Original Article

Congenital anterior glottic webs: a retrospective review of 59 cases with management and outcomes

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Contributions: (I) Conception and design: A Daniel, AT Cheng; (II) Administrative support: AT Cheng; (III) Provision of study materials or patients: A Lathif, A Daniel, AT Cheng; (IV) Collection and assembly of data: A Daniel; (V) Data analysis and interpretation: A Daniel, M Ellis; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Background: Congenital anterior glottic webs are rare anomalies which present with a wide spectrum of symptoms and are managed in endoscopic and open approaches. We present 37 years of a single centre experience in the management of congenital anterior laryngeal webs to establish which factors may influence outcomes.

Methods: A retrospective review looking at all anterior laryngeal webs managed at a quaternary referral centre across four decades. Patient demographic information, clinical signs, symptoms, co-morbidities, and management was recorded and outcomes analysed.

Results: A total of 59 patients were identified as having an anterior glottic web. 22q11.2 deletion syndrome was diagnosed in 61% of patients. Lower grade webs were commonly managed conservatively or with endoscopic division, while higher grade webs were managed by external laryngotracheal reconstruction (LTR). There was an association with recurrence and revision surgery with the grade of web. We found no associations with recurrence and revision surgery with age at diagnosis, age at time of first surgical procedure, sex, surgical technique or underlying genetic abnormality.

Conclusions: Congenital anterior glottic webs should be suspected when the neonate or young infant presents with dysphonia or respiratory distress. Diagnosis should be made on direct visualisation, and consideration for genetic analysis and cardiac workup should be made given the high association with congenital anterior glottic webs. Endoscopic surgical division should be reserved for low grade webs and open procedures for high grade webs irrespective of sex, age and underlying genetic condition.

Keywords: Laryngeal; glottic; webs; airway; paediatric

Received: 10 October 2020; Accepted: 02 March 2021; Published: 25 March 2021.
doi: 10.21037/ajo-20-76
View this article at: http://dx.doi.org/10.21037/ajo-20-76

Introduction

Congenital anterior glottic webs are rare anomalies seen in disrupted embryogenesis of the vocal cords. The development of these webs still remains unclear and are thought to be associated with abnormal development of either the vacuolization of the epithelial lamina, the laryngeal caecum or the pharyngotracheal duct (1). They present with a spectrum of symptoms and signs which can range from an altered cry to severe airway obstruction (2). They are characterised by their position (anterior or posterior), involvement of the subglottic area and whether it is congenital or acquired (3). Seymour Cohen proposed an internationally accepted staging system for characterising anterior glottic webs relying on the

Table 1 Cohen grading system for congenital anterior glottic webs

Grade	Vocal cord involvement	Thickness	Subglottic involvement
1	<35%	Uniform thin	Little or none
2	35–50%	Thin or moderately thick	Minimal
3	50–75%	Thick anteriorly and thin posteriorly	Extends to lower part of cricoid
4	75–90%	Uniformly thick	Extends to lower cricoid

degree of obstruction and extent of the web, the degree of involvement with the glottis and whether there was extension into the subglottis (*Table 1*) (3). This has implications on the functionality of the glottic mechanism, its effect on respiration, airway protection and vocal quality.

Anterior glottic webs can be found as an isolated congenital anomaly or as a part of a syndrome such as the 22q11.2 deletion syndrome (22q11.2DS) previously known as velo-cardio-facial syndrome (4). The management of anterior glottic webs involves achieving adequate respiration with a protective cough and improved phonation.

A range of surgical techniques have been proposed; endoscopic approaches include the use of knife and/or scissor division (cold steel), CO2 laser incisions, and protecting the newly created airway with keel placement and/or mitomycin C application (2). In higher grade webs, patients may present with severe respiratory distress at birth and this may require a tracheostomy followed by a staged endoscopic or external approach laryngotracheal reconstruction (LTR) (2).

Currently there is limited data given a lack of population cases to address questions related to outcomes of different management modalities, associations related to recurrence and revision surgery including underlying congenital diagnosis and phonation outcomes. The aim of this study is to present a retrospective analysis of 37 years experience at a quaternary referral paediatric hospital in the management of congenital anterior laryngeal webs. We describe the largest series to our knowledge and analyse the outcomes of endoscopic surgery on recurrence and revision surgery and the factors that lead to it in order to provide a management algorithm for other institutions. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/ajo-20-76).

