

Topical Mitomycin-C Use in Surgery of the Anterior Commisure

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ABSTRACT

Objectives: To review the efficacy of mitomycin c in the treatment of preexisting anterior glottic webs in patients undergoing microdirect laryngeal surgery over a six year period.

Methods: From 2004 through 2009 following treatment for recurrent respiratory papillomatosis or a persistent anterior glottic by either laser excision or microdebridement, twenty-five patients underwent topical application of 4mg/ml mitomycin – c to the anterior commisure. We retrospectively evaluated the efficacy of topical mitomycin – c in preventing web formation at the anterior glottis.

Results: Nineteen manifested anterior webs during treatment, whereas six were successfully treated with mitomycin c without developing a web. 84% demonstrated resolution of the AGW. Conversely three patients developed new web formation following application of mitomycin C, all of which were subsequently cleared. Only one patient was recalcitrant to therapy and required surgical lysis with keel placement. No patients developed laryngeal cancer during our study period.

Conclusion: Topical application of mitomycin appears to effectively limit the recurrence or progression of anterior glottic webs in a significant portion of patients.

INTRODUCTION

Endolaryngeal surgery for benign lesions at the anterior commisure is performed cautiously due to the risk of acquired glottic webs (AGW). AGW presents a difficult management dilemma due to the risks of airway compromise and impacts on voice (McGuirt, 1984). Conventional therapies of AGW have included intralesional kenalog injection, keel insertion, division followed by repeated dilation and mucosal grafting (Hsiao TY, 1999). In recent years a shift in management toward endoscopic laser lysis of laryngeal stenosis has resulted in significant improvements in voice outcomes (Knott, 2006), but has relied on the use of keel or sialastic stent placement to prevent the risk of glottic webbing (Monnier, 2005). While these adjuvant therapies have demonstrated acceptable outcomes they typically require tracheotomy placement and carry a risk of granulation formation requiring additional surgery (Edwards, 2007). Mitomycin C (MMC) is now routinely employed for prevention of scar formation in tracheal stenosis as well as subglottic and posterior laryngeal stenosis (Perepelitsyn, 2004). Limited animal models as well as in vivo human studies addressing its use for anterior glottic stenosis indicate it may prove to be a useful adjunct in the treatment of AGW.

METHODS AND MATERIALS

This study was approved by the Thomas Jefferson University Hospital IRB study number 09D.499.

A retrospective chart review was conducted to evaluate all patients over the age of 18 undergoing endoscopic surgery at the anterior commisure between January 1, 2004 and December 1, 2009. All procedures were performed at the lead investigators institution. All patients subjected to instrumentation at the anterior commisure with subsequent application of mitomycin c were included in the study. Instrumentation was most frequently cold steel, but could include microdebridement or laser excision. Patients with a history of adult or juvenile onset recurrent respiratory papillomatosis as well as those with previously known anterior glottic webs were included. Patients previously or concurrently undergoing treatment with cidofovir were also included. All patients with a known history of connective tissue disease, Wegner's disease and sarcoidosis were excluded.

Application of mitomycin C was performed subsequent to all other endoscopic instrumentation and immediately preceding the end of surgery (Fig 1). From 2004 until late 2007 patients were treated with a topical preparation of 4mg mitomycin/ml. This was applied to the anterior commisure for 2 minutes then removed for 1 minute and reapplied for an additional 2 minutes. From late 2007 until the conclusion of the study period mitomycin at a concentration of 1mg/ml was applied topically for a continuous 4 minute period.

Charts were reviewed for presence of and size of anterior glottic webbing and MMC application to the anterior commisure. Patients were noted to have resolved, improved, stable, worsened or new web formation, based on clinical or operative exam.

RESULTS

A total of twenty five patients were identified including eighteen male and nine female patients. Six patients were successfully treated with mitomycin following instrumentation at the anterior commisure and never manifested anterior webbing. The remaining nineteen patients were observed to have an anterior glottic web at some point during therapy (Table 1). 11 of these patients were initially taken to the OR for surgical treatment of an AGW. MMC resulted in resolution of AGW scarring in 17 of those 19 patients, 9 of which after only a single administration.

