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SHORT COMMUNICATION

Novel method of intralesional cidofovir injection into laryngotracheal papillomata

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Abstract

Laryngeal papillomatosis is characterised by multiple papillomata affecting the upper respiratory tract. This condition is difficult to treat due to its recurrent nature. Treatment often involves surgical debulking. A number of non-surgical treatments have been reported. Intralesional cidofovir, a cytosine nucleoside analogue with antiviral activity, has been used in an attempt to manage the condition. We present a novel technique of administering cidofovir in a case of recurrent laryngotracheal papillomata.

Key words: Larynx; Papilloma; Cidofovir; Injection

Introduction

Laryngeal papillomatosis is a rare condition characterised by multiple benign papillomata affecting the upper respiratory passages; it is often localised to the larynx.[1] The causative agent is the human papilloma virus. Viral subtypes 6 and 11 are predominately associated with symptomatic disease.[2] Human papilloma virus can affect the respiratory tract and genital region and may also have cutaneous manifestations.

The incidence of laryngeal papillomatosis varies between adults and children, being 2 per 100 000 and 4.5 per 100 000, respectively. It presents in infancy or early childhood with stridor and a change in voice or crying pitch.

Patients often require multiple courses of treatment due to the recurrent nature of the disease, which is also referred to as recurrent respiratory papillomatosis. Tracheostomies are generally avoided but are occasionally required. Traditional surgical treatment modalities include 'cold steel', laser, microdebrider and photodynamic therapy. There are alternative or adjunctive treatments available, including antiviral therapy (e.g. interferon), chemotherapy, retinoids and vaccination.[3]

Intralesional cidofovir has been used over the last decade to treat recurrent respiratory papillomatosis, since the first report in 1998.[1] Cidofovir is a cytosine nucleoside analogue with antiviral activity.[4] Many publications have reported promising results for intralesional cidofovir.[1,5–11] Side effects are rare, but include rash,[1] headache,[1] local inflammation[8] and potential nephrotoxicity; in animal studies, concerns have been raised about carcinogenicity. A few authors have described dysplasia after use,[1,2,10,12] and a 2–5 per cent rate of malignant change has been reported.[1,13] Recent general[14] and histological[15] reviews have suggested that the rate of malignant transformation with cidofovir is no higher than expected from the natural course of the disease; however, this remains contentious.

Surgical debridement with intralesional cidofovir is used for moderate to severe disease.[16] Currently, there is no literature on the method of administration of intralesional cidofovir. In the senior author's experience, and judging from reports from various centres, most clinicians appear to inject using a laryngeal needle after tumour debulking.

In this report, we share our experience of treating a particularly difficult, recalcitrant case of recurrent respiratory papillomatosis.

Case report

A 20-year-old woman had initially been diagnosed with laryngeal papillomatosis at the age of 18 months, due to stridor and a change in crying pitch. This condition had been very difficult to treat, and the patient had undergone a tracheostomy before the age of three years. Multiple attempts at surgical debulking with a laser had been attempted, without any significant improvement.

A second opinion had been sought at a specialist paediatric institute, and the patient had remained under their care for the next 13 years. Over this period, she had undergone over 250 surgical interventions (mainly involving KTP laser) plus adjuvant treatment with interferon. In the year prior to the current presentation, the patient had received systemic cidofovir to treat papillomas that had seeded further down her respiratory tree.

The patient's care had been transferred back to our centre when she reached the age of 16 years, with a tracheostomy still in situ. Initially, she had continued systemic cidofovir together with surgical management using a microdebrider.

At this stage, a literature review was performed, which brought to light reports of good results with intralesional cidofovir.[1,5–10] As a result, cidofovir was used intralesionally in an attempt to control the patient's recurrent, extensive papillomata in the larynx and upper trachea.

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Administration technique

Intralesional cidofovir was delivered under general anaesthesia. A ventilating Storz paediatric bronchoscope was used. We used a Cook brand disposable variceal injector[17] (Figure 1) (Cook, Medical Ltd, Cork, Ireland) to administer the cidofovir, using the side port of the Storz ventilating bronchoscope. The specific variceal injecting device used was a DVI-23 model, which is 200 cm in length and has a 5.0 Fr injector that requires a minimal channel size of 2.0 mm. This was used because the needle remained sheathed, thus decreasing the risk of iatrogenic injury or injection. When the needle tip was advanced, it had a range of 4 mm. Prior to use, the system was checked to ensure that the needle could be advanced; the system was then primed.

