International Journal of Pediatric Otorhinolaryngology (2008) xxx, xxx–xxx

ELSEVIER

International Journal of Pediatric Otorhinolaryngology

www.elsevier.com/locate/ijporl

Postoperative airway events of individuals with CHARGE syndrome

Kim Blake [a,*], Jillian MacCuspie [b], Timothy S. Hartshorne [e], Mononita Roy [b], Sandra L.H. Davenport [c], Gerard Corsten [d]

[a] Dept. of Pediatrics, Dalhousie University, Canada
[b] Medical Students Dalhousie University, Canada
[c] Sensory Genetics/Neurodevelopment, Bloomington, MN, United States
[d] Dept. of Anesthesia, Dalhousie University, Canada
[e] Dept. of Psychology, Central Michigan University, United States

Received 14 May 2008; received in revised form 7 October 2008; accepted 10 October 2008

KEYWORDS
CHARGE syndrome;
Airway events;
Postoperative

Summary

Objective: CHARGE syndrome is a heterogeneous genetic disorder comprising multiple congenital anomalies. Major clinical diagnostic criteria include ocular coloboma, choanal atresia/stenosis, characteristic ear abnormalities, and cranial nerve abnormalities. CHARGE syndrome is caused by a mutation in the gene *CHD7* located on chromosome 8. Patients with CHARGE syndrome require multiple anesthetics for surgical and otorhinolaryngology procedures. This study describes the postoperative anesthetic related airway events (i.e. re-intubations for apneas and desaturations, airway obstruction due to excessive secretions) of nine individuals with CHARGE syndrome.

Methods: Detailed chart audits were performed on nine patients diagnosed clinically with CHARGE syndrome who had undergone surgery at a single tertiary health centre. The CHARGE characteristics present in each individual, the number and types of surgeries and anesthetics, and the related postoperative airway events were determined.

Results: The mean ± age of the population at chart review was 11.8 years (±8.0). The total number of anesthetics was 147, with a mean of 16.2(±8.4). Of the 215 surgical procedures (mean 21.9, ±12.2), 30% were otorhinolaryngological. Postoperative airway events occurred after 35% of anesthetics. Surgeries resulting in the most airway events involved the heart (65%), the gastrointestinal tract (39%), and airway diagnostic scopes, i.e., bronchoscopy, laryngoscopy, and nasopharyngoscopy (36%). Combining multiple surgical procedures under one anesthetic did not increase

* Corresponding author at: IWK Health Centre, 5850/5980 University Avenue, PO Box 9700, Halifax, NS, Canada B3K 6R8. Tel.: +1 902 470 6499; fax: +1 902 470 6913.
E-mail address: kblake@dal.ca (K. Blake).

0165-5876/$ – see front matter
doi:10.1016/j.ijporl.2008.10.005

Please cite this article in press as: K. Blake, et al., Postoperative airway events of individuals with CHARGE syndrome, Int. J. Pediatr. Otorhinolaryngol. (2008), doi:10.1016/j.ijporl.2008.10.005

the risk of postoperative airway events. As individuals aged, they had fewer surgeries and anesthetics, as well as a lower risk of postoperative airway events.
Conclusion: Individuals with CHARGE syndrome face a significant risk of postoperative airway events with anesthesia, and this is exacerbated by the high number of surgeries they require. Surgeons and anesthesiologists should be aware of potential for postoperative airway events in individuals with CHARGE syndrome and plan accordingly.

1. Introduction

CHARGE syndrome is a heterogeneous genetic disorder. There are four major clinical criteria for CHARGE syndrome [1], which are rare in other conditions; ocular coloboma, choanal atresia or stenosis, characteristic ear abnormalities (external and/or internal, including temporal bone anomalies) [2] and cranial nerve dysfunction [3–5]. Minor criteria include genital hypoplasia, delayed or incomplete pubertal development, cardiovascular malformations, growth deficiency and short stature, orofacial cleft, tracheoesophageal fistula, and characteristic CHARGE facial features [1]. Clinical diagnosis of CHARGE syndrome can be based on a combination of major and minor criteria. Other occasional findings in CHARGE syndrome include structural renal anomalies, and immune systems disorders (similar to DiGeorge Syndrome), and hand, limb, spine, and neck deformities [1,6].

