

Topical Mitomycin-C for The Management of Acquired Glottic Web and Subglottic Stenosis

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Abstrak: Penatalaksanaan stenosis laring terutama ditujukan untuk mendapatkan jalan napas yang cukup dan kualitas suara yang baik. Untuk itu, penanganan secara endoskopis menjadi pilihan untuk kasus-kasus stenosis laring. Dibandingkan dengan penanganan secara bedah terbuka, pembedahan secara endoskopis lebih menguntungkan bagi penderita dan bila diperlukan dapat dilakukan berulang-ulang. Walaupun teknik pembedahan secara endoskopis telah mengalami banyak kemajuan, tingkat kegagalannya masih cukup tinggi. Penyebab utama dari kegagalan ini adalah pembentukan jaringan parut dan re-stenosis. Untuk menurunkan tingginya tingkat rekurensi stenosis laring pada pembedahan secara endoskopis, para peneliti telah berusaha memodulasi penyembuhan luka dan menghambat pembentukan jaringan parut. Sebagai zat anti-proliferasi, Mitomycin-C (suatu anti-metabolit yang berkhasiat sebagai obat anti-kanker dan anti-proliferasi) dapat menghambat aktivitas dan proliferasi fibroblast, karena itu mengurangi pembentukan jaringan parut.

Di sini kami laporkan satu kasus web glotik yang didapat dan stenosis subglotik pada seorang laki-laki berumur 43 tahun yang berhasil ditangani secara endoskopis dengan penggunaan mitomycin-C secara topikal. Penderita dirujuk ke RSUP H. Adam Malik akibat sesak napas dan suara serak 3 bulan setelah mengalami trauma laring akibat kecelakaan lalu lintas. Sesaat setelah mengalami kecelakaan, penderita ditrakeostomi dan seminggu kemudian berhasil dilakukan dekanulasi, tetapi kemudian perlahan-lahan timbul sesak napas bila penderita beraktivitas dan suara serak disertai dengan stridor inspiratoir. Tidak ditemukan penyakit sistemik pada penderita.

Pemeriksaan laringoskopi optik yang dilakukan pada waktu penderita masuk rumah sakit memperlihatkan web glotik yang berat, tetapi tidak ditemukan kelainan pada pemeriksaan CT Scan laring. Pada waktu dilakukan operasi mikrolaring ditemukan stenosis subglotik. Hanya sebagian jaringan parut subglotik yang dapat diangkat dan lapangan operasi diberi larutan mitomycin-C. Setelah operasi penderita dapat bernapas dengan lebih baik, tetapi masih agak sesak bila beraktivitas dan suara masih serak. Pemeriksaan ulang CT Scan yang lebih presisi mengkonfirmasi stenosis subglotik. Diputuskan untuk melakukan operasi lanjutan dua minggu kemudian. Pada saat operasi ditemukan sebagian web glotik terbentuk kembali. Dilakukan pembelahan web glotik dan pengangkatan seluruh jaringan granulasi pada daerah subglotik, diikuti pengolesan larutan mitomycin-C selama 10 menit. Hasilnya luar biasa. Selama dua bulan follow-up, penderita dapat bernapas tanpa kesulitan dan kualitas suaranya bertambah baik. Hanya ada sedikit suara serak dan tidak ditemukan tanda-tanda re-stenosis.

Kata kunci: web glotik yang didapat, stenosis subglotik, operasi mikrolaring, mitomycin-C

Abstract: The primary goal of management for laryngeal stenosis is to provide a patent airway and to achieve a good voice quality. For these reasons, endoscopic management has been a treatment option for laryngeal stenosis. Compared with open procedures, this approach benefits patients and if needed, tolerance to repeated procedures. Despite advances in endoscopic technique, the failure rate of endoscopic treatment of laryngeal stenosis remains high. The most frequent cause of failure is scar formation and restenosis. To reduce the high recurrence rate of laryngeal stenosis after endoscopic treatment, medical researchers have made some efforts to modulate wound healing and inhibit scar formation. As an antiproliferative agent, Mitomycin-C (an antimetabolite with antineoplastic and

antiproliferative properties) can inhibit fibroblast activity and proliferation, thereby reduce scar formation.

The successful endoscopic management of an acquired glottic web and subglottic stenosis in a 43-year-old man with topical mitomycin-C application is reported. He referred to H. Adam Malik hospital with dyspnea and husky voice 3 months after laryngeal trauma due to traffic accident. He was tracheostomized and decanulated in a week, but later he developed dyspnea on exertion and severe hoarseness with inspiratory stridor. There was no systemic disorder.

Optical laryngoscopy on admission revealed a severe glottic web, no disorder found by CT Scan. Subglottic stenosis found on microlaryngeal surgery. Only a part of the subglottic granulation tissue could be removed, and 2 mg/ml of mitomycin-C was applied to the surgery area. He could breathe easier after operation, but there was still a slight dyspnea on exertion and hoarseness. A more precise CT Scan confirmed subglottic stenosis. The second operation performed 2 weeks later, the glottic web was partially reformed. The web and granulation tissue in subglottic region was completely removed, followed with application of 2 mg/ml mitomycin-C for 10 minutes. The result was eventful. During 2 months follow up he could breathe without difficulty and his voice quality improved with a low degree of hoarseness. No re-stenosis found.

