Correlation between Ophthalmic Disorders and Congenital Cardiac Disease in Children with Down Syndrome

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INTRODUCTION

Down’s syndrome (DS), one of the most frequent chromosomal anomalies, is associated with dysmorphic features, congenital malformations and intellectual disability.

There are various clinical manifestations: congenital cardiac diseases are found in 40% of cases, gastrointestinal anomalies in 7% of cases, and intellectual disability can be present in a medium or serious form.

Both congenital cardiac diseases and ocular problems are particularly frequent, regarding both structure and function, such as refractive defects, accommodation, strabismus and cataract are particularly frequent.

However, in the literature few data, and none that is univocal, are found on a possible correlation between these two groups of pathologies.

In a group of children Bromham NR et al. observed a relationship between congenital cardiac diseases and myopia and nystagmus. No

ABSTRACT

BACKGROUND: Congenital cardiac diseases are particularly frequent in patients with Down’s Syndrome, like ocular anomalies. The purpose of this paper is to make a contribution regarding the possible correlation between single congenital cardiac disease and the frequently found eye disorders.

METHOD: 198 subjects (112 males and 86 females) with a 21 free trisome in the study of the karyotype were examined from both the cardiological and the ophthalmic point of view.

RESULTS: 60 subjects present a congenital heart disease: 21 patients an interatrial defect (DIA), 14 patients an interventricular defect (DIV) and 8 patients atriointeventricular septal defect (AVSD). The most frequent ocular anomalies found were myopia in 62 eyes, hypermetropia in 58 eyes and astigmatism in 54 eyes. In the DIA subjects hypermetropia is prevalent, and in those with DIV and/ or AVSD the other three anomalies (hypermetropia, myopia and astigmatism) are more or less equally frequent.

CONCLUSIONS: Our study confirms the frequent association between congenital cardiac diseases and ocular anomalies, above all refractive defects, in DS patients, and draws attention to the need for early ophthalmic screening to set going all the essential corrective actions for a better quality of life.

Key words: Down’s Syndrome; Congenital cardiac diseases; Ocular anomalies; Myopia; Hypermetropia; Astigmatism

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relationship with strabismus or other accommodation anomalies was observed. Stirn Kranje B[3], studying 65 Slovenian subjects with DS, noticed a relationship between cardiac disease and myopia and strabismus. He did not notice any statistically significant association with hypermetropia, although this refraction defect was the most frequent ocular anomaly, affecting 36.9% of subjects.

Afifi HH et al[10] noticed a statistically significant correlation between myopia and congenital cardiac diseases but without any correlation between refraction defect and type of congenital cardiopathy.

We therefore wanted to study the possible correlation between single congenital cardiac diseases and the ocular defects most frequently found in a group of DS patients.

MATERIAL AND METHODS

198 subjects were studied with an average age of 7.2 years (range 7 months-35 years), 112 males and 86 females, treated at the Regional Down’s Syndrome Reference and Genetic Chromosomal Pathologies - University of Palermo; they belonged to a homogeneous ethnic context. All the subjects presented a 21 free trisome in the karyotype study.

All subjects with congenital cardiac diseases were submitted to a complete ophthalmic examination with evaluation of visual acuity, biomicroscopy of the anterior segment, dilated fundus examination and orthoptic examination with study of ocular motility, degree of convergence and the cover and uncover test both close up and at a distance. Evaluation of refraction was carried out in cycloplegia in all patients through instillation of 3-5 drops of Cyclopentolate 1%.

Visual acuity (VA) was tested with an E chart and best-corrected visual acuity (BCVA) would be measured if the VA was less than 0.5. Cycloplegic refraction was determined by streak retinoscopy 30 min after the last drop to ensure maximal cycloplegic effect.

The refractive error was taken as the spherical equivalent (SE) in diopters (D) and calculated as the power of the sphere plus half the cylindrical power. Eyes with a SE from -0.75 to +1.75 D were classified as emmetropic. Myopia was defined as SE refractive error of at least -0.75 D and hypermetropia as +1.75 D or more.