Between 2001 and 2004, the Canadian Pediatric Surveillance Program identified 77 clinically confirmed cases of CHARGE syndrome in Canada, with an average national birth incidence of 3.5/100,000 live births [7]. However, the expected incidence with no gender difference, was estimated to be closer to 1:8500 by extrapolating from the Maritime Canadian data [8]. CHARGE syndrome is now known to be caused by a de novo genetic mutation in the gene *CHD7* located on the q12 arm of chromosome 8 [9]. The gene is speculated to have a role in the regulation of chromatin structure and gene expression, causing widespread effects in early embryonic development and accounting for the heterogeneous nature of the congenital anomalies in CHARGE syndrome [10]. However, approximately 40% of clinically diagnosed patients do not have a mutation in CHD7, suggesting that there may be genetic heterogeneity in the condition [11]. Statistically, advanced parental age has been found in concordance with sporadic cases of CHARGE syndrome [6,12].

Children with CHARGE syndrome undergo many surgical procedures often starting as a neonate [13] and are therefore potentially at high risk for postoperative anesthetic airway events [13]. It is known that tracheal intubation may be difficult in syndromes that have similar anatomic anomalies to CHARGE, such as Moebius sequence [14]. Many cranial facial syndromes have preoperative, inhalation concerns; however, it is also the postoperative airway events that are of concern in CHARGE syndrome. There has been concern that the CHARGE population are at increased risk for demise and airway events in the recovery phase of anesthesia [13].

By examining, in detail, medical records of nine patients with CHARGE syndrome who underwent surgery at one institution, we determined the number and type of anesthetics, surgeries and related airway events. The CHARGE clinical characteristics and surgical procedures that may correlate with the postoperative airway events were also determined.

2. Methods

The IWK Health Centre in Halifax, Nova Scotia, is a tertiary referral centre for patients with CHARGE Syndrome servicing the Maritime Canadian Provinces. Following Institutional Research Ethics Board approval, detailed chart reviews were performed on nine patients with a clinical diagnosis of CHARGE Syndrome. This cohort represents, as far as we know, the entire Maritime Canadian CHARGE syndrome population. Two additional patients, one who died in the neonatal period, and one born during the course of this study, were not included.

The charts were assessed for patient demographics including major and minor CHARGE clinical criteria, and age of the patient at the time of anesthesia. The anesthetic technique used, the number of surgical procedures per anesthetic, as well as nature of procedure performed were recorded. Surgical procedures were grouped into eight categories defined by the consensus of the investigating authors. Adverse postoperative airway events were also recorded. They were defined as airway events that occurred in the immediate postoperative recovery phase and were severe enough to have been recorded in the anesthesia record and

Please cite this article in press as: K. Blake, et al., Postoperative airway events of individuals with CHARGE syndrome, Int. J. Pediatr. Otorhinolaryngol. (2008), doi:10.1016/j.ijporl.2008.10.005

Table 1 Phentotypic CHARGE features of study cohort of nine individuals with CHARGE syndrome.