Keywords: acquired glottic web, subglottic stenosis, microlaryngeal surgery, mitomycin-C

INTRODUCTION

Narrowing or constriction of the larynx can occur in the supraglottic, glottic, or subglottic region.¹ Treatment is depend on the site of involvement and the degree of stenosis, and it ranges from endolaryngeal surgery to open surgical repair.² Traditionally, the treatment of choice for laryngeal web is laryngofissure and placement of a stent or keel.³ Endoscopic treatment of laryngeal stenosis continues to challenge the surgeon due to high failure rate. Scar formation and restenosis is the main cause of failure. Preliminary results of recent clinical trials using mitomycin-C in laryngotracheal stenosis showed promise.⁴

CASE REPORT

A 43-year-old man referred to H. Adam Malik Hospital with hoarseness and dyspnea on 18 March 2005. He had traffic accident on December 2004 where his neck struck the guide rail and need to be canulated because of dyspnea, stridor, hoarseness, hemoptysis and subcutaneous emphysema. He could be decanulated in a week, but later he developed severe hoarseness and dyspnea on exertion. He was referred to our hospital 3 months after the accident. On admission he presented a husky voice and biphasic stridor but was otherwise in good physical condition.

Optical laryngoscopy revealed a severe glottic web which could not be detected by CT Scan (Figure 1). The web then divided with microscissor and granulation tissue in the subglottis found. We were unable to remove all of the subglottic granulation tissue due to lack of preparation and bleeding. Two mg/cc of

mitomycin-C was topically applied to the vocal cord. The patient could breathe easily afterward, but there was still hoarseness and a slight dyspnea. A more precise CT Scan confirmed subglottic stenosis (Figure 2).

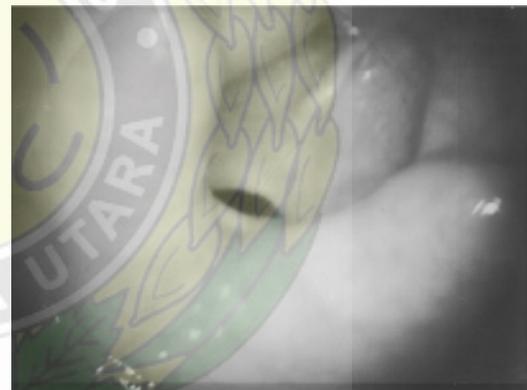


Figure 1. Glottic web on admission

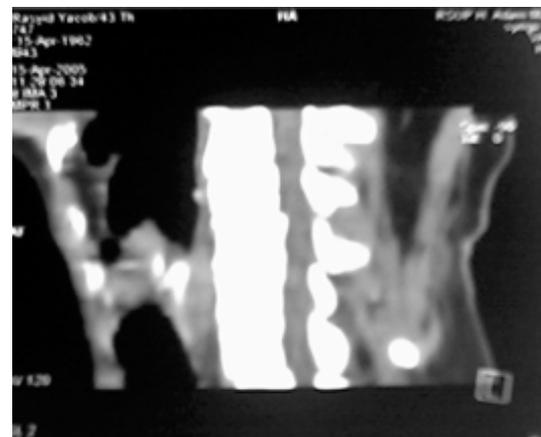


Figure 2. More precise CT Scan confirmed subglottic stenosis

At the second operation 2 weeks later we found the web was partially reformed (Figure 3), which was divided again. Granulation tissue in subglottic region was completely removed, followed with application of 2 mg/cc mitomycin-C for 10 minutes. The result was eventful. During 2 months follow up the patient could breathe without difficulty and his voice quality improved to a low degree of hoarseness. There was no evidence of restenosis (Figure 4).

