EXTENDED REPORT

Down's syndrome and early cataract

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Aims: To estimate the occurrence of early cataract among patients with Down's syndrome and to evaluate the clinical characteristics of the cases.

Methods: Cases with Down's syndrome were ascertained from a cohort of all Danish children between 0 and 17 years of age, who were diagnosed with cataract during the period 1977–2001 (n=1027). Information on the patients was obtained from the medical records.

Results: Of the total of 1027 cases with non-traumatic, non-acquired cataract there were 29 cases (13 males, 16 females) with Down's syndrome (2.8%). This corresponds to an occurrence of early cataract among patients with Down's syndrome of 1.4%; 27 had bilateral cataract and two had unilateral cataract. Half of the patients (n=14) underwent cataract surgery, of whom two had bilateral primary lens implantation. 10 patients had bilateral cataract observed soon after birth, and five of these underwent cataract surgery within the first 6 months of life.

Conclusion: The frequency of early cataract among children with Down's syndrome is estimated to be 1.4%, with cataracts requiring surgery during childhood being even rarer. In one third of the 29 cases, bilateral cataract was detected in the neonatal period.

Children with Down's syndrome are characterised by mental retardation and a special physiognomy and body stature. They also have a high frequency of various ocular anomalies. The clinical entity was first described by Down in 1866.¹ In Down's syndrome there is a surplus of genetic material from chromosome 21, in most cases as a full trisomy of the chromosome.² In Denmark the incidence of Down's syndrome is approximately one in 1000 children.³

In literature the occurrence of early cataract among children aged up to 17 years with Down's syndrome has been reported to be from 5% (Haugen O, personal communication, 2005) and up to 50%.^{4–9} In previous studies of congenital or infantile cataract, 3–5% of cases were associated with Down's syndrome.^{10–13} However, in ophthalmic literature there is a lack of population based data on occurrence and characteristics of early cataracts in Down's syndrome.

Based on a population based study of paediatric cataract cases in Denmark the primary aim of this paper was to estimate the frequency of early cataract among patients with Down's syndrome and report the age at diagnosis, age at surgery, and the clinical characteristics.

METHODS

This study is part of a larger national study on childhood cataract in Denmark. The present analysis focuses on the cases with Down's syndrome identified among the registered and validated cases of paediatric cataract. Cataracts after trauma, or considered to be caused by acquired systemic (for example, diabetes) or acquired ocular pathology (for example, uveitis) were not included.

All medical records of children (0–17 years old) diagnosed with non-traumatic, non-acquired cataract in the Danish National Register of Patients (NRP) during the period 1977 to 2001 were reviewed in order to validate the ophthalmic diagnosis. Since 1977 the NRP has registered all discharge diagnoses of patients admitted to public hospitals (inpatients) and also the surgical procedures performed. In addition, outpatients were registered from 1995. Further methodological details are provided elsewhere.^{14 15}

The cataract cases were classified according to aetiology, with (a) unknown, (b) genetic, (c) intrauterine infection, and (d) the result of chemical substances during embryogenesis as the four subgroups. The genetic cases were further subdivided into hereditary cataract, as confirmed by family history, and cataracts associated with syndromes/chromosomal abnormalities, including Down's syndrome.¹⁵ According to the description in the medical records, in general the cataract morphology groups were nuclear/zonular, posterior cortical, anterior polar, posterior polar, dense, cerulean, mixed (nuclear and posterior cortical) and "other." Age at diagnosis and age at surgery are given in days when below 1 year, in months at age 1–2 years, and rounded to whole number of years when above that age.

Children, who had a validated diagnosis of cataract and who had Down's syndrome were selected for the present analysis.

The total number of Down's syndrome cases during the study period was estimated as based on data from the Danish National Board of Health, which reported a birth prevalence of one per 1000 live births during 1981 to 2004.³ Using Danish birth statistic data for the study years 1977 to 2001, we estimated a total number of births to be 1 552 379 during the study period. The number of children with cataract and Down's syndrome born during the years 1977–2001 was 22. This number was used in the estimation of the frequency of early cataract in children with Down's syndrome. The remaining seven early childhood cataract cases out of the total of 29 were born before 1977.

RESULTS

During the study period, 1977–2001, a total of 1027 children aged 0–17 years had a validated diagnosis of non-traumatic, non-acquired cataract. In 60 cases the cataract was associated with syndromes/chromosomal abnormalities, with Down's syndrome as the most frequent entity. It was present in 29 cases (2.8% of the total series). From the population frequency of Down's syndrome it can be estimated that approximately 1550 cases with Down's syndrome were born