	Age at review (years)	Coloboma[a,b]	BPCA[a,b]	CN[a,b]	Ear[a,b]	Cleft palate	CVS	GERD	Feeding diff.	Facial palsy	T.F.	Gene
1	1.5[a]	+	−	+	+	−	m	+	+	+	−	Y
2	8	+	−	+	+	+	M	+	+	+	−	n/a
3	8	+	−	+	+	−	M	−	+	−	−	n/a
4	8	+	+	+	+	−	M	+	+	+	−	Y
5	8	+	−	+	+	−	m	+	+	+	−	Y
6	13	+	−	+	+	+	m	+	−	−	−	Y
7	11	+	−	+	+	+	M	+	+	+	−	n/a
8	28	−	−	+	+	+	m	+	+	−	+	n/a
9	21	+	−	+	+	+	M	−	+	+	+	Y

BPCA: bilateral posterior choanal atresia (does not include choanal stenosis or unilateral choanal atresia); CNS: cranial nerve dysfunction-olfactory nerve anomalies, sensorineural deafness, neurologically based swallowing problems; Ear: external, middle and/or inner ear anomalies. CVS: cardiovascular system; M: major (tetralogy of Fallot, double outlet right (ventricle); m: minor (patent ductus arteriosus, vascular ring); GERD: gastroesophageal reflux disease; Feeding diff.: not tolerating oral feeds, requiring tube feeding; TF: tracheoesophageal fistula; Gene: positive for CHD7 gene mutation (Y); n/a: not available.

[a] Patient moved at the age of 1.5 years, after which charts were unavailable.

[b] Major criteria for clinical diagnosis of CHARGE Syndrome.

require medical intervention and management by an anesthesiologist.

3. Statistical analysis

The data were examined to determine which, if any CHARGE clinical characteristics were predictive of postoperative anesthetic airway events and to enumerate the number and types of surgical procedures and anesthetics that CHARGE patients undergo. Continuous data are presented as means and standard deviations and categorical data are presented as percentages and proportions. Fisher's exact test was utilized for statistical analysis of categorical data, and $p < 0.05$ was considered significant.

4. Results

4.1. Demographics

The cases reviewed ($n = 9$) consisted of four females and five males. Age at the time of chart review ranged from 1.5 to 28 years (mean = 11.8, S.D. = 8.0). The mean age at the time of first surgical procedure ranged from 1 to 52 days with a mean age of 22 days (S.D. = 17.9).

The phenotypic features of these cases and the presence or absence of the *CHD7* gene mutation where data was available is presented in Table 1. The five individuals who had been tested for the gene mutation were positive, while the remaining four had not yet been tested. In total, the nine individuals underwent 215 surgeries (range 6—40)

Table 2 Number of surgeries, anesthetics, and postoperative airway events in nine (1—9) individuals with CHARGE syndrome.

	Number of surgeries	Number of anesthetics	Number of airway events	% anesthetics resulting in airway events
1	8	3	3	100
2	22	16	11	82
3	19	14	8	57
4	36	15	8	53
5	27	18	6	33
6	6	6[a]	1	25[b]
7	40	30	8	27
8	20	20	3	15
9	37	25	3	12
Total	215	147	51	35

[a] Records only available for four of six anesthetics.

[b] Of the available records, 25% of anesthetics resulted in airway events.

Please cite this article in press as: K. Blake, et al., Postoperative airway events of individuals with CHARGE syndrome, Int. J. Pediatr. Otorhinolaryngol. (2008), doi:10.1016/j.ijporl.2008.10.005

and 147 anesthetics (mean = 16.2, S.D. = 8.4, range 3—30) (Table 2). The mean number of surgeries per individual was 21.9 (S.D. = 12.2). There were five anesthesia records that did not specify the type of anesthetic used, and two of those did not have information regarding postoperative airway events.

4.2. Anesthetics and airway events

The mean length of anesthetics for all surgeries was 123.8 (S.D. = 31.6) min (range 87—195 min). The anesthetic techniques utilized are summarized in Table 3. Fifty-one of 145 anesthetics resulted in airway events (35%) that occurred postoperatively (Table 2). All but one individual underwent at least one anesthetic with multiple (two or more) surgical procedures.