Methods

A retrospective analysis was performed of children's medical records coded as having a glottic web at the Children's Hospital at Westmead from 1983 to 2020. Inclusion criteria include anterior glottic webs discovered on direct laryngoscopy in patients under 18 years of age at diagnosis. The exclusion criteria were webs of traumatic, infectious or granulomatous aetiology, non-anterior glottic webs, patient age over 18 years at diagnosis and if full patient data was not available. Demographic information, clinical signs, management and follow up data was collected from the medical records. Ethical approval for the study was granted by the Sydney Children's Hospital Network Human Research Ethics Committee (2020/ETH01068) and individual consent for this retrospective analysis was waived. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Low grade webs are defined as those classified as grade 1 or 2 on the Cohen system, grade 3 and 4 webs formed the definition of high grade webs. When used during an external LTR, the laryngeal keel consisted of autologous perichondrial tissue attached as part of anterior graft placement while silastic keels are used only in endoscopic placement. When used, mitomycin C was administered as a 0.4 mg/mL topical dose and applied for a total of 4 minutes.

The outcome measures were recurrence as defined from either a flexible nasendoscopic or laryngoscopic visualization of a recurrent web, and revision surgery as defined as requiring any further intervention on the airway (not including a diagnostic laryngobronchoscopy). We also measured the decannulation rate following tracheostomy.

Statistical methods

Continuous demographic variables are described with mean and standard deviation for normally distributed data, skewed data is presented with median and interquartile range. The outcome measures used in statistical analysis of patients undergoing division of anterior glottic web were recurrence and requirement for revision surgery. Categorical groups

Table 2 Characteristics of 59 patients with congenital anterior glottic webs. Multiple presenting symptoms were present for 8 patients and multiple synchronous airway lesions were present for 7 patients

Variable	n (%)
Incidence of presenting symptoms	
Dysphonia or aphonia	24 (40.7%)
Stridor	17 (28.8%)
Respiratory distress	16 (27.1%)
Recurrent croup	4 (6.8%)
Chronic cough	4 (6.8%)
Asymptomatic	1 (1.7%)
Not recorded	3 (5.1%)
Incidence of synchronous airway pathology	
No other synchronous lesion	26 (44.1%)
Subglottic stenosis	22 (37.3%)
Tracheobronchomalacia	11 (18.6%)
Laryngomalacia	6 (10.2%)
Laryngeal cleft	1 (1.7%)

were compared using the Chi square test where at least 10 subjects were present in each group, and Fisher's exact test otherwise. Patients were stratified by age into categories of less than or greater than one year.

Univariate analyses and reverse stepwise multivariate logistic regression analysis were performed of risk factors for recurrence and revision surgery. Covariates were excluded from the model if the change in likelihood ratio had significance greater than P=0.1. The level of statistical significance was taken as P<0.05. Statistical analysis of results was performed using SPSS version 24 (IBM, New York, USA).

Results

Study population

A total of 164 cases of glottic web were identified and following exclusions, 59 cases of congenital anterior glottic webs met the inclusion criteria. The median age at diagnosis was 2 months (IQR, 0–8 months), 29 patients (49.2%) were male. Dysphonia was the most common presenting symptom (40.7%) followed by stridor (28.8%) and respiratory distress (27.1%). The incidence of all presenting symptoms is shown in *Table 2*. There were multiple presenting symptoms for 8 (13.6%) patients. Glottic web was the sole airway abnormality for 26 (44.1%) patients. One concurrent airway lesion was present for 26 (44.1%) patients and two additional lesions were identified for 7 (11.9%) patients. The incidence of presenting symptoms and synchronous airway lesions is shown in *Table 2*.