Patients were subjectively evaluated for the extent of web involvement over the course of treatment. The majority of patients experienced resolution of the AGW following MMC application (Fig 2). An anterior web in one patient increased in size despite therapy with mitomycin and required subsequent open surgery with endolaryngeal keel placement. Three patients developed new webs during treatment all of which resolved with subsequent therapy. Only two patients had evidence of AGW at the time of last clinical evaluation, whereas twenty three patients did not demonstrate webbing at their last evaluation.

One patient had juvenile RRP but was an adult at the time of AGW formation. One patient who had previously undergone a renal transplant and was on well controlled long term immunosuppression was included in the study. Two patients had previously been treated for T2 laryngeal squamous cell carcinoma by primary radiation therapy. One patient with congenital glottic webbing treated with MMC was excluded from analysis, however did experience resolution of disease following a single treatment. No patients developed significant dysplasia or laryngeal cancer during the study period.

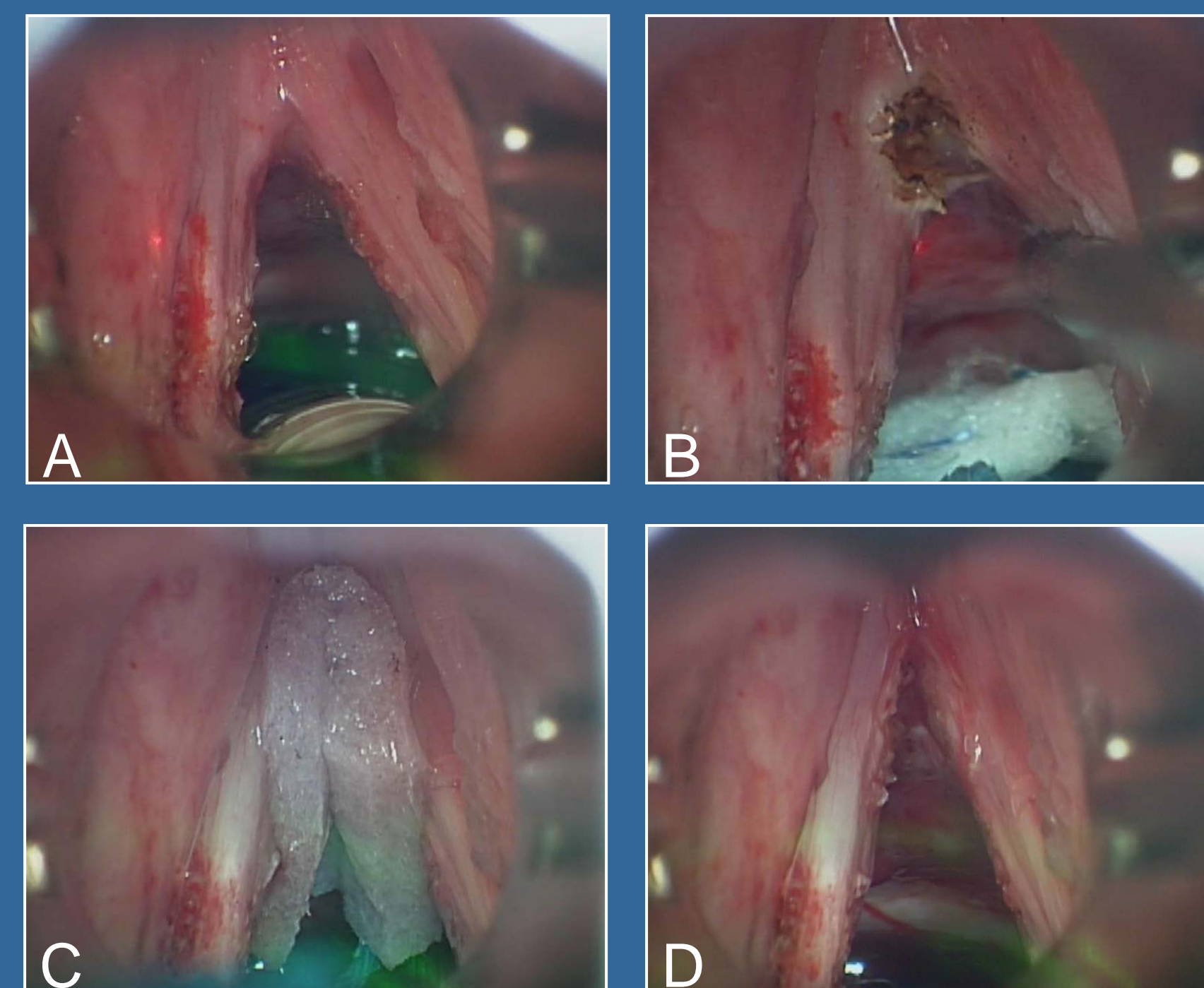


Figure 1. a) Preoperative glottic web secondary to previous papilloma excision. b) endoscopic laser excision of AGW. c) Application of mitomycin C. d) Post treatment appearance of anterior commisure.

	Sex	Age	Follow up (days)	Cidofovir	web recurrence p MMC	Treatments to clear	Time to clear? (days)	Notes	
1	M	36	251	Y	Y	2	16		
2	M	23	448	Y	N	1			
3	F	43	1418	N	Y	2	363		
4	M	30	1630	Y	Y	Failed		Keel placement	
5	M	36	239	Y	N	1			
6	M	33	1073	Y	Y	2	134		
7	F	63	1030	N	Y	Stable		XRT T2 SCCA	
8	F	52	5	Y	N	1			
9	F	32	781	Y	Y	2	303		
10	M	49	642	Y	N	1			
11	M	45	19	N	N	1			
12	F	46	103	N	Y	2	159		
13	M	39	781	Y	N	1			
14	F	37	897	N	Y	Improved		Dyspnea, marked improvement	
15	M	73	278	N	Y	1		spontaneous resolution	
16	F	18	675	Y	N	1			
17	M	31	603	Y	Y	3	517		
18	M	77	386	N	N	1		Leukoplakia bx, s/p XRT for Lung CA	
19	F	53	295	N	Y	2	291	Surgical Failed glottic closure	
		11M/8F 43		608	N	11Y/9N	1.5	255	

Table 1. Demographic and clinical data on 19 patients who manifested AGW during treatment with MMC.