The most common postoperative anesthesia airway event was decreased O_2 saturations requiring intervention ($n = 23$). Other postoperative events included excessive secretions resulting in airway obstruction and requiring continuous suctioning ($n = 13$), prolonged crackles and wheezing with coughing and concerns of aspiration ($n = 11$), arrhythmias or other heart rate abnormalities ($n = 9$), decrease in respiratory rate or erratic breathing ($n = 7$), stridor ($n = 6$), failed extubations ($n = 4$), metabolic acidosis ($n = 2$), atelectasis ($n = 1$), and pneumothorax ($n = 1$).

Table 4 presents the number of single and multiple procedures and anesthetics the population underwent as well as the rate of airway events present after each anesthetic. Single procedure anesthetics resulted in airway events 39% (37/94) of the time, while 25% (13/51) of all multiple procedure anesthetics resulted in airway events, which was not statistically significant (fisher exact test $p = 0.103$). Postoperative anesthetic-related airway events had the highest rate of occurrence following procedures involving the heart (13/20, 65%), the gastrointestinal tract (12/31, 39%), and diagnostic scopes involving the airway (laryngoscopy, bronchoscopy, or nasopharyngoscopy) (8/22, 36%) (Table 5). Airway events occurred at least once during each type of surgical procedure, except for those involving the eyes (Table 5).

An anesthetic-related postoperative airway event was more likely to occur when the individual had feeding difficulties requiring a G-tube or a Nissen fundoplication (Table 6). Individuals with a cleft palate (repaired or not), underwent 97 anesthetics with 27 of these resulting in postoperative airway events. Individuals without a cleft palate underwent 48 anesthetics, with 25 of these resulting in postoperative airway events. A significantly higher risk of postoperative airway events was in the no cleft palate group, than individuals with a cleft palate or repaired cleft palate (Fisher's exact test $p = 0.0057$).

Of the three patients in our study who had a tonsillectomy and adenoidectomy (T and A), two had subsequent improved postoperative recovery with shorter recovery times, fewer airway problems and no unplanned admissions to ICU>. One had no change in their postoperative recovery, but this patient had more severe problems with postoperative anesthesia airway events before they had a T and A.

Table 3 Anesthetic technique utilized during surgical procedures performed on nine individuals with CHARGE syndrome.

	# of anesthesias	% of total (total = 142[a])
Inhalational induction		
Halothane	47	32.6
Sevoflurane	37	25.7
Isoflurane	66	45.8
Intravenous induction (hypnotics)		
Propofol	48	33.3
Thiopentol	18	12.5
Ketamine	40	27.8
Midazolam	14	9.7
Muscle relaxants		
Succinylcholine	32	22.2
Pancuronium	12	8.3
Rocuronium	26	18.1
Vecuronium	15	10.4
Mivacurium	13	9.0
Atracuronium	3	2.0
Neostigmine	22	15.3
D-Tubocurarine	4	2.8
Prostigmine	1	0.7
Opioids		
Morphine	14	9.7
Fentanyl	42	29.2
Sufentanyl	16	11.1
Meperidine	5	3.5

[a] There are five anesthetics where there is no anesthetic record.

Table 4 Frequency of surgical procedures per anesthetics with resulting postoperative airway events in nine individuals with CHARGE syndrome.

Number of surgical procedures per anesthetic	Frequency	Percent resulting in airway events
1	94	39% ($n = 37/94$)
2	36	22% ($n = 8/36$)
3+	15	33% ($n = 5/15$)

Please cite this article in press as: K. Blake, et al., Postoperative airway events of individuals with CHARGE syndrome, Int. J. Pediatr. Otorhinolaryngol. (2008), doi:10.1016/j.ijporl.2008.10.005

Table 5 Number and types of surgical procedures performed on nine individuals with CHARGE syndrome and resulting rate of postoperative airway events.

