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OCULOPLASTICS AND ORBIT

Congenital lacrimal fistula associated with Down syndrome

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Abstract
Background The aim of this work is to investigate the prevalence and clinical characteristics of congenital lacrimal fistula in Down syndrome patients.
Methods The medical records of 198 Down syndrome patients who were referred to a tertiary ophthalmology clinic from 2000 to 2010 were retrospectively reviewed to identify patients with congenital lacrimal fistula. The demographic data, clinical features, clinical management, and clinical outcomes were recorded. The main outcome measures were the presence and laterality of fistula, accompanying adnexal and oculomotor abnormalities including congenital nasolacrimal duct obstruction (NLDO), the type of surgery performed, and surgical outcome. The prevalence of congenital lacrimal fistula in Down syndrome patients was calculated upon this data.
Results Congenital lacrimal fistula was identified in 8/198 (4.04 %) patients, 4 (2.02 %) of whom presented with bilateral lacrimal fistula. All patients that had lacrimal fistula complained of tearing from their eyes. Congenital NLDO was observed in seven of eight patients with lacrimal fistula. Five patients underwent excision of the lacrimal fistula for the improvement of cosmesis, and three of these patients also underwent lacrimal silicone intubation for NLDO. Another patient received lacrimal silicone intubation for NLDO without excision of the lacrimal fistula. Excision of the lacrimal fistula was successful in all patients; however, tearing persisted after surgery in two patients with uncorrected NLDO.
Conclusions Congenital lacrimal fistula occurs more frequently in Down syndrome patients and therefore these patients should be thoroughly examined for this abnormality. Down syndrome patients with congenital lacrimal fistula should be also examined for NLDO, because this condition is frequently observed in these patients.

Keywords Congenital lacrimal fistula · Down syndrome · Epiblepharon · Epicanthal fold · Nasolacrimal duct obstruction

All authors have full control of all primary data and agree to allow Graefes Archive for Clinical and Experimental Ophthalmology to review author's data upon request.

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Introduction

Down syndrome, caused by trisomy 21, the most common chromosomal anomaly, has been associated with a number of ophthalmic features [1]. The lacrimal drainage system is often affected and the incidence of nasolacrimal duct obstruction is 5–30 % [2–6].

The incidence of lacrimal fistula is approximately one in 2,000 live births. Although systemic diseases are not associated with this abnormality, a few associated disorders have been identified [7–15]. Sullivan et al. reported five cases of lacrimal fistula in Down syndrome patients, and Keseru et al. reported a single case of bilateral lacrimal fistula associated with Down syndrome [11, 14]. Two Down syndrome patients were included in a series of 67 patients with congenital lacrimal fistula in a study by Welham et al. [16]. Satchi et al. reported a case of a Down syndrome patient with a double lacrimal puncta and lacrimal fistula [17].

A review of English literature (PubMed search) showed only nine cases of Down syndrome-associated lacrimal fistula, published in four articles, and only one of nine cases had bilateral lacrimal fistula [11, 14, 16, 17]. In this study, we investigated the prevalence and clinical characteristics of congenital lacrimal fistula in Down syndrome patients.

Materials and methods

The medical records of all Down syndrome patients who were referred to the pediatric ophthalmology clinic of Seoul National University Hospital and Seoul National University Bundang Hospital for ocular evaluation from 2000 to 2010 were retrospectively reviewed to identify patients with congenital lacrimal fistula. The demographic data, clinical features (the presence and laterality of fistula and accompanying adnexal and oculomotor abnormalities including congenital nasolacrimal duct obstruction), the type of surgery performed, and surgical outcome of Down syndrome patients with congenital lacrimal fistula were recorded. The prevalence of congenital lacrimal fistula in Down syndrome patients was calculated upon this data.

Written informed consent was obtained from all patients. The study protocol was reviewed and approved by the Institutional Review Board of Seoul National University Bundang Hospital and was conducted in accordance with the Declaration of Helsinki.