22q11.2 DS was diagnosed in 36 patients (61.0%) and other genetic abnormalities were diagnosed in a further 4 patients (6.8%). A positive family history was present for 2 patients (3.4%). The proportion of high grade webs was greater in patients with synchronous airway lesions (57.5%) compared with those having solely an anterior glottic web (23.0%), (Fisher's exact, P=0.008). There was no association between the grade of glottic web and presence of 22q11.2 DS (Chi square, P=0.928), any genetic syndrome (Chi square, P=0.412), cardiac comorbidity (Chi square, P=0.928), positive family history (Fisher's exact, P=0.318), gender (Chi square, P=0.879), age group at diagnosis (Fisher's exact, P=1.000) or age group at treatment (n=36, Chi square P=0.979). Congenital heart anomalies were diagnosed in 24 patients (40.7%) in which 79.2% (19/24) of those diagnosed were also found to have 22q11.2 DS (Fisher's exact P=0.023). Common cardiac lesions included atrial septal defects (8 patients, 13.6%) and ventricular septal defects (7 patients, 11.9%). Other less common cardiac conditions found included coarctation of aorta (4 patients, 6.8%) and Tetralogy of Fallot (3 patients, 5.1%). Low grade webs (grade 1–2) as a whole were more common than higher grade webs (grade 3–4) with grades 1 and 2 comprising 25.4% and 32.3% respectively and grades 3 and 4 comprising 28.8% and 13.6% of congenital anterior glottic webs as highlighted in *Table 3*.

Overall surgical and endoscopic management summary

The median age at time of surgery for grade 1 webs was 39 months (IQR, 6–72 months), grade 2 webs was 3 months (IQR, 1.25–16.5 months), grade 3 was 6 months (IQR, 3–4 months) and grade 4 was 2 months (IQR, 0–4 months). Endoscopic surgical division of web was performed for 30 patients (50.8%); 22 patients (73.3%) underwent a cold steel division with 8 patients (26.7%) undergoing a laser division (*Table 3*). Following cold steel dissection, mitomycin C was administered for 3 patients and a further 3 patients had insertion of a keel.

LTR was performed as the initial management for 13 patients (22%) whom all had high grade webs (grade

Table 3 Summary of management of anterior glottic webs by grade and management modality

Classification	Grade of web	Number of patients	Number divided endoscopically	Number managed with LTR	Number managed conservative
Low grade	1	15 (25.4%)	2 (13.3%)	0 (0.0%)	13 (86.7%)
	2	19 (32.2%)	19 (100%)	0 (0.0%)	0 (0.0%)
High grade	3	17 (28.8%)	7 (41.2%)	10 (59.8%)	0 (0.0%)
	4	8 (13.6%)	2 (25%)	3 (37.5%)	3 (37.5%)*

*These patients had a tracheostomy placement at time of birth.

Table 4 Recurrence and Revision surgery rate following endoscopic division of web (n=59)

Classification	Grade of web	Number of patients	Number divided endoscopically	Web recurrence rate	Revision surgery rate
Low grade	1	15 (25.4%)	2 (13.3%)	0 (0.0%)	0 (0.0%)
	2	19 (32.3%)	19 (100%)	6 (31.6%)	5 (26.3%)
High grade	3	17 (28.8%)	7 (41.2%)	7 (100%)	6 (85.7%)
	4	8 (13.6%)	2 (25%)	2 (100%)	2 (100%)

3–4). It is the senior author's preference to do a single stage LTR and avoid a tracheostomy. Three of these patients subsequently developed recurrence of anterior web and one patient required a further endoscopic excision of the residual web. Of the patient's with grade 4 webs who did not have their web treated, 2 of the 3 died around birth due to comorbidities, and the third is awaiting a planned LTR. Tracheostomy was required for 15 patients (25.4%) of which 13 were diagnosed with a high grade laryngeal web (86.7%). Of the patients with low grade webs requiring tracheostomy insertion, one patient concurrently had severe laryngomalacia which was managed with laser supraglottoplasty complicated by posterior glottic stenosis requiring tracheostomy insertion. The other patient had tracheostomy insertion as a bridge to laser division treatment of a grade 2 web. All of those patients with high grade webs had a tracheostomy insertion prior to management of the web. Out of the 15 patients who had tracheostomy placement, 13 (86.7%) of those were successfully decannulated.

Endoscopic management of anterior glottic webs

A total of 21 patients with low grade webs and 9 patients with high grade webs underwent endoscopic surgical division. High grade webs had significantly higher rates of recurrence (Fisher's exact P<0.001) and revision surgery (P=0.002) than low grade webs as highlighted in *Table 4*.

The overall recurrence rate following endoscopic surgical division was 50%. Eight (61.5%) of the 13 cases requiring revision presented with a high grade web. In univariate logistic regression analysis, a high grade web was a significant predictor for recurrence [OR 4.31, 95% confidence interval (CI): 1.32–14.02, P=0.012] and requirement for tracheostomy insertion (OR 12.57, 95% CI: 2.46–64.31, P<0.0001).