Categorization of surgical procedures	Number of surgical procedures	Number of airway events	% of surgical procedure resulting in airway events
Ears	46	1	2.2
Gastrointestinal tract	31	12	38.7
Nose/throat	30	6	20.0
Dental	26	1	3.8
Diagnostic scopes	22	8	36.4
Heart	20	13	65.0
Eyes	6	0	0
Other	34	10	29.4
Total	215	51	23.7

Minor ear procedures: debridement of ears, examination under anesthesia (EUA), myringotomy tubes; diagnostic scopes (airway): nasopharyngoscopy, laryngoscopy, bronchoscopy; gastrointestinal tract: gastrostomy/jejunostomy tube, Nissen fundoplication, G button insertion and change; nose/throat: cleft lip/palate repair, choanal atresia repair and redilatations, tonsillectomy, adenoidectomy; dental: cleaning, cavities, extractions; heart: total repair, shunts, vascular ring and patent ductus ligations; eyes: examination under anesthesia, insertion of weights in eyelid; other: nephrotomy tube insertion/repair, hernia repair, circumcision, removal of granuloma, CT scan, lung scan, transthoraic echocardiogram, X-ray, skin biopsy, MRI, cochlear implant.

Table 6 Feeding procedures or surgical measures required and rates of postoperative airway events in nine individuals with CHARGE syndrome.

	Number of anesthesias	Airway event	No airway event	Significance
G/J tube	82	36	46	Yes, $p = 0.0092$
No G/J tube	63	15	48	
Nissens fundoplication	79	33	46	Yes, $p = 0.049$
No Nissens fundoplication	66	18	48	

As they aged, the number of surgical procedures individuals underwent as well as the number of anesthetics generally decreased (Table 7), along with the number of postoperative airway events. After age 7, surgical procedures for these individuals skipped some years, but there were only two complications for the additional 24 anesthetics.

5. Discussion

The numerous structural and functional anomalies associated with CHARGE syndrome have many implications for surgical and anesthetic care. In the neonatal period, bilateral posterior choanal atresia, cyanotic heart disease [15] and tracheoesophageal fistula [16] require emergency surgery and can be a

Table 7 Mean surgeries, anesthetics undergone, and postoperative airway events resulting from anesthetics as nine individuals with CHARGE syndrome aged.

Age	Mean surgeries	Mean anesthetics	Mean complications from anesthetic	Mean % complications from anesthetic	Total % complications from anesthetic
0—1[a]	5.9(±3.2)	4.7(±2.4)	2.2(±1.7)	46.8% (2.2/4.7)	48% (20/42)
1—2[a]	3.7(±1.7)	2.3(±1.3)	1.3(±1.3)	56.5% (1.3/2.3)	54% (12/22)
2—3	3.5(±2.3)	2.4(±1.9)	0.8(±0.7)	33.3% (0.8/2.4)	32% (6/19)
3—4	2.5(±1.8)	1.5(±1.0)	0.8(±0.8)	53.3% (0.8/1.5)	50% (6/12)
4—5	2.5(±2.4)	1.4(±1.0)	0.3(±0.4)	21.4% (0.3/1.4)	18% (2/11)
5—6	1.3(±1.0)	0.9(±0.6)	0.1(±0.3)	11.1% (0.1/0.9)	14% (1/7)
6—7	1.9(±1.6)	1.0(±0.7)	0.3(±0.4)	30.0% (0.3/1.0)	25% (2/8)
7+	7.6(±8.8)	4.8(±5.8)	0.4(±0.5)	8.3% (0.4/4.8)	8.3% (2/24)

[a] Means for these age groups are representative of nine individuals. The remainders are for eight individuals only, with the exception of age 7+, where data was only available for five individuals.

Please cite this article in press as: K. Blake, et al., Postoperative airway events of individuals with CHARGE syndrome, Int. J. Pediatr. Otorhinolaryngol. (2008), doi:10.1016/j.ijporl.2008.10.005

challenge for the surgeon and anesthesiologist. The patient with CHARGE syndrome moves through an ordeal of numerous surgeries and procedures that require multiple anesthetics, many of which may lead to postoperative airway events.

