry, Righ-тон Speedy-K, Japan), an ocular motility examination, a cover/uncover test performed at 0.5 and 6.0 m, measuring the objective angle of deviation with a synoptophor (Synoptophor Oculus, Germany), and measuring the A-scan axial length (Ultrasound A/B Scanner UD-6000, Tomey). The screening of visual acuity was accomplished with standard Snellen vision charts or, in small children, with a picture chart. The patients’ eyes were examined in mydriasis by an ophthalmologist using a fundus camera. Digital fundus images were obtained with a digital fundus camera (Visucam Lite Zeiss).

The first was a pair of twelve-year old twins with “mirror-image” myopic astigmatism in one eye and emmetropia in the other. The children were born from the first full-term regular pregnancy, with no eye disorder family history. The twins’ monocular poor vision was accidentally revealed at the age of seven.

The Twin 1 best corrected visual acuity (BCVA) of the amblyopic eye was 0.5, while the Twin 2 was BCVA 0.3. The visual acuity of the children’s unaffected eyes was 1.0. Ophthalmoscopy revealed extensive chorioretinal atrophy (conus myopicus) in the right eye fundus of the Twin 1 (Figure 1) and in the left eye fundus of the Twin 2 (Figure 2). The Twin 1 developed right eye myopic astigmatism and emmetropia in the left eye [right -4.0/-2.0 (180), left plano/-
The Twin 2 developed left eye myopic astigmatism and emmetropia in the right eye [right plano/-0.25 (180), left -6.0/-3.50 (180)]. The cover-uncover test was conducted and no objective deviation was found. A-scan axial length measurements were 26.22 mm/23.29 mm in the Twin 1 and 23.61 mm/26.67 mm in the Twin 2. The keratometer readings were 41.00 D/43.25 D in the right eye and 42.00 D/42.50 D in the left eye of the Twin 1 and 41.75 D/42.25 D in the right eye and 41.00 D/44.50 D in the left eye of the Twin 2.

The second was a pair of six-year old twins with “mirror-image” esotropia and hypermetropic astigmatism. The children were born from the first regular full-term pregnancy, with no eye disorder family history, and an eye turn observed at the age of two.

The children’s best corrected visual acuity was 0.8 in the unaffected eye and 0.1 in the amblyopic eye. The Twin 1 developed the left eye esotropia with bilateral hypermetropic astigmatism [right +3.75/+2.25 (100), left +4.00/+0.75 (80)] (Figure 3a). The Twin 2 developed the right eye esotropia with bilateral hypermetropic astigmatism [right
+3.00/+1.75 (100), left +3.50/+2.75 (80)] (Figure 4a). The angle of deviation was 40 prism diopeters in both children. Esotropia was surgically corrected. The findings of the Twin 1 left eye were medial rectus muscle recession of 7.0 mm and lateral rectus muscle recession of 7.0 mm (Figure 3b). The findings of the Twin 2 right eye were medial rectus muscle recession of 6.5 mm and lateral rectus muscle recession of 6.5 mm (Figure 4b). The post-operative angle of deviation was 1 prism diopter in the Twin 1 and orthophoria was gained in the Twin 2. A-scan axial length measurements were 21.22 mm/21.29 mm in one twin and 21.67 mm/21.61 mm in the other. The keratometer readings were 41.00 D/41.50 D in the right eye and 42.00 D/42.50 D in left eye of one twin and 41.00 D/42.50 D in the right eye and 41.50 D/42.25 D in the left eye of the other twin.

**DISCUSSION**

The refraction of the eye may change in the course of life. In the first months of life preterm children more frequently suffer from myopia [6, 7], astigmatism, anisometropia [7], mainly anisomyopia [8] compared to full-term infants (Fletcher and Brandon, 1955; Graham and Gray, 1963; Dobson et al., 1981; Scharf et al., 1986; Rodriguez et al., 1992; Quinnet et al., 1992) [7].