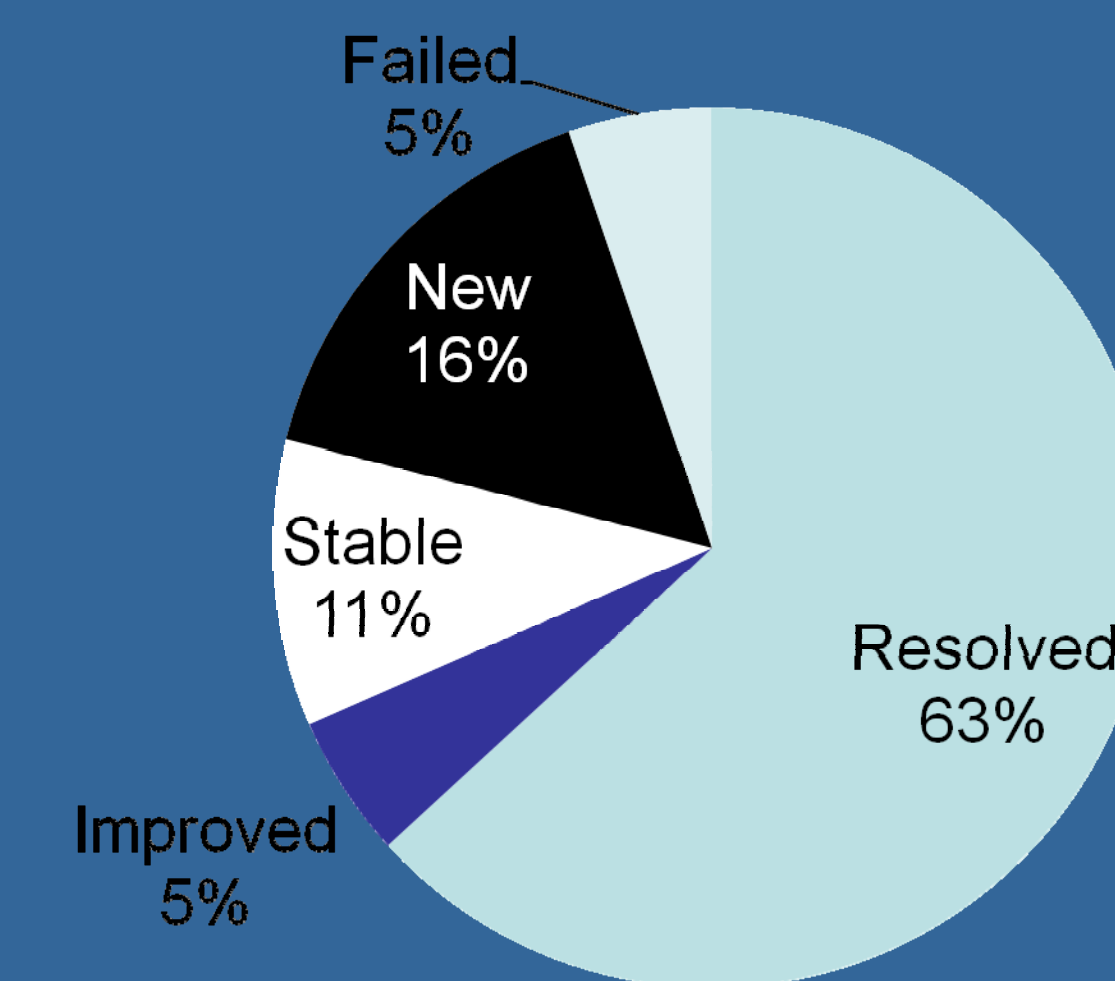


Figure 2. Clinical response to MMC therapy in 19 patients that developed AGW. All 3 patients who developed new webbing during therapy subsequently cleared the AGW and were web free at the last clinic visit.

DISCUSSION

Following initial enthusiasm for the use of MMC in the anterior glottis has had limited but encouraging results (Roh, 2005; Spector, 2001). Animal models appear to indicate MMC is a useful tool to prevent scarring when operating at this area. However traditional surgical lysis of anterior glottic lesions persist. Previous studies using surgical lysis followed by keel insertion report recurrence of AGW between 10 and 62% (Edwards, 2007; Lichtenberger, 1994) In our cohort more than 80% of the patients treated with MMC demonstrated objective and sustained resolution of the AGW.

Six patients underwent surgery at the anterior commisure without subsequent development of AGW, whereas three developed new webbing after MMC application. All of these patients were able to be treated more aggressively than if MMC was not used.

MMC primarily acts to inhibit DNA translation thus exerting an effect to decrease proliferation of fibroblasts. Additionally it has been shown to induce fibroblast apoptosis and limit angiogenesis. Topical application appears to be safe for use in the head and neck with little or no systemic side effects (Veen, 2009). In our cohort there were no incidences of malignant degeneration, or worsening dysplasia. Previous reports examining MMC in patients developing webs following SCCA confirms our results (Knott, 2006).

We recognize inherent limitations to this study. Firstly the retrospective nature of the review limited more sensitive assessment of web size. Many of the patients also received concurrent or metachronous cidofovir injections, the impact of which is unclear.

CONCLUSIONS

- MMC is effective in treating anterior glottic webs in more than 84% of patients
- More than half of patients that demonstrated a resolution of AGW following MMC did so after a single treatment
- MMC allows for more aggressive surgery at the anterior commisure
- MMC results in less morbidity and faster recovery than traditional keel prostheses

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