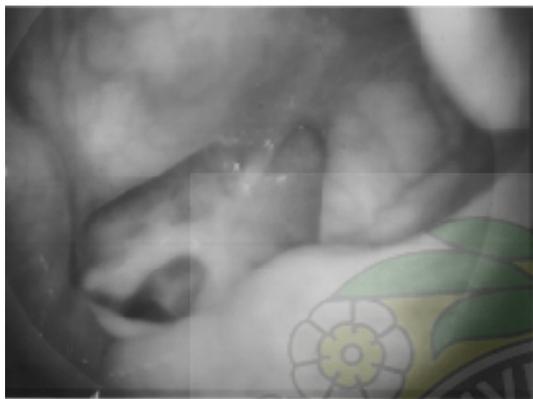


Figure 3. Before 2nd operation

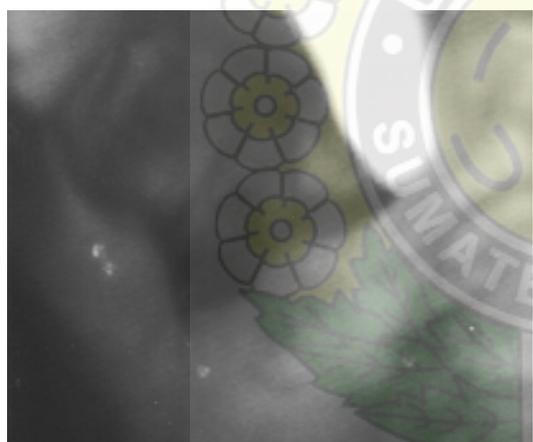


Figure 4. After 2 months follow-up

DISCUSSION

In adults laryngeal stenosis are sometimes result of a motor vehicle accident where the larynx strike hard object causing a fracture of the laryngeal framework and laceration or disruption of the mucosa. Primary repair should be undertaken as soon as possible, as healing by secondary intention and subsequent scarring may produce an acquired laryngeal stenosis.¹ Laryngeal fracture is characterized by history of a blow to the neck, hoarseness, inspiratory or expiratory stridor (or both), hemoptysis and subcutaneous emphysema.⁵ Our patient had a history of laryngeal trauma and showed all signs of laryngeal fracture 3 months before. He underwent tracheostomy, but was not followed

by laryngeal exploration. Chronic laryngeal stenosis is said to be established if the patient has not got a satisfactory airway 4 weeks after an injury.⁶

The ultimate long term goal in the treatment of established acquired subglottic stenosis is to restore an adequate airway and maintain voice function; surgery should not worsen the voice.^{1,2,7} Treatment must be individualized and appropriate for each case; there is no standard operative procedure. Many methods of treatment have been used depending on the severity of the stenosis, age, general progress, and the wishes of patient.^{1,2} Endoscopic management has been a treatment option. Compared with open procedures, this approach benefits patients as a result of less morbidity, shorter hospital stay, earlier return to work, and if needed tolerance to repeated procedures.⁴ Cotton and Andrews postulated conservative endoscopic treatment should be considered before deciding on an open surgical reconstructive technique. Open surgical techniques are usually considered only in patients who are tracheotomy dependent.⁷ These reasons led us to perform endoscopic treatment for the patient.

Granulation tissue may require removal at one or two further endoscopic procedures to prevent partial re-formation of the web.¹ In this case we performed repeated procedures due to subglottic stenosis was undiagnosed prior to surgery by laryngoscopy and first radiological assessment. There was not enough preparation to remove all the granulation tissue found in the operation. The remnant granulation tissue in subglottis seemed to triggered re-formation of the glottic web after the first operation.

Despite advances in endoscopic technique, the failure rate of endoscopic treatment of laryngeal stenosis remains high. The most common cause of failure is scar formation and restenosis. All surgical techniques result in some degree of mechanical injury to laryngeal mucosa, produces inflammatory response, which ultimately results in fibroblast proliferation and scar formation. To reduce the high recurrence rate of laryngeal stenosis after endoscopic treatment, medical researchers are interested in agents capable to modulate wound healing and inhibit scar formation. A number of pharmacologic agents have shown promise. For example, 5-fluorouracil and beta-aminopropionitrile have demonstrated ability to inhibit collagen cross-linking and reduce scar formation in animal models. Steroids have long been known to affect the healing process and

inhibit scar formation primarily through the ability to suppress inflammatory response.⁴

Mitomycin-C is an antimetabolite produced by *Streptomyces caespitosus*. It possesses antineoplastic and antiproliferative properties. As an antiproliferative agent it can inhibit fibroblast activity and proliferation both in vitro and in vivo, thereby reduce scar formation. Mitomycin-C has been long-standing, successfully used by ophthalmologists to prevent restenosis in glaucoma surgery, dacryocystorhinostomy and pterygium recurrence. Several recent reports demonstrate safety and suggest mitomycin-C efficacy in the treatment of laryngotracheal stenosis. A study by Perepelytsin and Shapshay indicate that adding mitomycin-C to the treatment regimen significantly increases the success rate of endoscopic treatment of acquired upper airway stenosis from less than 20% (with steroid injection) to 75%.⁴ Many authors suggested that topical mitomycin-C is an effective adjuvant agent in the treatment of laryngotracheal stenosis.^{3,4,8-10}

Human and animal studies have demonstrated the efficacy and safety of topical mitomycin in the treatment of airway stenosis at concentrations ranging from 0.4 mg/cc to 10 mg/cc. McCurdy and Simpson reported complications due to local toxicity of mitomycin-C occurred in 4 of 66 patients (6%) manifested by accumulation of fibrinous debris at the operative site resulting in partial airway obstruction. A significantly higher percentage of complications occurred when supersaturated mitomycin-C (10 mg/cc) was used.¹¹ We used cottonoid sponge soaked with mitomycin-C 2 mg/cc and topically applied to the surgical site for 10 minutes. No complications or side effects observed 72 hours after the procedure. Patient was controlled for 2 months, and there was no evidence of re-stenosis.

The results of surgical treatment are determined by the overall size of the web and by the anterior thickness. Involvement of the glottis in subglottic stenosis has been found to have unfavourable effect on outcome. Voice outcomes vary according to the method of treatment and degree of stenosis, but generally are unchanged or improved.^{1,2} However, in this case a partial voice improvement from husky voice to slight hoarseness achieved and a patented airway provided by microlaryngeal surgery and topical application of mitomycin-C.

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