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ORIGINAL ARTICLE

후두유두종증의 예후인자: 20년간의 임상 경험을 통한 분석

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Prognostic Factor of Laryngeal Papillomatosis: 20 Years Experience

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Background Laryngeal papillomatosis, which is caused by human papillomavirus, is the most common benign neoplasm of the larynx. However, the prognosis of this disease remains really unpredictable. The aim of this paper is to determine whether any clinical features at the time of diagnosis could predict its course.

Material and Method Eighty-six patients treated at our institution during the last 20 years were analyzed retrospectively. All patients had microsurgery under general anesthesia. All patients' follow-up period was more than 1 year. We divided the patients into 1) Juvenile versus adult group based on their age 20, 2) single surgical method with laser versus dual surgical method with laser and microdebrider group, and 3) single subsite versus multiple subsites group. And we compared the therapeutic outcome.

Results The recurrence rate was 100% (15 patients) in the JP group and 56% (40 patients) in the AP group. Juvenile versus adult group was the only independent prognostic factor by univariate, and multivariate analysis. Microdebrider resection technique and multiple subsites were not associated with treatment result. Time period from the first surgery to recurrence detection was different statistically only for the age group. The number of surgery in the JP group ranged from 1 to 31 (mean 8.8). In the AP group the number of surgery ranged from 1 to 25 (mean 3.7). It was statistically different.

Conclusion Prognosis for the laryngeal papillomatosis remains unpredictable. Only patients' age was the only independent prognostic factor.
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KEY WORDS Larynx · Papillomatosis · Prognosis.

Introduction

Laryngeal papillomatosis is the most common benign tumor of the larynx. Although it is a benign disease, it has an unpredictable clinical course, tends to recur and spread throughout the aerodigestive tract, and can undergo malignant conversion. This is a disease of virus called human papilloma virus (HPV). However, no known single therapy or combination of therapies that can reliably eradicate HPV from respiratory tract. So, it is impossible yet to predict the course of this disease.

The aim of this paper is to review retrospectively 86 laryngeal papillomatosis patients treated in 1989-2008 at the Korea University Hospital and to determine the results of treatment and whether any clinic al factor may predict the course of the disease.

Materials and Methods

We reviewed eighty-six patients who had treament in our department during the last 20 years. These included 60 male

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patients, and 26 female patients. Their mean age was 41 years. All patients had microsurgery under general anesthesia. In some special cases which required inspection of the posterior part of the glottis and subglottis, jet ventilation or apnea technique was performed. All patients' follow-up period was more than 1 year (mean 6.2 years; 1.0-32.4 years).

We divided the patients into 1) Juvenile versus adult group based on their age 20, 2) single surgical method with laser versus dual surgical method with laser and microdebrider group, and 3) single subsite versus multiple subsites group according to the staging system (Table 1).[1] And we compared treatment results.

Some of the patients had already had several surgical interventions for laryngeal papillomas in other medical institutions. In this paper only the operations performed in our department are evaluated.

In the JP group, papillomatosis were excised not at the first sign of disease or recurrent growth but at the moment when the phonatory and respiratory disorder became clinically obvious. The aims of surgery in the JP group were 1) meticulous removal of papillomas to maintain a stable airway, and 2) preservation of the voice. The aims of surgery in the AP group were slightly different: 1) radical removal of papillomas and restoration of the voice, and 2) prevention of possible malignancy of papillomas.

All patients underwent endolaryngeal microsurgery. We started to use microdebrider from 2004. We used microdebrider combined with laser in 17 patients, and laser only for 69 patients. Patient's age was not statistically different between two groups. We combined Interferon treatment when the patients need more than four surgery per year, rapid growth with airway obstruction, distal multiple spread (JP- 2 patients, AP-4 patients).

We compared the recurrence rate among these prognostic factors using the Kaplan-Meier method, Cox regression analysis. Statistical analysis was performed by using SPSS for Windows (version 12.0; SPSS Inc., Chicago, IL, USA). Statistical significance was set at $p < 0.05$.

