The effects of quadrivalent human papillomavirus vaccination in recurrent respiratory papillomatosis (RRP)

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Introduction

Recurrent respiratory papillomatosis (RRP) is a benign neoplasm of the respiratory tract involving the formation of laryngeal papillomata¹. Frequent surgical resection is required in order to maintain airway patency and improve voice quality. Papillomata are associated with benign human papillomavirus (HPV) subtypes -6 and -11² and, hence, the quadrivalent HPV vaccine (Gardasil®) has been proposed as an adjuvant therapy³ to prevent new papilloma formation at additional sites. There is currently a relative lack of data for the efficacy of the vaccine in this role.

Aims

In this case series, we aim to observe the effects of therapeutic HPV vaccination with Gardasil® on the frequency of surgical procedures in patients with RRP.

Methods

Patient selection

- Adults (18+ years old)
- Confirmed HPV-positive RRP

Gardasil® vaccine

- General practitioners asked to administer at 0, 1 and 4 months.

Data collection

- Clinic and surgical notes
- Contact with GPs

Results

Patients identified

Patient	Gender (M/F)	Age of Diagnosis (years)	Juvenile/Adult -onset	Presenting Complaint	Extent of papillomata	Surgical modalities		Vaccination Age (years)	Adjuvants	Pre-vaccination			Post-vaccination		
						Helica cautery	Microdebrider			Follow-up period (years)	No. of surgical procedures	Procedures/ year	Follow-up period (years)	No. of surgical procedures	Procedures /year
1	M	24	AoRRP	Hoarseness	Vocal cords	x		25	None	1.76	2	1.14	0.11	0	0.00
2	F	64	AoRRP	Hoarseness	Vocal cords	x		65	None	5.33	2	0.38	1.57	0	0.00
3	F	<31	AoRRP	Hoarseness	Left arytenoid and vocal cord	x	x	45	None under this clinic	14.10	4	0.28	3.11	0	0.00
4	M	7	JoRRP	Hoarseness	Vocal cords to trachea		x	34	None under this clinic	14.72	12	0.82	3.12	2	0.64
5	M	26	AoRRP	Hoarseness	Vocal cords	x	x	34	None under this clinic	6.40	8	1.25	1.47	1	0.68
6	F	26	AoRRP	Hoarseness	Vocal cords and supraglottis		x	26	None	1.00	2	2.00	0.53	0	0.00

Average frequency of procedures pre- and post- Gardasil

Procedures by year pre- and post- Gardasil

Discussion/Summary

Literature review

- Juvenile-onset RRP – 5 case reports: 3 showed complete remission within follow-up periods^{5,7,8}; 2 showed increased inter-surgical interval^{4,9}. One uncontrolled intervention study of 9 patients showed no change in clinical course in the year before and after Gardasil¹⁶.
- Adult-onset RRP – 2 case series. Significant increase in inter-surgical interval. Complete remission in 40 - 85% without recurrence at 2 years follow up.

Results summary

- 3 or 4 patients had no further procedures after Gardasil®.
- 2 patients had fewer procedures after Gardasil®.

Limitations

- Small number of patients
- Relatively short follow-up period

Future prospects

- Larger, multi-centre studies with longer follow-up are needed to establish what constitutes best practice in the management of RRP.

References

- ¹DERKAY, C.S. and WIATRAK, B., 2008. Recurrent Respiratory Papillomatosis: A Review. *The Laryngoscope*, **118**(7), pp. 1236-1247.
- ²MOUNTS, P., SHAH, K.V. and KASHIMA, H., 1982. Viral etiology of juvenile- and adult-onset squamous papilloma of the larynx. *Proceedings of the National Academy of Sciences of the United States of America*, **79**(17), pp. 5425-5429.
- ³LUVELY, J.M. and SHAH, R.K., 2013. Recurrent respiratory papillomatosis: A possible role for the HPV vaccine? *Journal of the American Academy of Physician Assistants*, **26**(5).
- ⁴BAUMANIS, M.M. and ELMARAGHY, C.A., 2016. Intersurgical interval increased with use of quadrivalent human papillomavirus vaccine (Gardasil) in a pediatric patient with recurrent respiratory papillomatosis: A case report. *International journal of pediatric otorhinolaryngology*, **91**, pp. 166-169.
- ⁵FORSTER, G., BOLTZE, C., SEIDEL, J., PAWLITA, M. and MULLER, A., 2008. Juvenile laryngeal papillomatosis-immunisation with the polyvalent vaccine gardasil. *Laryngo-rhino-otologie*, **87**(11), pp. 796-799.
- ⁶HERMANN, J.S., WEOCK, L.Y., MONTEIRO NURMBERGER, J., SANTOS JUNIOR, G., FRANCISCO DOS, CAMPOS PIGNATARI, A.C. and NAGATA PIGNATARI, S.S., 2016. Effectiveness of the human papillomavirus (types 6, 11, 16, and 18) vaccine in the treatment of children with recurrent respiratory papillomatosis. *International journal of pediatric otorhinolaryngology*, **83**, pp. 94-98.
- ⁷MESZNER, Z., JANKOVICS, I., NAGY, A., GERLINGER, I. and KATONA, G., 2015. Recurrent laryngeal papillomatosis with oesophageal involvement in a 2 year old boy: successful treatment with the quadrivalent human papillomavirus vaccine. *International journal of pediatric otorhinolaryngology*, **79**(2), pp. 262-266.
- ⁸MUDRY, P., VAVRINA, M., MAZANEK, P., MACHALOVA, M., LITZMAN, J. and STERBA, J., 2011. Recurrent laryngeal papillomatosis: successful treatment with human papillomavirus vaccination. *Archives of Disease in Childhood*, **96**(5), pp. 476-477.
- ⁹SULLIVAN, C., CURTIS, S. and MOUZAKES, J., 2017. Therapeutic use of the HPV vaccine in Recurrent Respiratory Papillomatosis: A case report. *International journal of pediatric otorhinolaryngology*, **93**, pp. 103-106.
- ¹⁰YOUNG, D.L., MOORE, M.M. and HALSTEAD, L.A., 2015. The use of the quadrivalent human papillomavirus vaccine (gardasil) as adjuvant therapy in the treatment of recurrent respiratory papilloma. *Journal of Voice*, **29**(2), pp. 223-229.
- ¹¹CHIRILIA, M. and BOLBOAGA, S.D., 2014. Clinical efficiency of quadrivalent HPV (types 6/11/16/18) vaccine in patients with recurrent respiratory papillomatosis. *European Archives of Oto-Rhino-Laryngology*, **271**(5), pp. 1135-1142.

Laryngeal papilloma photograph from: <http://www.entdoctor.com.au/sites/default/files/images/other/conditions/papilloma-pre-treatment-abduction.jpg>

Acknowledgements

The authors would like to thank Mich Maroney for her help contacting GPs and locating clinical notes.