In this study, the detailed chart review of nine individuals with CHARGE syndrome serviced by the only tertiary care hospital in the Maritime Provinces revealed that 35% of anesthetics resulted in postoperative anaesthesia airway events. These airway events ranged in severity from re-intubation and admission to Intensive Care Unit to obstruction of the airway with excessive secretions and desaturation requiring medical management and action by the anesthesiologist. The majority of airway events were found to occur after surgical procedures that involved the cardiovascular system, diagnostic scopes (laryngoscopy, bronchoscopy, and nasopharyngoscopy), and procedures involving the gastrointestinal tract. Airway events were found to have occurred at least once after almost every type of surgical procedure except those involving the eyes. Anatomical anomalies of the upper airways may be one reason for the postoperative airway events [13]. We hypothesize that the difficulties in handling oral secretions, which may be the result of cranial nerve anomalies, may also play an important role. Cranial nerves IX and X have been implicated as having abnormal function and so may prevent swallowing and coping with an increase in secretions that often occur after anesthesia [3].

In an earlier study Stack and Wyse found that individuals experienced more anesthesia related airway events as they age [17]. In contrast, the CHARGE population in this study experienced fewer surgeries, fewer anesthetics, and a lower percentage of anesthetic-related airway events as they aged. This may have been the result of this population undergoing more multiple procedures under a single anesthetic, or that the surgical procedures most associated with anesthetic airway events, such as cardiovascular and gastrointestinal, are most likely to occur earlier in the child with CHARGE's life.

Individuals with CHARGE who required a Nissen fundoplication or a gastrostomy/jejunostomy tube insertion were found to be at significantly higher risk for anesthetic airway events than those who did not. It has been postulated that the CHARGE population is at significant risk for severe gastroesophageal reflux and increased upper airway secretions [18]. Those with severe feeding difficulties require tube feeding for an extended period, sometimes for years [19].

In our population, individuals with a cleft palate in our sample (even when repaired) were less likely to experience anesthetic airway events than those who did not have a cleft palate. In general, cleft palate is not recognized as having any sort of protective effect for anesthetic airway events. However, it is possible that the children with cleft palate (even following repair) may have an impact on postoperative complications because of the associated wider nasopharyngeal air space, especially compared to those children with CHARGE who have had choanal atresia. As children with CHARGE also have neurologic dysfunction, poor motor control of swallowing and gastroesophageal reflux, having a wider nasopharyngeal air space may allow better drainage of secretions that would otherwise contribute to postoperative airway complications. In one of the few studies of an adolescent and adult population of CHARGE syndrome individuals, Blake et al. found that oral facial clefts were three times more prevalent (57%) in the study group than in the estimated population frequency of clefting (15–20%) [20]. One hypothesis from this study was that the cleft palate, even when repaired, could be a survival phenomenon because the clefting produced a large anatomical space [20].

Patients with CHARGE may have problems with airway obstruction due to enlarged or prominent tonsils and adenoids. Anecdotal comments from families of individuals with CHARGE indicate that once their children had a tonsillectomy and or adenoidectomy they coped much better with their airway during and after anesthesia. These children were noted by their parents to have improved sleep, less snoring, less waking with cough, and improved postoperative recovery. This requires further investigation, especially as limited literature exists on this issue.

Gene positive individuals with CHARGE who do not have the complete clinical spectrum as defined by major and minor clinical criteria may not have the same pattern of problems with anesthesia as individuals at the severe end of the CHARGE phenotypic spectrum [21]. However, it is possible that they have not been challenged with as many surgeries and anesthetics. This is yet to be determined, and a prospective study of the milder CHARGE phenotype population is needed.