Hypermetropia [6, 7] and astigmatism can be found in newborns and sucklings, but these two disorders are noted to rapidly decrease in the first year of life [7], while myopic refraction is extremely rare (about 1%) at this age [6]. During the preschool period, hypermetropia from +3.0 to +4.0 D at birth decreases to +0.50, emmetropia that may even turn into myopia [6].

In the past decades the prevalence of myopia in young adolescents has been rising and accounts for 10-25% and 60-80% in industrialized Western and Eastern societies [9]. Worldwide 1.6 billion people are estimated to have myopic refractive error, and this number is expected to increase to approximately 2.5 billion by the year 2020 [10]. This indicates that myopia is becoming a significant global health problem [11].

Astigmatism relatively rarely occurs as an isolated refractive error (simple, compound and mixed astigmatism make up about 20% of all astigmatisms). Over 80% of astigmatism combines with hypermetropia/myopia and can change in the course of life [6].

Anisometropia, an unequal refraction of both eyes [6], can cause amblyopia. Anisohypermetropia more commonly causes anisometric amblyopia than anisomyopia [8, 12]. The prevalence of anisometropia varies depending on the definition and ranges from 20 to 80% of the total population. Anisometropia between the two eyes >2.50 D is present in 20% of people with myopia ≥6 D. Scientific studies have reported anisometropia between the two eyes >10 D (unilateral myopia) and familial anisometropia, >20 D in a mother, her sisters and daughters [13].

Okamoto et al. [14] reported “mirror image” myopic anisometropia in two pairs of monozygotic twins. De Jong et al. [13] described anisometropia of more than 20 diopeters in both left eyes of a pair of monozygotic 64-year-old twins. Dirani et al. [15] described monozygotic twins with “mirror-image” congenital esotropia and discordant refractive errors. One had right congenital esotropia surgically corrected during childhood, and the other had left congenital esotropia surgically corrected at the age of 3 and 6. Dirani et al. [16] described “mirror image” congenital esotropia with concordant hypermetropia in monozygotic twins. Dirani et al. [17] described female monozygotic twins aged 54 years discordant for myopia; one twin presented with bilateral high myopia and her identical twin had no significant refractive error. Atilla and Erkam [18] reported microesotropia in twins as a unique example of the role of heredity in primary microstrabismus. Yoon et al. [19] reported that the concordance rate in monozygotic twins is high, especially in refractive or non-refractive accommodative esotropia and intermittent exotropia, where genetic factors can be responsible for the development of these types of strabismus.

Primarily genetic factors are responsible for the development of a refractive error and contribute up to 84-86% of the cases of myopia and hypermetropia and 50% and 60% of the cases of total and corneal astigmatism, respectively [4].

Investigation of twins has become a very popular method of genetic testing in the early 20th century, when science has not yet had access to DNA. Earlier research, mainly in the form of individual studies and clinical trials (Blatt 1924; Jablonski 1922; Steiger 1913) [13, 20], identified great similarities in refractive errors between monozygotic twin pairs, and pointed to the role of genetic factors in the development of refractive anomalies. The first classic twin study aiming at researching refractive anomalies is said to have been conducted on 52 twin pairs by Walter Jablonski at the beginning of the 20th century [20]. Karlsson (1974) points out the coincidence of refractive anomalies in approximately 95% 29% MZ and DZ pairs of twins. Possible discordant refraction in MZ twins is explained by different intrauterine environments, skewed X-chromosome inactivation, incomplete genetic penetrance, variable expressivity due to environmental exposures, postgenomic events such as changes in the regulation of DNA methylation and intrapair epigenetic variation [10]. Ever since 1937, when applied in neurology and psychiatry (Hill, 1973) [21], diagnostic or therapeutic ultrasound has been used in almost all branches of medicine. The introduction of ultrasound biometrics contributed to the considerations of the influence of genetic and other factors on the development of refraction anomalies [10, 22-25].