Laser division was initially performed for 8 patients, of whom 7 (87.5%) experienced recurrence and 6 (75%) required revision surgery. For the 22 patients undergoing cold steel division recurrence occurred in 8 (36.4%) and revision surgery was required for 7 (31.8%) patients. Laser division was associated with a significantly higher rate of recurrence (Fisher's exact, P=0.021) and revision surgery (Fisher's exact, P=0.047) than cold steel division, however a higher proportion of patients undergoing laser division had high grade webs (57.1%) than patients undergoing cold steel division (22.7%). Adjusting for grade of web in reverse stepwise multivariate logistic regression analysis the surgical division technique used does not significantly predict recurrence or revision surgery however the numbers involved in the analysis were small.

The number of patients receiving mitomycin C or keel insertion were too small to analyse statistically. It is notable

Table 5 Univariate logistic regression analysis predicting recurrence and revision surgery following endoscopic division of congenital laryngeal web in children

Covariate	Recurrence			Revision surgery		
	OR	95% CI	Sig.	OR	95% CI	Sig.
High grade web	*	–	–	32.000	3.052–335.509	P<0.0001
Age under one year at diagnosis	0.738	0.200–1.393	P=0.736	0.833	0.119–5.820	P=0.854
Age under one year at treatment	0.080	0.908–1.083	P=0.908	1.000	1.000–1.000	P=1.000
Male gender	2.000	0.485–8.241	P=0.333	1.375	0.343–5.510	P=0.653
22q11.2 deletion syndrome	0.500	0.113–2.210	P=0.354	0.476	0.111–2.040	P=0.314
Genetic diagnosis	0.773	0.175–3.651	P=0.773	0.833	0.187–3.723	P=0.811
Cardiac comorbidity	0.750	0.181–3.115	P=0.692	0.786	0.188–3.290	P=0.741
Synchronous airway lesion	2.357	0.580–9.576	P=0.225	1.875	0.467–7.526	P=0.372

Significance determined by change in likelihood ratio. *Odds ratio for recurrence with high grade web not shown as all cases recurred. OR, odds ratio; CI, confidence interval.

that none of the three patients treated with mitomycin C experienced recurrence however all presented with grade 2 (low grade) webs. Three patients were treated with a silastic keel, two of which recurred and required revision surgery, both had grade 3 (high grade) webs.

Risk factors for recurrence and revision surgery

The rate of recurrence of web following endoscopic surgical division was 50%. All 9 cases of high grade webs that were surgically divided recurred, and 8 (88.9%) required revision surgery (*Table 4*).

With reverse stepwise multivariate logistic regression analysis, the only covariate which contributed to either model was the severity of the grade of web (*Table 5*). In this study population, patient demographics and co-morbidities are not associated with either of the outcome measures analysed.

Discussion

To our knowledge, this is the largest cohort study of congenital anterior glottic webs to date and based on the current findings, an algorithm for diagnosis and treatment of the condition has been proposed.

This study population is comparable with Cohen's and Lawlor's cohort with equal gender distribution, age of presentation and correlation with family history (3,5). 22q11.2 DS has been previously found to be associated with anterior glottic webs (4,6) and in this study 61.0% of children had 22q11.2 DS. The rate of recurrence or revision surgery for anterior glottic webs has not been described specifically for children with a diagnosis of 22q11.2 DS. Our findings suggest 22q11.2 DS is not a predictor for surgical outcome, nor is the presence of any genetic syndrome and this should not be used for prognostication of the laryngeal web. We found a significantly higher rate of recurrence and revision surgery following endoscopic laser excision than with cold steel, however, after adjustment for the grade of web, this difference was not statistically significant. In this study, the only covariate which predicted a poor endoscopic outcome was the initial grade of web. All patients following endoscopic treatment for high grade webs had clinically significant recurrence of the web and all but one had revision surgery. Patient age and gender were not associated with recurrence, suggesting that delaying treatment on the basis of a patient's age is not required to achieve a favorable outcome. The patient's family history and genetic predisposition was also not associated with poor outcomes and families of a patient who is otherwise fit to undergo the procedure should not be dissuaded from a surgical approach based on the child's co-morbidities.

