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Treatment of recurrent respiratory papillomatosis with argon plasma coagulation

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Abstract
Extension of recurrent respiratory papillomatosis (RRP) to the lower airway in children is life-threatening and an extremely difficult condition to treat. We present the case of a seven-year-old girl with progressive RRP since the age of two. Repeated CO_2 laser treatment and interferon-alpha treatment could not prevent tracheotomy and spread to the trachea. We used argon plasma coagulation (APC) with flexible endoscopy for the first time for the treatment of RRP. APC gives a controlled limited penetration into the tissue and good control of bleeding. There is no carbonization or vaporization which makes it a suitable method for the treatment of lower airway RRP. After a few treatments with APC, we gained very good control of the disease with no side-effects or complications. The described application of APC seems to be a promising way to treat lower airway RRP.

Key words: Papillomatosis, recurrent respiratory; Airway obstruction; Laser surgery; Argon plasma coagulation

Introduction

Recurrent respiratory papillomatosis (RRP) is a virally-induced disease characterized by recurrent proliferation of benign squamous papillomas within the respiratory tract. The larynx is mostly involved and represents the most common location for benign neoplasm of the larynx (Willging, 1995). Two forms are described, the juvenile onset and the adult onset. Patients with juvenile papilloma are usually between the ages of two and five years. The juvenile form of the disease presents as multiple lesions, which are unpredictable in their response to treatment and tend to have a higher rate of recurrence. Both the adult and juvenile forms are histologically identical (Doyle *et al.*, 1994). The lesions are friable and bleed easily. Molecular hybridization techniques have identified over 60 types of human papillomavirus (HPV) but type HPV 6 and HPV 11 are associated with respiratory tract papillomatosis. HPV 11 is the most common type and is reported to be associated with more aggressive disease (Padayachee and Prescott, 1993; Pou *et al.*, 1995). Recurrence cannot be predicted because of latent infection in morphologically normal tissue adjacent to papillomas (Abramson *et al.*, 1987). Spontaneous resolution of the disease has been reported with puberty, but remains controversial (Benjamin and Parsons, 1988). Extensive disease with acute respiratory distress is not uncommon, when the lower airway is affected and requires tracheostomas and surgical ablation every one to two months. The mortality is reported to be eight per cent (Morgan and Zeitsch, 1986). There is no universally effective treatment for RRP. The mainstay of treatment for RRP is repeated vaporization with CO_2 laser. Any type of surgical treatment carries the risk of laryngeal and lower airway stenosis. Various treatment approaches including radiation, ultrasound, vaccines, steroids, podophyllin and levamisol have been tried but have been abandoned (Willging, 1995). Anti-viral drugs such as acyclovir and ribavirin, 13-cis-retionoic acid and photodynamic laser therapy have shown some response but further evaluation is needed (Feyh *et al.*, 1993; Morrison and Evans, 1993; Morrison *et al.*, 1993; Lippmann *et al.*, 1994). Chemotherapeutic drugs have been used but toxic side effects are severe (Mehta and Herold, 1980). Alpha-interferon has gained widespread use and is now the best studied adjuvant approach. But response duration and rebound effects limit the value (Lundquist *et al.*, 1984; Gerein *et al.*, 1987; Kashima *et al.*, 1988; Walther and Herberhold, 1993). Therefore, new approaches for controlling RRP are needed.

Argon plasma coagulation (APC) represents an alternative and innovative method for the treatment of RRP especially in the lower airway. APC has been used so far in open surgery for treating superficial haemorrhages from parenchymatous organs. It is only recently that it has been introduced into flexible endoscopy (Farin and Grund, 1994; Grund *et al.*, 1994). No treatment of airway papillomatosis has been reported yet using APC.

High frequency electric current is used for non-contact tissue coagulation via ionized argon gas. The penetration depth of around 2 mm is constant and predictable, thus avoiding unnecessary damage of the tracheal cartilage. It is very effective for haemostasis. The absence of the vaporization effect, produced by lasers, is offset by a pronounced desiccation of the tissue with APC, which prevents hazardous perforations. We report the successful use of APC on a seven-year-old child with RRP, which showed progressive involvement of the lower airway and had had an unsuccessful trial of α-interferon.