Results

Presentation

The JP group consisted of 15 patients. The AP group consisted of 71 patients. The JP patients presented with two main symptoms: hoarseness (11 patients) and dyspnea (4 patients). In the AP group the main complaint of patients was hoarseness (60 patients). No patient suffered from respiratory distress. Less common presenting symptoms include sore throat, and globus sensation. It was not uncommon that the misdiagnosis of asthma, croup, allergies, bronchitis, or vocal nodule/ polyp was entertained at the first visit hospital (JP group-9 patients; 60%. AP group-7 patients; 1%) before a definitive diagnosis was made. The mean duration of symptoms before the first operation was 12 months (JP group), and 10.6 months (AP group).

Number of primary papilloma lesion

The vocal fold was usually the first and predominant site of papilloma lesions. Seventy-one patients had a single subsite, 15 patients had multiple subsites. Patient's age was not statistically difeerent between two groups.

Recurrence & Prognostic factor

Recurrence requiring surgical intervention amount to 100% in JP patients and 56% in AP patients. Fifty-seven percent of laser-only treatment group had a recurrence, 94% of laser with microdebrider treatment group had a recurrence. The reason for high recurrence rate in microdebrider group is that we started this instrument recently, and used usually for more aggressive condition. Sixty-one perecnt of single subsite group had a recurrence, 65% of multiple subsite group had recurrence. Juvenile versus adult group was the only independent prognostic factor by univariate, and multivariate analysis. Microdebrider resection technique and multiple subsites were not associated with treatment result (Table. 2).

Time period from the first surgery to recurrence detection was different statistically only for the age group. The number

Table 1. Demographics of three different patient group. Patients are divided into groups based on their age, treatment methods, number of primary sites

	Age group		Device group		Multiplicity group	
	JP	AP	Laser only	Laser with microdebrider	Single subsite	Multiple subsites
Sex	Male 9 Female 6	Male 50 Female 21	Male 47 Female 22	Male 13 Female 4	Male 47 Female 24	Male 13 Female 2
Age (years)	2-16 (mean 8)	21-79 (mean 47.4)	2-79 (mean 40.2)	2-66 (mean 41.6)	2-79 (mean 39.7)	3-66 (mean 44.3)
Total	15	71	69	17	71	15

JP: juvenile papillomas, AP: adult-onset papillomas

of surgery in the JP group ranged from 1 to 31 (mean 8.8). In the AP group the number of surgery ranged from 1 to 25 (mean 3.7). It was statistically different. Laser-only treatment group had 3.4 surgery, laser with microdebrider treatment group had 9.3 surgery. The reason for high number of surgery in microdebrider group is that, as mentioned before, we started to use this instrument usually for more aggressive, recently. Mean number of surgery was 4.5 for single subsite group and 5.1 for multiple subsites group. There was no significant difference statistically (Table. 3).

Tracheotomy

Only one JP patient had a tracheotomy due to the urgent dyspnea. However, it has been suggested that tracheotomy may activate or contribute to the spread of disease lower in the respiratory tract. Thus, we always try to avoid unless absolutely necessary. When a tracheotomy is unavoidable, we consider decannulation as soon as the disease is managed effectively with endoscopic techniques.

Complication

There were no serious complications related to surgery. Glottic web was the only complication with 8 patients (JP group-4, AP group-4).

Malignancy

We get the surgical specimen as a first step in surgical procedure. Only one AP gourp patient had a malignant tumor after several surgical intervention.

Discussion

The pattern of the growth rate of papillomas is really irregular and unpredictable. The disease may undergo spontaneous remission, persist in a stable state requiring only periodic surgical treatment, or may be aggressive, requiring surgical treatment every few days to weeks and consideration of adjuvant medical therapy. Knowing that HPV may persist in clinically normal mucosa for a long time, especially in the active more aggressive form, eradication is not possible and, therefore, treatment should be conservative.[2)]

Despite there being no significant histological differences between juvenile and adult onset laryngeal papillomatosis, It has been claimed that the juvenile form of the disease carries a higher risk of recurrence than does the adult-onset disease.[3)] Therefore two clinical types of laryngeal papillomas may be distinguished: 1) juvenile papillomas (JP), 2) adult-onset papillomas (AP). The age of 20 years marks the border between the JP and AP groups.[4)] Juvenile papillomas usually develop on the vocal cords. As the disease progresses, papillomas extend to the supraglottic and infraglottic regions and the trachea. With growth, papillomas lead to progressive laryngeal stenosis. When papillomas are removed they recur quite quickly and spread into the unaffected portions of the larynx. With maturation, JP can regress spontaneously. Adult-onset papillomas (AP) manifest themselves clinically mainly with hoarseness. Laryngeal stenosis is rarer than in JP. Data from the specialist literature indicate that approximately 1.7−7% of AP cases are liable to become malignant.[4)] There