Consent

Written informed consent to participate in this study was obtained from a parent of the patients.

Statistical Analysis

The data are expressed as mean ± SD. The correlations between the ophthalmic disorder with congenital cardiac disease were examined by means of linear regression analysis. Values of $p < 0.05$ were considered as significant.

RESULTS

60 patients, amounting to 30.3%, present a congenital cardiopathy, most frequently an interatrial defect (DIA), present in 14 patients and an atrioventricular septal defect (AVSD) in 8 patients. These three cardiopathies constitute 71.6% of all cases (Table 1). The other group is constituted by single cardiopathies like steno-mitrail insufficiency, tricuspidal insufficiency, etc.

As can be seen from Table 2, in subjects with congenital heart diseases, the most frequent ocular anomaly is myopia, found in 62 eyes, followed by hypermetropia (58 eyes) and astigmatism (54 eyes). Regarding the latter, hypermetropic astigmatism (Table 3) prevails over myopic. Lastly, in 44 eyes, strabismus is present.

In subjects without congenital heart diseases, astigmatism is the most frequent ocular anomaly, found in 96 eyes, followed by strabismus (78 eyes), hypermetropia (56 eyes) and myopia (52 eyes).

Examining the associations between the single congenital cardiac diseases and the ocular anomalies (Table 4), it appears evident that in subjects with DIA hypermetropia, Myopia and Astigmatism are more

| Cardiopathy | Myopia | Hypermetropia | Astigmatism | Strabismus | Amblyopia | Nystagmus | Cataract |
|-------------|--------|---------------|-------------|------------|-----------|-----------|----------|
| DIA         | 11     | 16            | 9           | 11         | 7         | 7         | 6        |
| DIV         | 7      | 7             | 6           | 4          | 3         | 1         | 0        |
| AVSD        | 3      | 4             | 4           | 3          | 4         | 0         | 1        |
| Fallot Tetralogy | 2   | 1             | 2           | 1          | 1         | 0         | 0        |
| PDA         | 2      | 3             | 3           | 0          | 0         | 0         | 0        |
| Other group | 6      | 2             | 3           | 3          | 2         | 1         | 1        |
DISCUSSION

This is the first study whose aim is to verify the presence of a correlation between specific congenital cardiac diseases and ocular disorders in subjects with DS. Other authors[1,2,3] have addressed their attention to the presence or otherwise of a correlation between cardiac pathology in general and ocular disorders, above all formulating the hypothesis that it is associated with myopia, nystagmus and astigmatism.

The data we obtained underline the presence of a statistically significant correlation (p = 0.003) between DIA and myopia, DIA and hypermetropia and DIA and strabismus; by contrast, no correlation has been observed with astigmatism, amblyopia, nystagmus and cataract.

The same data are observed in relation to interventricular patency (p = 0.001), while no correlation was found between AVSD and examined ocular anomaly.

The correlation between DIA and hypermetropia and DIV and hypermetropia observed by us could very probably depend on the greater prevalence in our patients of this refractive defect, found in 33 eyes of DS subjects with congenital cardiology.

The discordance with what has been observed by others[4], who have found no correlation between this refraction defect and congenital cardiac diseases although in their sample too it was frequent, perhaps due to peculiar ethnic characteristics. In this connection, the group of DS patients studied by Afifi HH and coll. is historically constituted by subjects coming from an isolated region on the banks of the river Nile and, therefore, as the authors hypothesize, could be the consequence of a genetic mutation that has remained unchanged in time. Al-Jarallah AS[5] also advances the hypothesis that the consanguinity of the parents may have a role in the appearance of cardiology, at least in the Saudi population studied. This hypothesis appears to be confirmed by the fact that, although the presence of an extra copy in all or part of chromosome 21 causes a 1.5-fold increase in the expression of some genes with a genetic unbalance, this situation does not always give rise to a heart development anomaly. In this connection, while it is true that around 40% of people with Down’s syndrome present some form of congenital heart disease (CHD), it is also true that half of all people with DS have normal hearts. Consequently, it can be hypothesised that the genetic unbalance mentioned, as Reeves R[6], suggest, is the consequence of genetic, environmental and stochastic influences, or that in order to manifest itself it requires some interaction with genes located on other chromosomes rather than chromosome 21[7].