Patients with CHARGE face a significant risk of airway events following anesthesia, and the high number of surgical procedures that they require exacerbates this risk. In many instances, two or more surgical procedures were combined under one anesthetic. This was not found to increase the risk of anesthetic related complication. Thus, combining procedures to reduce the number of anesthetics CHARGE patients undergo may be a useful strategy in risk reduction. Regardless of the

Please cite this article in press as: K. Blake, et al., Postoperative airway events of individuals with CHARGE syndrome, Int. J. Pediatr. Otorhinolaryngol. (2008), doi:10.1016/j.ijporl.2008.10.005

type of surgical procedure, or the phenotypic features of patients with CHARGE, anesthesiologists should be aware that these patients might face an increased risk of postoperative airway events when receiving anesthesia.

6. Limitations

The generalizability of this study may be limited due to the small sample size of the population cohort. However, this cohort seems to be comparable to the Canadian CHARGE syndrome population as a whole [8]. Although we are unaware of the *CHD7* gene mutation status of four of the nine individuals in this study, there is a known positive correlation with the combination of cardiovascular malformation, coloboma, and facial asymmetry (which these individuals had) with the occurrence of the *CHD7* mutation. This study was retrospective in nature and relied on chart reporting. Our meticulous review of individual charts uncovered a greater number of details therefore are probably more representative of the complications related to anesthesia than the information available with questionnaires from larger Canadian studies [8].

7. Conclusions

Individuals with CHARGE syndrome who meet the clinical diagnostic criteria undergo frequent surgical procedures requiring multiple anesthetics throughout their lifetime. Postoperative airway events are common and can occur during or after multiple types of surgical and otorhinolaryngology procedures. Combining multiple procedures under one anesthetic does not lead to an increased risk of postoperative airway events. We propose this as a useful strategy to lower the number of anesthetics and the overall risk of airway events. Postoperative airway events can occur at any age, and happen regardless of the complexity of surgical procedure. Nissen's fundoplication, or gastrostomy and junostomy feeding individuals with CHARGE may be at particular high risk for postoperative airway events. Anesthesiologists should be aware of the high risk of postoperative airway events faced by individuals with CHARGE syndrome and plan accordingly.

Conflict of interest

The authors state that there are no conflicts of interest.