Abbreviations: IOL, intraocular lens; NRP, National Register of Patients

Table 1 Early cataract cases with Down's syndrome

Case no	Sex	Age at cataract diagnosis*	Eye	Morphology	Age at surgery*	Congenital heart defects
Bilateral						
1	F	at birth	R	Dense	50 d	Yes
			L	Dense	71 d	
2	M	at birth	R	Mixed	137 d	No
			L	Posterior cortical	57 d	
3	F	at birth	R	Nuclear/zonular	107 d	Yes
			L	Nuclear/zonular	107 d	
4	F	at birth	R	Dense	137 d	yes
			L	Dense	153 d	
5	M	at birth	R	Dense	130 d	no
			L	Other		
6	M	at birth	R	Dense	9 m	no
			L	Nuclear/zonular	11 m	
7	M	at birth	R	Posterior cortical	2 y	yes
			L	Cortical	2 y	
8	F	at birth	R	Nuclear/zonular	3 y	no
			L	Nuclear/zonular	3 y	
9	F	at birth	R	Nuclear/zonular	4 y	no
			L	Nuclear/zonular	4 y	
10	F	3 y	R	Nuclear/zonular	9 y	yes
			L	Nuclear/zonular	5 y	
11	F	4 y	R	Posterior cortical	13 y	no
			L	Posterior cortical	13 y	
12	F	13 y	R	Other	14 y	yes
			L	Other	14 y	
13	M	uncertain† (<15 y)	R	Dense	16 y	yes
			L	Other	17 y	
14	F	at birth	R	Other		no
			L	Dense‡		
15	F	9 m	R	Cortical		no
			L	Cortical		
16	M	14 m	R	Other		no
			L	Other		
17	M	4 y	R	Dense		yes
			L	Dense		
18	M	4 y	R	Other		no
			L	Other		
19	M	7 y	R	Nuclear/zonular		yes
			L	Nuclear/zonular		
20	F	10 y	R	Other		no
			L	Other		
21	F	uncertain† (<12 y)	R	Other		no
			L	Nuclear/zonular		
22	M	12 y	R	Other		yes
			L	Other		
23	M	14 y	R	Cerulean		yes
			L	Cerulean		
24	M	14 y	R	Cerulean		yes
			L	Cerulean		
25	F	16 y	R	Cerulean		no
			L	Cerulean		
26	M	17 y	R	Cerulean		no
			L	Cerulean		
27	F	17y	R	Cerulean		no
			L	Cerulean		
Unilateral						
28	F	17 y	L	Dense	17 y	no
29	F	uncertain† (<6 y)	L	Anterior polar		yes

*d, days; m, months; y, years.

†The cataract had been diagnosed before the age given, but no previous medical record was available.

‡Because the cataract was only dense in the left eye, surgery was not performed.

during the period 1977–2001.³ Twenty two cases in the present study were born during this period (see Methods), making up a frequency of around 1.4% as valid for early age cataract in Down's subjects, and a frequency of congenital cataracts of less than 1%.

The 29 cases were made up of 13 males and 16 females. In table 1 the characteristics of the cases are summarised. One child (case 3) had, in addition to trisomy of chromosome 21, a trisomy of chromosome X. Another child was known to have mosaicism for trisomy 21 (case 8).

Twenty seven of the 29 children with Down's syndrome and cataract had bilateral cataract and two had unilateral

cataract. Ten patients (one third) had bilateral cataract observed when first examined soon after delivery. Eight cases out of the total number presented with dense cataract either bilaterally or unilaterally, five of these at birth. Five cases with a cerulean dot type of cataract were first recorded at age 14–17 years.

Fourteen patients representing 26 eyes out of the 56 eyes with cataract in the Down's series underwent cataract surgery at a median age of 2 years (range 50 days to 17 years). Of the 27 bilateral cases 12 had bilateral surgery and one unilateral surgery; one of the two cases with unilateral cataract was operated on at age 17 years. Two cases

had bilateral primary intraocular lens implantation (IOL, cases 11 and 12). Of the 10 Down's cases with bilateral cataract observed neonatally 11 eyes of six patients had a density that led to cataract surgery within the first year of life. In one of the remaining four cases surgery was not performed with the reason given that the bilateral cataract was dense in only one eye (case 14); the remaining three cases had bilateral cataract surgery performed between age 2 years and 4 years (cases 7, 8, and 9).

The age at cataract diagnosis for the 19 cases first observed after the neonatal period ranged from 9 months to 17 years of age (median age 12 years). One patient aged 4 years at diagnosis developed dense bilateral cataracts, but eye surgery in general anaesthesia had been considered to carry too high a risk because of serious heart defects (case 17). The child was blind and died at the age of 18 years.

Six of the 12 bilaterally operated cases had subsequent surgery for secondary cataract, bilaterally in four and unilaterally in two. Three of the 29 patients also had strabismus surgery (cases 12, 25, and 26).

Case 7 had bilateral dissection of the cataracts. Eventually he had bilateral ocular exenteration performed at age 11 because of painful chronic uveitis. Case 9 had secondary IOL implantations 15 years after the primary cataract surgery, but soon hereafter had a right eye trabeculectomy performed for glaucoma. Four eyes in two patients with early cataract surgery later developed retinal detachment, after latencies of 10 years and 15 years, respectively (cases 6 and 13). Case 28 underwent vitrectomy because of vitreous opacities 15 months after the primary cataract surgery and developed retinal detachment 8 years later.