Once appropriate views of the papillomata were obtained, the variceal injector was inserted down the side channel of the bronchoscope. The injector was advanced to lie upon a papilloma (Figure 2), an assistant advanced the tip into the

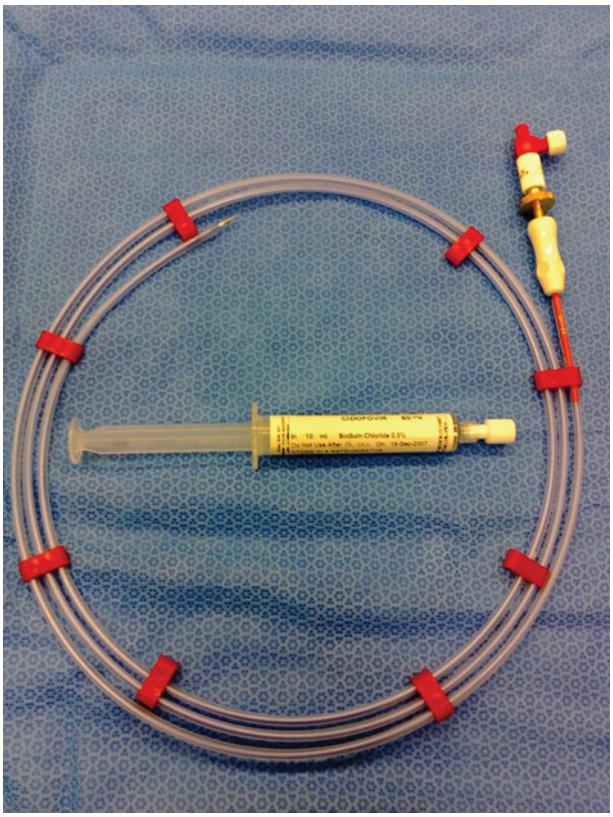

FIG. 1
Variceal injector prepared for use with cidofovir.

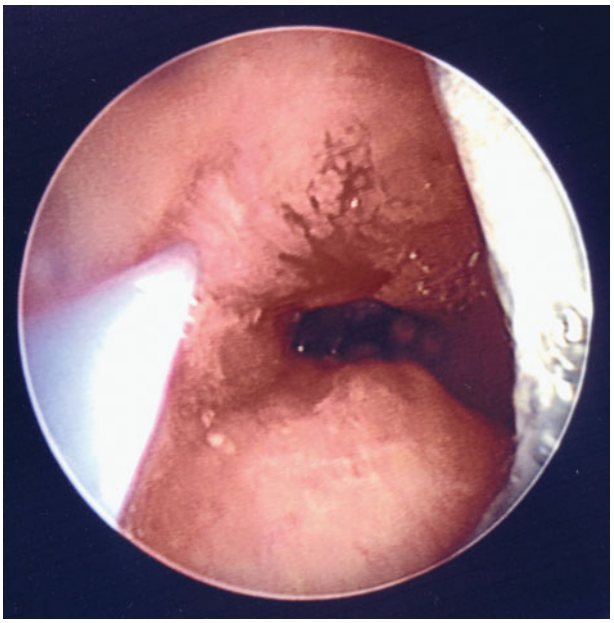

FIG. 3
Endoscopic view of variceal injector advanced into a lesion.

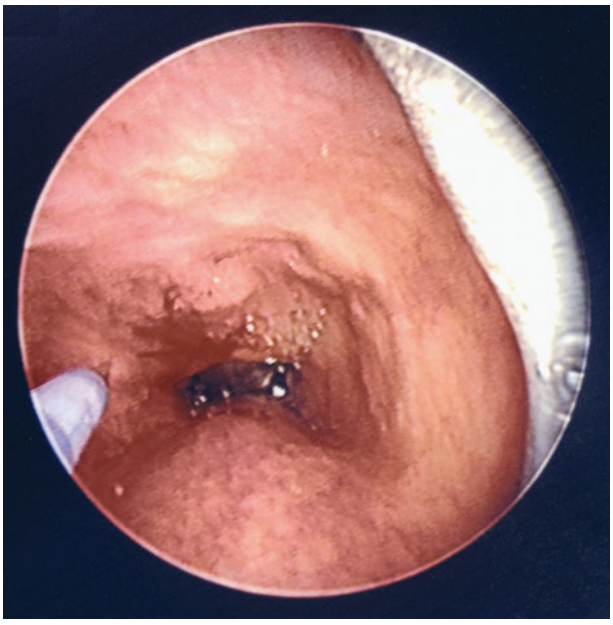

FIG. 2
Endoscopic view of variceal injector in trachea. The tip of the needle is visible.

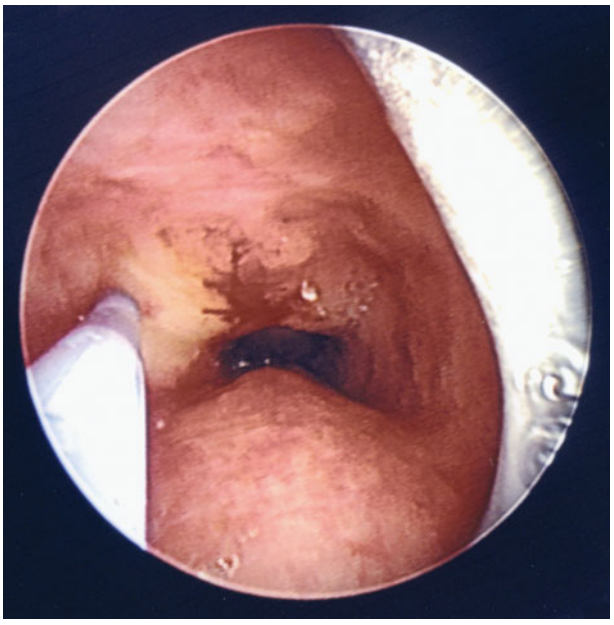

FIG. 4
Endoscopic view showing successful injection of cidofovir, with blanching of the lesion.

