Efficacy of Long-term Interferon-alpha Therapy in Adult Patients with Recurrent Respiratory Papillomatosis

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Introduction

First described in the seventeenth century as a "wart in the throat", recurrent respiratory papillomatosis (RRP) is a rare disease characterized by the growth and relentless recurrence of benign squamous papillomas in the respiratory tract. The lesions most commonly involve the oral cavity, oropharynx, and larynx, and only 5% of these tumors extend more distally to involve the trachea. Involvement of the lung parenchyma is rare, occurring in less than 1% of cases. Malignant transformation into squamous cell carcinoma occurs in 3-5% of patients, and may be idiopathic or due to exposure to carcinogens, immunosuppressants, radiation, or smoking.

The age distribution of RRP is bimodal, with juvenile onset (<5 years) or adult onset (>20 years), and the prevalence of this disease is about 3 to 5 per 100,000...
In general, no disease-specific definitive medical therapy is available for RRP. Therefore, standard treatment consists of endoscopic laser excision of all visible papilloma from affected areas of the respiratory tract, as warranted by the patient’s symptoms. The disease is noted for its highly unpredictable course, with rapid growth, spread within the respiratory tract, spontaneous resolution, and the constant possibility of airway obstruction requiring urgent intervention to maintain patency. Due to the clinical variability of RRP, several methods of adjuvant therapy have been reported, including interferon-alpha (IFN-α), indole-3-carbinol, methotrexate, cidofovir, acyclovir, ribavirin, cis-retinoic acid, and photodynamic therapy.

Since 2002, Samsung Medical Center’s guidelines have mandated regular injection of IFN-α in adult patients with RRP. After initial laser therapy, patients receive subcutaneous injection of 6 million units of IFN-α every 2 months, and are evaluated regularly by bronchoscopy and/or computed tomography (CT).

To describe and evaluate the efficacy of long-term IFN-α therapy in adult patients with RRP, patient data were investigated in the present study.

Materials and Methods

1. Patients

The study population included patients with RRP referred for laser therapy from January through December 2002. All patients were diagnosed by bronchoscopy and histopathology. The protocol was approved by the Institutional Review Board of Samsung Medical Center and patients gave their informed consent to use IFN-α as part of their adjuvant treatment for RRP. Patients’ medical records were reviewed and clinical characteristics, number of laser treatments before and after IFN-α injection, adverse events of IFN-α, and clinical outcome were investigated.

2. Diagnostic procedure

Patients were evaluated by chest radiography, spirometry, bronchoscopy, and biopsy at the time of referral. Bronchoscopy showed multiple wart-like papillomas scattered in the central airways, which showed a typical bunch-of-grapes appearance. Pathology confirmed the diagnosis of papilloma.

3. Technique of bronchoscopic intervention and IFN-α injection

All patients underwent bronchoscopic intervention with rigid bronchoscopy under general anesthesia. After induction of general anesthesia, patients were intubated with a rigid bronchoscope tube (Hopkins; Karl-Storz, Tuttingen, Germany). A flexible bronchoscope (EVIS BF 1T240; Olympus, Tokyo, Japan) was then introduced through the rigid bronchoscope, and the tumor was mechanically removed by suction. Then, a 20 watt Nd-YAG laser (Model 1000; LaserSonics, Milpitas, CA, USA) was applied using a G56D noncontact fiber (LaserSonics) to cauterize the base of the papilloma and control bleeding. Laser cauterization was minimized to prevent unnecessary injury to the normal mucosa and future development of new papilloma.

After bronchoscopic intervention, patients received subcutaneous injection of 6 million units of IFN-α (Roche, Basel, Switzerland) every 2 months until complete remission of RRP.

4. Follow-up procedure and definition of outcome

After laser therapy and IFN-α injection, patients were regularly evaluated by bronchoscopy every three to six months and/or chest CT every twelve months. In addition, further bronchoscopic intervention was carried out as needed to maintain airway patency.

Clinical outcome was evaluated based on patients’ symptoms, chest radiography, bronchoscopy, and/or CT findings. Response to treatment was classified as complete, partial, or no remission, which were defined as no evidence of disease for at least 6 months, stable and reduced need of laser therapy, and the same or increased (aggravated recurrence) need of laser therapy after IFN-α injection, respectively.