Results

Of 377 Down syndrome patients who visited the pediatrics clinic of Seoul National University Hospital and Seoul National University Bundang Hospital, 198 patients were referred to the ophthalmology clinic for routine ocular examination. Lacrimal fistula was noted in eight (4.04 %) patients, and bilateral lacrimal fistula was noted in four (2.02 %) of these eight patients. Two of these eight patients (25 %) also had lower canalicular obstruction, and seven of these eight patients (87.5 %) had congenital nasolacrimal duct obstruction, which was confirmed by lacrimal probing and lacrimal irrigation intraoperatively or at outpatient clinic. Six of eight patients (75 %) had upper eyelid epiblepharon, four of eight patients (50 %) had lower eyelid epiblepharon, and four of eight patients (50 %) had prominent epicanthal fold. One of these eight patients (12.5 %) had punctal agenesis and two patients (25 %) had exotropia. The cases are summarized in Tables 1 and 2.

All patients experienced tearing from their eyes, but not from their lacrimal fistula opening. Six of the eight patients underwent surgical management. Within this cohort of surgically treated patients, five underwent excision of the lacrimal fistula for cosmetic reasons, three also underwent lacrimal silicone intubation for combined nasolacrimal duct obstruction, and one received lacrimal silicone intubation without lacrimal fistula excision. Lacrimal silicone intubation could not be performed for the left eye of case 3, due to upper punctal agenesis and complete nasolacrimal duct obstruction that could not be probed. The patient's parents refused further surgery such as dacryocystorhinostomy. Among six patients who underwent surgical management, two underwent bilateral upper lids epiblepharon repair and another two patients underwent bilateral upper and lower lids epiblepharon repair. Two of eight patients did not undergo any surgical procedure, because one of them was very young and the parents of the other refused surgical management.

The mean age of the patients at surgery was 54.3 months (range, 14–94 months), and the mean period of postoperative follow-up was 41.8 months (range, 10–124 months). The relatively high mean age of patients at surgery was due to late referral. The lacrimal fistula was well obliterated in all five patients who underwent surgical excision (Fig. 1). Two patients complained of persistent tearing from their eyes after surgical management, and one patient showed upper punctal agenesis and complete obstruction of the nasolacrimal duct that could not be overcome by probing during the surgery. The other patient did not undergo lacrimal silicone intubation because he showed good passage for lacrimal irrigation. However, the patient was diagnosed as bilateral partial nasolacrimal duct obstruction afterward.

Discussion

Lacrimal fistula was found in eight (4.04 %) of 198 Down syndrome patients. Four (2.02 %) of these patients showed bilateral lacrimal fistula, and seven (87.5 %) showed accompanying nasolacrimal duct obstruction. The prevalence of lacrimal fistula was remarkably higher in our sample of Down syndrome patients than in the general population (0.05 %) [8]. In our study, four (50 %) of the eight Down syndrome patients had bilateral lacrimal fistula. Although the incidence of bilateral lacrimal fistula in the general

Table 1 Case summary of congenital lacrimal fistula in patients with Down syndrome