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lesion, and cidofovir was slowly injected (Figure 3). Once the lesion blanched (Figure 4), the injection was halted and the tip re-sheathed, and new papillomata were sought. This process was repeated as necessary until all relevant lesions had been treated.

Reported complications of such mucosal injections include ulceration, necrosis of injected tissue, venous thrombosis and stricture formation.

However, at the time of writing our patient had received 15 courses of treatment with no adverse consequences. Following the first few treatments, her papillomata decreased significantly in size, enabling decannulation after 14 years of tracheostomy dependence. Her frequency of treatment has decreased from monthly to three-monthly since commencement of intralesional cidofovir therapy.

Conclusion

In cases of recurrent respiratory papillomatosis, the use of a variceal injector to administer intralesional cidofovir is a cheap, safe and easily accessible method with no adverse effects in our experience. In our centre, we now use this method for all our patients requiring intralesional cidofovir to treat laryngotracheal papillomatosis.

References

1 Snoeck R, Wellens W, Desloovere C, Van Ranst M, Naesens L, De Clercq E *et al*. Treatment of severe laryngeal papillomatosis with intralesional injections of cidofovir [(*S*)-1-(3-hydroxy-2-phosphonylmethoxypropyl)cytosine]. *J Med Virol* 1998;**54**:219–25

2 Pudszuhn A, Welzel C, Bloching M, Neumann K. Intralesional cidofovir application in recurrent laryngeal papillomatosis. *Eur Arch Otorhinolaryngol* 2007;**264**:63–70

3 Pawlita M, Gissmann L. Recurrent respiratory papillomatosis: indication for HPV vaccination? [in German] *Dtsch Med Wochenschr* 2009;**134**(suppl 2):100–2

4 Shehab N, Sweet BV, Hogikyan ND. Cidofovir for the treatment of recurrent respiratory papillomatosis: a review of the literature. *Pharmacotherapy* 2005;**25**:977–89

5 El-Hakim H, Waddell AN, Crysdale WS. Observations on the early results of treatment of recurrent respiratory papillomatosis using cidofovir. *J Otolaryngol* 2002;**31**:333–5

6 Neumann K, Pudszuhn A, Welzel C, Bartel-Friedrich S, Passmann M. Intralesional cidofovir injections for recurrent laryngeal papillomatosis: first results [in German]. *Laryngorhinootologie* 2003;**82**:700–6

7 Schraff S, Derkay CS, Burke B, Lawson L. American Society of Pediatric Otolaryngology members' experience with recurrent respiratory papillomatosis and the use of adjuvant therapy. *Arch Otolaryngol Head Neck Surg* 2004;**130**:1039–42

8 Bielamowicz S, Villagomez V, Stager SV, Wilson WR. Intralesional cidofovir therapy for laryngeal papilloma in an adult cohort. *Laryngoscope* 2002;**112**:696–9

9 Chung BJ, Akst LM, Koltai PJ. 3.5-Year follow-up of intralesional cidofovir protocol for pediatric recurrent respiratory papillomatosis. *Int J Pediatr Otorhinolaryngol* 2006;**70**:1911–17

10 Dikkers FG. Treatment of recurrent respiratory papillomatosis with microsurgery in combination with intralesional cidofovir – a prospective study. *Eur Arch Otorhinolaryngol* 2006;**263**:440–3

11 Bielecki I, Mniszek J, Cofała M. Intralesional injection of cidofovir for recurrent respiratory papillomatosis in children. *Int J Pediatr Otorhinolaryngol* 2009;**73**:681–4

12 Wemer RD, Lee JH, Hoffman HT, Robinson RA, Smith RJ. Case of progressive dysplasia concomitant with intralesional cidofovir administration for recurrent respiratory papillomatosis. *Ann Otol Rhinol Laryngol* 2005;**114**:836–9

13 Kimberlin DW. Current status of antiviral therapy for juvenile-onset recurrent respiratory papillomatosis. *Antiviral Res* 2004;**63**:141–51

14 Broekema FI, Dikkers FG. Side-effects of cidofovir in the treatment of recurrent respiratory papillomatosis. Eur Arch Otorhinolaryngol 2008;**265**:871–9

15 Lindsay F, Bloom D, Pransky S, Stabley R, Shick P. Histologic review of cidofovir-treated recurrent respiratory papillomatosis. *Ann Otol Rhinol Laryngol* 2008;**117**:113–17

16 Tanna N, Sidell D, Joshi AS, Bielamowicz SA. Adult intralesional cidofovir therapy for laryngeal papilloma: a 10-year perspective. *Arch Otolaryngol Head Neck Surg* 2008;**134**:497–500

17 Disposable varices injector by Cook. In: http://www.cookmedical.com/esc/content/mmedia/16386_0106DVI.pdf [January 2010]

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