References

[1] K.D. Blake, S.L. Davenport, B.D. Hall, M.A. Hefner, R.A. Pagon, M.S. Williams, et al., CHARGE association: an update and review for the primary pediatrician, Clin. Pediatr. (Phila) 37 (3) (1998) 159–173.
[2] J. Amiel, T. Attiee-Bitach, R. Marianowski, V. Cormier-Daire, V. Abadie, D. Bonnet, et al., Temporal bone anomaly proposed as a major criteria for diagnosis of CHARGE syndrome, Am. J. Med. Genet. 99 (2) (2001) 124–127.
[3] K. Blake, T. Harthorne, C. Lawand, N. Dailor, J.W T.Thelin, Cranial Nerve Manifestations in CHARGE Syndrome, Am. J. Med. Genet. A. 146A (5) (2008) 585–592.
[4] M. Jongmans, L. Hoefsloot, K. van der Donk, R. Admiraal, A. Magee, I. van der Laar, et al., Familial CHARGE syndrome and the CHD7 gene: a recurrent missense mutation, intrafamilial recurrence and variability, Am. J. Med. Genet. A. 146A (1) (2008) 43–50.
[5] D. Sanlaville, A. Verloes, CHARGE syndrome: an update, Eur. J. Hum. Genet. 15 (4) (2007) 389–399.
[6] A.L. Tellier, V. Cormier-Daire, V. Abadie, J. Amiel, S. Sigaudy, D. Bonnet, et al., CHARGE syndrome: report of 47 cases and review, Am. J. Med. Genet. 76 (5) (1998) 402–409.
[7] K. Blake, J.M. Graham Jr., C. Prasad, I.M. Smith, CHARGE Association/Syndrome, Can. Pediatr. Surveill. Prog. Res. (2003) 20–24.
[8] K.A. Issekutz, J.M. Graham Jr., C. Prasad, I.M. Smith, K.D. Blake, An epidemiological analysis of CHARGE syndrome: preliminary results from a Canadian study, Am. J. Med. Genet. A 133 (3) (2005) 309–317.
[9] L.E. Vissers, C.M. van Ravenswaaij, R. Admiraal, J.A. Hurst, B.B. de Vries, I.M. Janssen, et al., Mutations in a new member of the chromodomain gene family cause CHARGE syndrome, Nat. Genet. 36 (9) (2004) 955–957.
[10] T. Woodage, M.A. Basrai, A.D. Baxevanis, P. Hieter, F.S. Collins, Characterization of the CHD family of proteins, Proc. Natl. Acad. Sci. U.S.A. 94 (21) (1997) 11472–11477.
[11] S.R. Lalani, A.M. Safiullah, S.D. Fernbach, K.G. Harutyunyan, C. Thaller, L.E. Peterson, et al., Spectrum of CHD7 mutations in 110 individuals with CHARGE syndrome and genotype–phenotype correlation, Am. J. Hum. Genet. 78 (2) (2006) 303–314.
[12] K.D. Blake, D. Brown, CHARGE association looking at the future—the voice of a family support group, Child Care Health Dev. 19 (6) (1993) 395–409.
[13] K.D. Blake, I.M. Russell-Eggitt, D.W. Morgan, J.M. Ratcliffe, R.K. Wyse, Who's in CHARGE? Multidisciplinary management of patients with CHARGE association, Arch. Dis. Child. 65 (2) (1990) 217–223.
[14] W.A. Ames, T.M. Shichor, M. Speakman, R.M. Zuker, C. McCaul, Anesthetic management of children with Moebius sequence, Can. J. Anaesth. 52 (8) (2005) 837–844.
[15] R.K. Wyse, S. al-Mahdawi, J. Burn, K. Blake, Congenital heart disease in CHARGE association, Pediatr. Cardiol. 14 (2) (1993) 75–81.
[16] M. Kutiyanawala, R.K. Wyse, R.J. Brereton, L. Spitz, E.M. Kiely, D. Drake, et al., CHARGE and esophageal atresia, J. Pediatr. Surg. 27 (5) (1992) 558–560.
[17] C.G. Stack, R.K. Wyse, Incidence and management of airway problems in the CHARGE Association, Anaesthesia 46 (7) (1991) 582–585.
[18] C. Dobbelsteyn, D.M. Marche, K. Blake, M. Rachid, Early oral sensory experiences and feeding development in children with CHARGE syndrome: a report of five cases, Dysphagia 20 (Spring (2)) (2005) 89–100.
[19] C. Dobbelsteyn, S.D. Peacocke, K. Blake, W. Crist, M. Rachid, Feeding difficulties in children with CHARGE syn-

Please cite this article in press as: K. Blake, et al., Postoperative airway events of individuals with CHARGE syndrome, Int. J. Pediatr. Otorhinolaryngol. (2008), doi:10.1016/j.ijporl.2008.10.005

drome: prevalence, risk factors, and prognosis, Dysphagia 23 (2) (2008) 127–135.
[20] K.D. Blake, N. Salem-Hartshorne, M.A. Daoud, J. Gradstein, Adolescent and adult issues in CHARGE syndrome, Clin. Pediatr. (Phila) 44 (2) (2005) 151–159.
[21] M.C. Jongmans, R.J. Admiraal, K.P. van der Donk, L.E. Vissers, A.F. Baas, L. Kapusta, et al., CHARGE syndrome: the phenotypic spectrum of mutations in the CHD7 gene, J. Med. Genet. 43 (4) (2006) 306–314.

Please cite this article in press as: K. Blake, et al., Postoperative airway events of individuals with CHARGE syndrome, Int. J. Pediatr. Otorhinolaryngol. (2008), doi:10.1016/j.ijporl.2008.10.005