According to the latter hypothesis, the appearance of congenital cardiac diseases may be due to the formation of variations in the epidermal growth factor (EGF), which codes for a protein expressed during heart development. In this connection, missense mutations in CRELD1 have been found in DS patients who are AVSD carriers.

By contrast, there is a widespread consensus on the fact that the genetic anomaly involves a simultaneous repercussion in the regular development of the heart and the eye; in our case study the association between congenital heart and ocular anomaly can be found in all subjects.

In our opinion, such a high frequency of association is of major interest in so far a the longevity of these patients today has significantly increased in comparison to a few decades ago, thanks to progress in heart surgery, with a life expectancy that is only slightly inferior to that of the rest of the population (over 60 years). It therefore becomes necessary to act in a timely way on the ocular problems present in that, if not corrected, they may interfere negatively with binocular vision and therefore with a person’s quality of life. The visual defect should also be corrected as soon as possible to improve integration at school and to allow the young patients to socialize with others. The importance of early treatment is such that some authors[8] believe that all the children with DS should be submitted to visual screening for the first time at one month and subsequently at one year, at 2-3 years, at the beginning of school and subsequently every 5 years. According to others[9,10], in subjects with CHD screening should be annual, at least until the beginning of the school cycle. The Committee on Genetics Health Supervision for Children with Down Syndrome (Pediatrics 2011;128;393) suggests an eye test within the first month of life given the elevated frequency of congenital cataract.

CONCLUSION

The results of our study confirm the frequent association between congenital cardiac diseases and ocular anomalies, above all refractive defects, in patients with DS. The need for ophthalmic screening in DS patients is even more important in those with congenital cardiac disease in that only timely identification of ocular anomalies can set going all the essential corrective actions for a better quality of life.

REFERENCES

1. Bromham NR, Woodhouse JM, Cregg M, Webb E, Fraser WI. Heart defects and ocular anomalies in children with Down's syndrome. Br J Ophthalmol 2002 Dec; 86(12): 1367-1368. [PMID: 12446367]
2. Stirn Kranjc B. Ocular abnormalities and systemic disease in Down syndrome. Strabismus. 2012 Jun; 20(2): 74-77. [PMID: 22612356]
3. Afifi HH, Abdel Azeem AA, El-Bassyouni HT, Gheith ME, Rizk A, Bateman JB. Distinct ocular expression in infants and children with Down syndrome in Cairo, Egypt: myopia and heart disease JAMA Ophthalmol. 2013 Aug; 131(8): 1057-1066 [PMID: 23764677]
4. Al-Jarallah AS. Down’s syndrome and the pattern of congenital heart disease in a community with high parental consanguinity. Med Sci Monit. 2009 Aug; 15(8): CR409-12. [PMID: 19644417]
5. Reeves R, Baxter L, Richtsmeier J. Too much of a good thing: mechanisms of gene action in Down syndrome. Trends Genet 2001; 17: 83-88 [PMID: 11173117]
6. Shapiro BL. Down syndrome—a disruption of homeostasis. Am J Med Genet 1983; 14: 241-269 [PMID: 620605]
7. Haugen OH, Hovding G, Riise R. Ocular changes in Down syndrome. Tidskr For Lægeforen. 2004 Jan 22; 124(2): 186-188. [PMID: 14743254]
8. Creavin AL, Brown RD. Ophthalmic abnormalities in children with Down syndrome. J Pediatr Ophthalmol Strabismus. 2009 Mar-Apr; 46(2): 76-82. [PMID: 19343968]
9. Roizen N, Mets MB, Blondis TA. Ophthalmic disorders and congenital cardiac disease in children with Down syndrome Dev Med Child Neurol. 1994 Jul; 36(7): 594-600.

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