There is a positive correlation between the ocular biometric parameters, particularly axial length and vitreous body length, and the degree of myopia [21]. The emphasis has also been placed on the influence of genetic/non-genetic factors on myopia prevalence in different ethnic groups, retinal pathology associated with severe forms of myopia [10], the association of myopia and genetic disorders (Marfan’s syndrome) [10, 26]. It has also been concluded that environmental risk factors [6, 10, 11, 27, 28, 29], growing anthropometric measures [30], higher
education [31], urbanization [32] contribute to the development of myopia. There have been fewer reports on the analysis of a genetic component to hypermetropia [4, 10].

In the case of astigmatism, Teikari et al. [1989] and Valluri et al. [1999] [25] discovered that there was no difference in the heritability of astigmatism in MZ and DZ twins, which indicates little influence of genetic factors on the development of astigmatism. On the other hand, Nance et al. [1982] and Sorsby et al. [1962] claimed that there was a significantly higher correlation for astigmatism between MZ twin pairs compared to DZ twin pairs, while Hammond et al. [4] reported that the correlation for astigmatism was almost four times larger in MZ twin pairs compared to DZ twin pairs. Conical curvature, conical astigmatism, and conical topography were obtained from computerized videokeratoscope. Correlation analysis was performed to investigate the symmetry of the refractive error, corneal curvature, corneal astigmatism, and anterior corneal aberrations between right and left eyes of each twin pair. These results suggest that conical astigmatism and spherical aberration possess a greater genetic predisposition than those of other refractive errors and higher order [33]. The latest studies explain that interindividual variations in corneal astigmatism and the curvature of the cornea are caused by genetic factors and point to the need to identify the genes involved in the aetiology of astigmatism [25].

We presented two pairs of identical male twins with “mirror image” astigmatism and esotropia. In this study we identified great similarities in refractive anomalies between the pairs of twins. Also we pointed to the role of genetic factors in the development of refractive error, as well as the type of strabismus.

Premature retinopathy screening at the Eye Clinic in Niš (started in 2008) creates conditions for further follow-up of the refractive state of children’s eyes in general, and especially in twins. Furthermore, in order to make any valid conclusion about the number and types of refractive errors in twins, particularly in terms of the importance of genetic factors, it is necessary to compare the obtained data with the ones relevant to the rest of the population. We hope that this paper will initiate further investigation of refraction anomalies in twins and future multicentre studies, which, to our knowledge, have not been conducted in our country so far.

REFERENCES

Кратак садржај
Увод Једнојајечани близанци чине 0,2% светске популације и 8% свих близанаца. Тзв. mirror image варијанта јавља се код 25% ових близанаца. Студије на близанцима имају посебно место у хуманој генетици због могућег поређења ефеката генетских и других фактора. Приказујемо два пара једнојајечаних близанаца са mirror image астигматизmom и езотропијом.

Приказ болесника Први пар близанаца били су дванаестогодишњи деца са mirror image миопним астигматизmom. Код првог близанца утврђен је миопни астигматизам десног ока, а код другог левог ока. Други пар једнојајечаних близанаца били су шестогодишњи деци са езотропијом и хиперметропним астигматизмом. Код првог близанца установљена је езотропија левог ока, а код другог десног ока. Езотропија је хируршки коригована.

Закључак Овим радом указано је на улогу генетских фактора у развоју рефракционе грешке и типа стабилизацији. Рефракционе аномалије (миопија, хиперметропија и астигматизам), као комплекс хетерогених поремећаја, идеалне су за генетска испитивања. Познавање генетског механизма са држаног у рефракционим грешкама омогућава лечење, као и би се спречило напредовање или додатно испитивање интеракција гена – фактора окружења. Надамо се да ће овај рад иницирати додатна испитивања рефракционих аномалија код близанаца и будуће мултицентричне студије, којих у нашој земљи, према нашим сазнањима, досад није било.

Кључне речи: mirror image близанци; рефракционе аномалије; езотропија

Једнојајечани близанци са mirror image анизометропијом и езотропијом
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