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Case report

A three-year-old girl presented to her local physician with a two-month history of hoarseness. At that time she had no stridor or respiratory distress and there was no history of maternal condylomata acuminata. On laryngoscopy no pathology could be detected. Suddenly after six months a stridor developed which led to a tracheostomy and the diagnosis of respiratory papillomas. The papillomas were initially confined to the supraglottic larynx. They were surgically removed and the tracheostomy was closed. In the following years she had lesions regularly removed from the larynx. The time interval between treatment was four to six months at the beginning but became shorter. At the same time the mother's compliance was decreasing and she only appeared in the hospital when a severe stridor developed. The increasing necessity of surgical removal with the CO_2 laser and the multilocular occurrence of the papillomas led to a progressive stenosis of the larynx, followed by a second tracheostomy. At this time the patient was six years old. Since then the papillomas have spread to the trachea, from where it was increasingly difficult to remove them with a CO_2 laser or a KTP laser (Figure 1). Adjuvant therapy with interferon-α was started but no convincing clinical effect was seen. One year later we decided to use APC for further treatment.

Materials and methods

Our equipment for APC consists of an APC probe, an argon gas source and a high-frequency surgical unit (APC 300, ICC 350, Erbe Elektromedizin, Tuebingen, FRG). We used a flexible Teflon tube with an outer diameter of 2.0 mm, which was put into the working channel of the flexible endoscope. The distal end of the Teflon tube carries a ceramic nozzle to prevent tissue adherence. The flow rate of the argon gas through the Teflon tube can be adjusted and was set at 1.0 l/min as standard. The rate of gas flow was adjusted during the procedure according to the needs. The working principle is, that high-frequency electrical current is fed from a probe tip through the ionized argon plasma without contact with the tissue, resulting in superficial, thermal coagulation. The brightly shining ionized argon plasma can be guided under visual control.

We used general anaesthesia with low oxygen concentration for safety reasons. After removal of the 5 mm cannula in the tracheostoma of the patient the flexible endoscope with the APC-tube was introduced in intermittent phases of apnoea. The papillomatous lesions were treated with several short intervals (around a second) of APC activation until the desiccated zones on the lesions or on the adjacent mucosa were visible. When thicker papillomatous lesions had to be removed, we used a little round-shaped soft brush on the thin desiccated zone after APC treatment in order to expose the underlying remaining mass for further APC passages. Thus, thick lesions can be removed by several APC passages in a controlled and safe way. Macroscopically normal mucosa was avoided. Any bleeding which occurred whilst using the endoscope or touching the papillomas was controlled immediately by APC. Each session lasted about 20 minutes and was repeated every three weeks for a total of four sessions. The child arrived at the hospital with her mother directly before the operation and was discharged on the same day without any problems.

Result

Control endoscopy after four sessions revealed no papillomatous lesions of the mucosa. Many of the lesions seen at the initiation of the therapy were removed (Figure 2). Following the fourth session, we were able to increase the treatment intervals to every two months. No increased formation of crust was seen in the trachea. There was no stenosis of the trachea due to the APC treatment or permanent damage to the mucosa. We did not see uncovered tracheal cartilage. The cumulative amount of argon gas flow through the probe in each session decreased from 2.1 litres in the first session to 0.3 l by the fourth

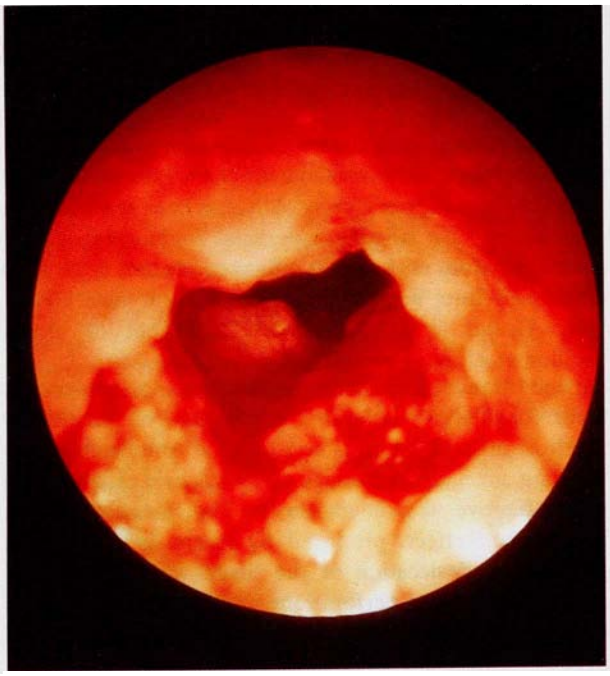

FIG. 1

RRP of the trachea in a seven-year-old girl before the initiation of the APC therapy. A marked stridor was present due to the obstructing papillomas.