Case	Sex	Age at diagnosis	Chief complaints	Laterality	Combined adnexal and oculomotor disorders	Operation	Age at surgery	Surgical outcome	Persistent symptoms
1	M	3 months	Tearing	Bilateral	BUL epiblepharon Exotropia	Excision of lacrimal fistula (both eyes) BUL epiblepharon repair Epicanthoplasty (both eyes)	3 years	Well-obliterated fistula	Tearing (both eyes)
2	M	13 months	Tearing	Bilateral	Both NLDO Both lower canalicular obstruction	Excision of lacrimal fistula (both eyes) Bicanalicular silicone intubation (both eyes)	14 months	Well-obliterated fistula	None
3	F	7 years	Tearing	Bilateral	Both NLDO BUL and BLL epiblepharon Prominent epicanthal fold Exotropia	Excision of lacrimal fistula (both eyes) Bicanalicular silicone intubation (right eye) BUL and BLL epiblepharon repair Z-epicanthoplasty (both eyes)	7 years	Well-obliterated fistula	Tearing (left eye)
4	M	9 months	Tearing	Left	Both NLDO BUL and BLL epiblepharon	–			Tearing (both eyes)
5	M	4 years	Tearing	Bilateral	Both NLDO Prominent epicanthal fold	Bicanalicular silicone intubation (both eyes)	4 years		None
6	M	4 years	Tearing	Right	Both NLDO BUL and BLL epiblepharon Prominent epicanthal fold	–			Tearing (both eyes)
7	F	5 years	Tearing	Left	Left lower canalicular obstruction BUL and BLL epiblepharon Prominent epicanthal fold	Excision of lacrimal fistula (left eye) Bicanalicular silicone intubation (both eyes) BUL and BLL epiblepharon repair Epicanthoplasty (both eyes)	5 years	Well-obliterated fistula	None
8	F	3 years	Tearing	Left	BUL epiblepharon	Excision of lacrimal fistula (left eye) BUL epiblepharon repair Epicanthoplasty (both eyes)	5 years	Well-obliterated fistula	None

BUL: bilateral upper lids, BLL: bilateral lower lids, LU: left upper, NLDO: nasolacrimal duct obstruction

Table 2 Adnexal and oculomotor abnormalities in Down syndrome patients with congenital lacrimal fistula

Abnormality	No. of patients (%)
Nasolacrimal duct obstruction	7 (87.5 %)
Upper eyelid epiblepharon	6 (75 %)
Lower eyelid epiblepharon	4 (50 %)
Prominent epicanthal fold	4 (50 %)
Exotropia	2 (25 %)
Canalicular obstruction	2 (25 %)
Punctal agenesis	1 (12.5 %)

population is unknown, Song et al. reported that only one patient had bilateral lacrimal fistula among 14 patients with lacrimal fistula but without Down syndrome [18]. Thus, it is likely that bilateral lacrimal fistula is more frequent in Down syndrome patients than in the general population.

Nasolacrimal duct obstruction was noted in seven (87.5 %) of eight patients with lacrimal fistula and Down syndrome in this study. The prevalence of nasolacrimal duct obstruction in Down syndrome patients with lacrimal fistula (87.5 %) was higher than that of Down syndrome population without lacrimal fistula (5–30 %), and was also higher than that of the general population with lacrimal fistula (27–36 %), even after considering the reported high prevalence of nasolacrimal duct obstruction in Down syndrome patients [2–6, 16, 18].

In most cases, congenital lacrimal fistula is not generally associated with systemic diseases, but it has been reported to be associated with thalassemia, preauricular fistula, hypospadias, a balanced 6p and 13q translocation, CHARGE syndrome, VACTERL, naso-orbital meningocele, ectrodactyly-ectodermal dysplasia-clefting syndrome, or Down syndrome [7, 9–15]. Our cases showed that congenital lacrimal fistula occurs in Down syndrome patients; thus, a careful examination for congenital lacrimal fistula as well as for other well-known ocular disorders should be carried out in these Down syndrome patients.

The incidence of epiblepharon is about 61 % in Asian Down syndrome patients and is much higher than in non-Down syndrome Asian patients [6, 19]. The high incidence of upper eyelid epiblepharon (75 %) and lower eyelid epiblepharon (50 %) in current study is thought to be one of the characteristic ocular findings in Asian patients with Down syndrome. The direct association between epiblepharon and congenital lacrimal fistula could not be proven in this case series.

A prominent epicanthal fold was observed in four (50 %) of the eight patients with lacrimal fistula. The prominent epicanthal fold is a typical finding in Down syndrome (61–96.7 %) [6, 20], and it may conceal fistula openings, because the lacrimal fistula opening is sometimes located within this fold (Fig. 2). The prominent epicanthal fold accompanied by tearing may also cause skin maceration, inflammation, discharge, and cosmetic problems by tears welled up between the opposing skin layers. Therefore, prominent epicanthal folds in all Down syndrome patients should be examined carefully to identify hidden lacrimal fistula openings.