Table 2. Recurrence of laryngeal papillomatosis. Only patient's age has a prognostic value. JP patients are at the greatest risk for recurrence. Microdebrider resection technique and multiple subsite are not predictable prognostic value

	Age group		Device group		Multiplicity group	
	JP	AP	Laser only	Laser with microdebrider	Single subsite	Multiple subsites
Recurrence (+)	15 (100%)	40 (56%)	39 (57%)	16 (94%)	45 (63%)	10 (67%)
	4.6 mo	14.6 mo	8.1 mo	20.9 mo	9 mo	24.4 mo
Recurrence (−)	0 (0%)	31 (44%)	30 (43%)	1 (6%)	26 (37%)	5 (33%)
		29 mo	30 mo	1 mo	30.3 mo	22.4 mo
p−value						
Univariate analysis	.000*		.141		.659	
Multivariate anaylsis	.000*		.06		.51	

JP: juvenile papillomas, AP: adult-onset papillomas

Table 3. Numbers of surgery were greater with JP group and laer with microdebrider group. The number of laryngeal procedures performed may not only reflect the severity of the disease, but also the effectiveness of the surgery and the patient's ability to accept hoarseness. The reason for high number of surgery in microdebrider group is that, we start this instrument recently, and use usually for more aggressive condition

	Age group			Device group			Multiplicity group		
	JP	AP	p-value	Laser only	Laser with microdebrider	p-value	Single subsite	Multiple subsites	p-value
Number of surgery	8.8	3.7	.004*	3.4	9.4	.000*	4.5	5.1	.952
Disease relapse time	4.6 mo	20.9 mo	.02*	17.6 mo	19.7 mo	.674	16.8 mo	23.7 mo	.266

JP: juvenile papillomas, AP: adult-onset papillomas

is, so far, no explanation as to why very aggressive courses of the disease have been often observed in juvenile recurrent laryngeal papillomatosis. It can be assumed developing immune system protect adult, children's immune system is not strong enough. There need more studies to be proved.

The treatment of laryngeal papillomatosis is still based on surgery, although it is an infectious disease. Endolaryngeal microsurgery with a gentle technique, avoiding excessive surgical trauma, makes it possible to remove papillomata on the vocal cords surrounding and close to the subglottic area with minimal damage to the underlying tissue and normal laryngeal structures. Massively involved lesion cannot be completely removed because it is impossible to determine where the normal tissue begins. In such cases, conservative approach are to be expected better long-term results with regard to voice and airway preservation compared with radical surgical approaches.

In JP patients it is more reasonable to excise papillomas not at the first sign of disease or recurrent growth but at the moment when the phonatory and respiratory disorder becomes clinically obvious. The goal of surgery is to maintain a safe airway with serviceable voice while avoiding excessive scarring. The aim of surgery in JP group were 1) maintain airway, 2) voice preservation. In AP patients the tactics for the surgical management of laryngeal papillomatosis are slightly different. Single papillomatosis should be removed when they border on normal tissue. Multiple and extended papillomas should be removed in the same manner as in JP patients. However, malignant degeneration of papillomas must be considered as a risk factor, which emphasizes the importance of repeatedly removing recurrent papillomas. Increasing airway distress was an absolute indication for surgery in both groups of patients. Increasing hoarseness was an indication for surgery in the AP group; however, this symptom was not decisive in the JP group. Indications for surgery in the JP group were determined individually after evaluation of the patient's age, general status and other symptoms.[4] The younger the patient, the faster the symptoms of airway distress occur, and intervals between repeated surgery become shorter.

Until now the greatest progress in the treatment of laryngeal papillomatosis has been the use of laser surgery. It has been favored over conventional instruments because of its hemostatic ability (while vaporizing papillomas) and its relative precision. Recently, the use of a laryngeal and tracheal microdebrider has been reported to be superior to laser surgical approaches on the basis of safety (airway fire, inadvertent laser injury) and lower costs.[2,5] We started to use an endoscopic microdebrider. However, regarding the recurrence rate, it doesn't improve recurrence rate based on our data.

In summary, the prognosis for the disease remains rather unpredictable. Only patients' age was the only independent prognostic factor.

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