FIG. 2

The trachea of a seven-year-old girl after the second treatment session with APC, only a few papillomas remain.

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TABLE I
APPLICATION DATA OF ARGON PLASMA COAGULATION

Session No.	1	2	3	4
Cumulative time of action	115 sec	83 sec	51 sec	17 sec
Cumulative amount of argon gas used (litre)	2.11	1.51	0.91	0.31

session (Table I). The time of activation of the APC which corresponds to the actual time of argon plasma flow was continuously decreasing from 115 seconds at the first session to 17 seconds in the fourth session.

The rate of the argon gas flow was in the range of 0.8 to 1.6 l/min depending on the location and the lesion. For a more defined and localized lesion we chose a lower gas flow. Lesions at the tracheostoma were treated with a higher gas flow. We have now extended the time interval for treatment to every three months.

Discussion

Treatment of progressive RRP in children is a challenging task for any ENT surgeon. The fact that surgical removal could not prevent recurrence gave rise to various systemic treatment trials but without success (Willging, 1995). Surgical removal is still the mainstay for treatment. Various forms of surgery are used but they all have disadvantages. Beside the removal with cup-forceps, but which may lead to incomplete removal, because of limited vision by bleeding, a few forms of laser applications are in use. The CO_2 laser has been successfully used with a micro-laryngoscope and a microscope for lesions in the supraglottic larynx, but has its limits in the lower airways in children. Flexible endoscopy is required for the treatment of papillomatous lesions in the lower airways. Lesions in the trachea could therefore be treated with KTP or a Nd:YAG laser because both laser systems work with flexible fibres. The KTP laser is potentially of advantage, when no deep penetration is required. But the weak effect on haemostasis carries the risk of bleeding in the lower airway and the use of yellow spectacles for eye protection makes it more difficult to distinguish normal mucosa from pathologic mucosa. The Nd:YAG laser is able to coagulate the tissue, which is of advantage. But its use in a flexible endoscope for RRP in the trachea is limited by the fact that the transition between coagulation and vaporization depends on the distance from the tip to the tissue. This distance is difficult to maintain as constant and therefore the penetration depth through vaporization is difficult to control. Perforation can occur.

Tissue damage in APC remains low and is controllable, in comparison to laser-treated tissue, where the deep thermal effect cannot be predicted in the tracheal wall (advantages of APC are seen in Table II). Since argon is chemically inert, there is no tissue carbonization. Tissue vaporization is not possible with APC, since endogenous heating of the tissue is automatically limited by the electrically insulating effect of the desiccated coagulation layer that is formed. The effect limited to the surface is desirable because of the nature of the disease. The virus-infected cells are principally found in the mucosa. The absence of vaporization with APC avoids a possible risk of infecting further airway structures by vapour-containing virus particles.

TABLE II
ADVANTAGES OF ARGON PLASMA COAGULATION IN RRP

- Effective haemostasis through coagulation
- Non-contact application with good visual control
- Usable in flexible endoscopy
- Depth of penetration and thermal trauma is limited
- No carbonization of tissue
- No vaporization of tissue
- Low risk of perforation and damage of cartilage
- Low cost compared to other treatment forms

The argon gas flow at the tip of the probe has the additional advantage of improving visibility, as a bleeding lesion may be controlled by blowing away the blood. Further advantage of APC concerns mobility and cost. APC has already been proved to be an efficient tool for endoscopic treatment of gastrointestinal neoplasms and is now being investigated in various surgical fields (Sessler *et al.*, 1995).

Our reported case showed that APC treatment is a very safe and efficient procedure for the treatment of recurrent papillomatosis in the lower airways. Its advantages for the treatment of supraglottic disease has still to be investigated. Therefore it is of importance that APC should be used gradually and with care. This will ensure that adequate treatment will evolve.

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