Congenital lacrimal fistula is mostly asymptomatic and tends to be overlooked, but active treatment may be indicated if tearing, inflammation, or cosmetic problems occur by lacrimal fistula, because it can be well obliterated by surgical treatment even in Down syndrome patients. However, even after successful obliteration of fistula, tearing may not be completely resolved owing to concomitant conditions such as nasolacrimal duct obstruction, epiblepharon,

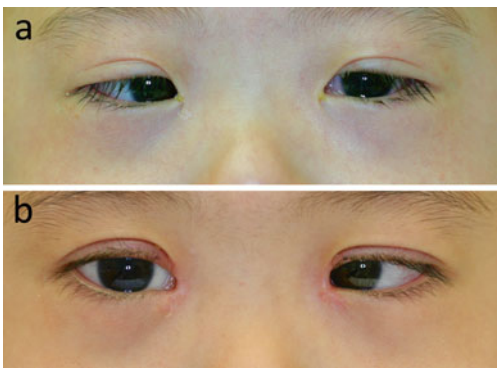

Fig. 1 A Down syndrome patient diagnosed with bilateral congenital lacrimal fistula and bilateral upper eyelid epiblepharon. (**a**) Note the bilateral lacrimal fistula and discharge at the fistula opening. (**b**) The patient underwent surgical excision of the bilateral lacrimal fistula, upper eyelid epiblepharon repair, and z-epicanthoplasty. Six weeks after the surgery, lacrimal fistula was well obliterated

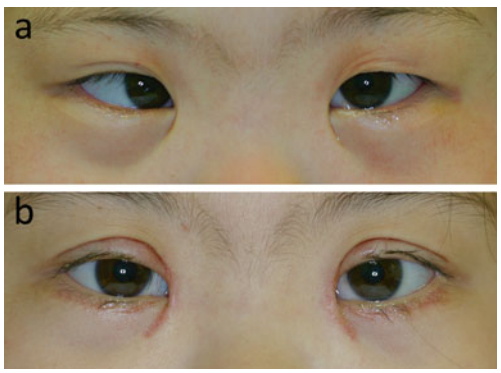

Fig. 2 A Down syndrome patient diagnosed with bilateral congenital lacrimal fistula, bilateral upper and lower eyelid epiblepharon, and prominent epicanthal folds. (**a**) Note that the prominent epicanthal folds are masking the lacrimal fistula opening. (**b**) Excision of bilateral lacrimal fistula, repair of upper and lower eyelid epiblepharon, and z-epicanthoplasty was performed. Three months after the surgery, lacrimal fistula was well obliterated, and epiblepharons were corrected

or prominent epicanthal fold, because these conditions frequently coexist with congenital lacrimal fistula and can cause not only cosmetic problems but also tearing and skin problems. Thus, these conditions should be evaluated carefully for appropriate management.

This study has a few limitations. First, it may be difficult to draw a meaningful conclusion from eight patients, even though the eight patients are the largest series of congenital lacrimal fistula in Down syndrome to the best of our knowledge. Second, prevalence of congenital lacrimal fistula in Down syndrome patients in current study maybe biased, because approximately only half of the Down syndrome patients from the pediatric clinic were referred to a single ophthalmology clinic and asymptomatic patients with fistula only may not be referred. Third, the high proportion of comorbidity of both congenital lacrimal fistula and nasolacrimal fistula might be overstated; because fistula alone may be asymptomatic and it is possible some lacrimal fistula patients without nasolacrimal duct obstruction were not referred.

In conclusion, the prevalence of lacrimal fistula is higher in Down syndrome patients than in the general population, and the fistula is frequently bilateral in these patients. Down syndrome patients should be thoroughly examined for congenital lacrimal fistula and for nasolacrimal duct obstructions, because those with congenital lacrimal fistula are likely to have accompanying nasolacrimal duct obstruction.

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