The surgical management of children with congenital anterior glottic webs can often be challenging and given the rarity of the disease process, there is limited literature to help guide the clinician in the diagnosis and treatment. The goals of treatment for congenital anterior glottic webs include adequate respiration, achieving appropriate airway

protection and improvement of voice quality (7). External approach surgical management with laryngofissure and keel placement or LTR with stenting are well described (8-10). Autogenous perichondrial tissue keels have been previously described by the senior author (9) and provides a scaffold which allows the underlying epithelial migration to occur. When epithelial cover is completed, they may slough off, leaving healthy mucosal surfaces which allows potentially better vocal quality. However, in recent years various endoscopic approaches have been developed (11,12) for treatment of lower grade webs. Based on our data, we would recommend an endoscopic approach for lower grade webs and single stage external approach LTR for grade 3 and 4 webs. These conclusions are also similarly reported by Chen *et al.* [2017] in which grade and thickness of congenital and acquired webs had high associations with recurrence (12). Tracheostomy was also used at times as a bridge to LTR for children with high grade webs and is an important aspect of management in securing the airway if required.

In our series, the three patients who had keel placement were performed in other institutions and subsequent follow up was in our institution. The division of the web leaves potentially two opposing raw mucosal surfaces. By employing a keel, there is a physical separation between raw surfaces to prevent recurrence (13). Keels described have often been made of or coated with silicone, plastic or polytetrafluroethylene. Previous papers, while limited discuss its use in adults, traumatic webs or in subglottic stenosis/other laryngeal pathologies (13,14). More data is required to discuss its potential use in congenital glottic webs. Mitomycin C is an anti-neoplastic antibiotic that inhibits cell division and prevents scarring by interrupting the proliferative stage of wound healing. Currently there is a lack of well described literature on the outcomes of mitomycin C with only a few case series on the subject (15,16). Our study showed a trend towards potential positive benefits with no recurrence in congenital webs, but the numbers were too small to claim statistical significance. Further studies are required with a greater number of patients to determine its benefits for future use. Similarly, our data found a significantly higher rate of recurrence and revision surgery following laser excision than with cold steel, however, after adjustment for the grade of web, this difference was not statistically significant. Currently there are only a few studies on Co2 laser treatment for congenital webs (17), further research is required to compare the rate of recurrence and revision between cold steel and laser excision to determine which if any has greater prognostic benefits.

Recommended management algorithm

After initial diagnosis, children should be referred for chromosomal microarray and cardiology review, given the high predominance of 22q11.2 deletion and congenital cardiac anomalies. Chromosomal microarray results detect all 22q11 deletions, but also gives the opportunity to find other genetic diagnoses. The results also further support the use of cold steel excision in grade 1 and 2 webs with LTR reserved for grade 3 and 4 webs.

Although definitive data is lacking to support the use of mitomycin C, the senior author favours its use when there is evidence of recurrent cicatrisation from repeated surgery. Tracheostomy should be considered on children with severe stenosis with clinically severe respiratory distress at birth. When it is time to consider tracheotomy decannulation, an LTR would be considered.

Suggested future studies should look into outcomes of voice quality given its implications on intellectual and psychosocial impacts in children. Research into adjuncts to endoscopic surgery should also be explored, including the use of mitomycin C or other anti-fibroblastic agents, to further optimise clinical outcomes, in providing a stable respiratory airway effective in respiration, feeding, airway protection and phonation.

Limitations

The study is limited by its retrospective nature which often does not given insight into surgeon and patient decision making. Furthermore, this cohort study is relatively small making data analysis difficult and larger numbers are required to address future questions including the use of CO_2 laser, glottic keels and mitomycin C.

Conclusions

Congenital anterior glottis webs should be suspected when the neonate or young infant presents with dysphonia or respiratory distress. Diagnosis is made on direct visualisation and consideration for genetic analysis and cardiac workup should be made given the high association with congenital anterior glottis webs, Endoscopic surgical division should be reserved for low grade webs and open

procedures for high grade webs irrespective of sex, age and underlying genetic condition.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/ajo-20-76

Data Sharing Statement: Available at http://dx.doi.org/10.21037/ajo-20-76

Peer Review File: Available at http://dx.doi.org/10.21037/ajo-20-76

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/ ajo-20-76). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Ethics approval was obtained from the SCHN ethics committee (2020/ETH01068) and individual consent for this retrospective analysis was waived.

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doi: 10.21037/ajo-20-76
Cite this article as: Daniel A, Ellis M, Lathif A, Reddy R, Wilson M, Cheng AT. Congenital anterior glottic webs: a retrospective review of 59 cases with management and outcomes. Aust J Otolaryngol 2021;4:7.