Regarding ocular anomalies other than cataract, three eyes in two patients had keratoconus (cases 11 and 15) and one child had bilateral microphthalmos (case 25). Five children had nystagmus. Seventeen children had strabismus, 15 (88%) of these having esotropia, nine of which were described as intermittent or alternating; only two cases were specified as exotropia. Data on preoperative refractive errors were available in 19 cases, though with the values given possibly influenced when lens pathology was observed. There were seven cases with myopia (equivalent sphere < -0.5 D, of which three cases ≤ -7 D), nine cases with hyperopia (equivalent sphere $\geq +0.5$ D, with two cases $\geq +4$ D), two cases with emmetropia (± 0.5 D of spherical equivalent), and 11 of the cases also had astigmatism (≥ 1 D, five cases having ≥ 3 D).

As for systemic disease manifestations among the 29 cases, 13 (45%) had heart disease (table 1), one had Hirschsprung bowel disease, and one had hearing loss and hypothyroidism.

DISCUSSION

Some authorities recommend an ophthalmic evaluation in infants with Down's syndrome within the first 6 months of life, with subsequent follow up examinations to be performed every 1–2 years during childhood and adolescence.¹⁶ The stated aim is early detection and therapy of high ametropia, strabismus, nystagmus and cataract, evidently to secure best possible visual development in a group of patients who usually do not present obvious clues or forward specific visual complaints.

Since cataract is one of the reasons for such screening strategies, it is important to know the actual frequency of the disease. In the literature the occurrence of cataract in Down's children range from 5% (Haugen O, personal communication, 2005) to 50%.^{4–9, 16} In a recent UK study of congenital and infantile cataract, of any background, ($n = 243$) 5.4% were Down's patients, with eight out of the 13 cases (61.5%) being diagnosed in the neonatal period.¹³ In clinical Down's cohort studies Haugen and co-workers reported two cases observed

among 54 subjects examined at age 14–26 years who both had bilateral cataract surgery with IOLs inserted.¹⁷ In our study only three out of the 14 operated cases had IOLs inserted, and in two patients as a primary procedure. In the third patient it was a secondary procedure, with glaucoma to develop later. Regarding our low IOL implantation frequency, it should be recalled that most cases in our series were from an era where IOL implantation was generally not advocated in small children. Today Down's syndrome patients are considered ideally suited to IOL implantation because of the difficulty many of these patients have in wearing contact lenses or spectacles.

Our own nation based data support that early cataract is a rare event in Down's syndrome, though one third of the 29 children with Down's had their cataracts diagnosed already at birth. The 29 cases made up a total of 2.8% of all non-traumatic, non-acquired cataract cases and the estimated frequency of early cataract in Down's syndrome cases was 1.4%. Taking into account only the cataracts diagnosed soon after delivery and the cataracts requiring surgery during childhood, the occurrence was even lower ($< 1\%$). Nevertheless, early ophthalmic examination in patients with Down's syndrome is pertinent, also because of the increased frequency of other treatable ocular manifestations.

Some Down's children with minor cataracts probably escaped recognition in the present context, since the identification of cases was based on a population of paediatric cataract registered at hospitals. This implies the inclusion of mainly advanced cases where surgery should be considered. Optically insignificant opacities in patients with Down's syndrome, as the apparently most prevalent childhood lens pathology observed,^{18–19} were probably ignored in the very young children and therefore not registered as early cataract in the NPR.

The frequency of Down's syndrome in Denmark has been estimated to be approximately one per 1000 children based on nationally registered data on both Down's syndrome and births during a more than 20 year period (1981–2004). In a recent US report the frequency of Down's syndrome was found to be approximately one in 800 children.²⁰ The apparent inconsistency may be due to differences in surveillance and case findings, in data coverage (the Danish data being nationally based), and in access to health care (free access in Denmark, also including early prenatal diagnostics and subsequent measures possibly to be taken). Further, there was a difference regarding study periods (1999–2001 in the US study).

Compared with data regarding other ophthalmic and/or systemic disorders in our series, it seems justified to state that no definite association was found between cataract and heart defects or to other systemic findings in the patients with Down's syndrome.^{16, 21–23} As would be expected, the literature has indicated an increased frequency of strabismus in patients with Down's syndrome and cataract when compared to unselected groups of children with Down's syndrome,^{4, 7–9} however, with a similar predominance of esotropia.

Summing up, early cataract is only rarely seen in patients with Down's syndrome. Textbook frequencies of cataract in Down's syndrome (15–75%) are apparently based on all ages or mainly on adults.^{18, 24, 25} As for neonatal cataract, Sorsby gave the much lower figure of 8%, though many were optically insignificant according to the lens morphology specifications given. Altogether, there is support for the bulk of Down's cataract cases being of adolescent or presenile onset.

We provide a population based frequency of 1.4%, and when considering primarily optically significant cataract of very early age the frequency does not exceed 1%. We suggest that this figure should be taken into consideration when

planning the monitoring of ocular anomalies in children with Down's syndrome.

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Birgitte Haargaard and Hans C Fledelius have no competing interests.

The study was approved by the scientific ethics committees for Copenhagen and Frederiksberg (reference no (KF) 01-253/00), and permission to receive data from the national registries was obtained from the Danish Data Protection Agency (reference no 2000-41-0825).

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