British Association of Paediatric Otorhinolaryngology members experience with recurrent respiratory papillomatosis

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Summary

Objectives: To establish current practice in the treatment of recurrent respiratory papillomatosis (RRP) in the UK.

Methods: Consultant members of the British Association of Paediatric Otorhinolaryngology (BAPO) were sent a questionnaire on current practice concerning the management of recurrent respiratory papillomatosis in the paediatric population.

Results: The response rate was 39.4% perhaps reflecting the relatively small number of otolaryngologists who treat this condition. Data were analysed from 41 respondents representing 27 departments for a total of 103 patients. A total of 13 patients (12.6%) received adjuvant medical therapies with the antiviral agent cidofovir accounting for 10 patients. Distal spread of RRP has occurred in 27 (26.2%) patients. There were six reported deaths due to progressive RRP. Various lasers (CO₂, KTP, and pulsed dye) are the preferred method of surgical removal of RRP in children. Spontaneous ventilation (65.3%) is the preferred method of anaesthesia. Half of the consultants do not routinely send for HPV subtyping and 75% send lesions for histological examination if there is a change in growth pattern. Two thirds of respondents do not routinely treat their patients with antireflux medication.

Conclusion: There is a need for the establishment of a centralized national base to which all treating consultants can report their cases. The time has come for national multicenter controlled trials on the use of adjuvant interventions for the treatment of both severe and less severe RRP disease. Both of the above can be organized under the umbrella of BAPO.

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1. Introduction

Recurrent respiratory papilomatosis is the most common benign neoplasm in the larynx and the second most common cause of hoarseness among paediatric patients [1]. Although benign in histology, epithelial proliferations may result in progressive hoarseness, stridor, airway obstruction, and respiratory distress rendering RRP a serious and potentially life threatening disease. Human papilloma viruses type 6 are 11 are the most common aetiological agents, with HPV-11 conferring a most aggressive course to RRP [2]. The incidence of RRP is estimated at 4.3 per 100,000 [3]. Vaginally delivered firstborn children to teenaged mothers have an increased risk for RRP [4]. Age at diagnosis is the most important determinant of disease severity, with patients younger than 3 years old requiring significantly more annual surgeries. These younger children are also more likely to have multicentric disease and have a higher incidence of tracheotomy [5].

The larynx is the most commonly affected site with distal tracheobronchial and pulmonary involvement rare. Malignant transformation has been described associated with HPV-11 [6].

Current treatment aims to maintain a patent airway and acceptable voice, while preventing complications such as laryngeal scarring or stenosis. Surgical treatment remains the principal modality, with patients requiring a mean of 4.4 procedures during their first year of diagnosis [7].

Ongoing trials are showing a promising role for adjuvant medical therapy with alfa interferon, indole 3 carbinol, cidofovir, acyclovir, cis-retinoic acid, mumps vaccine, and photodynamic therapy.

The impact of RRP on patients, their families and the health care system is considerable, with an estimated $109 million annual expenditure in the USA [3].

During 2002, ASPO surveyed their members regarding treatment of RRP and published the results in 2004 [8]. Spurred by the work of our colleagues from across the Atlantic, we decided to characterize the current surgical and medical management of RRP in the UK, by surveying the members of BAPO.

2. Methods

A postal survey regarding the experience with paediatric patients with RRP was sent to 104 BAPO Consultant members from December 2003 to March 2004. A further e-mail based reminder was sent during the month of April 2004. Membership affiliation was obtained from the BAPO register and cross-checked with the ENT UK members list. The questionnaire used was the same one as used by Prof. Derkay for his American Society of Pediatric Otolaryngology (ASPO) survey and was kindly provided by the author. Duplicate responses were excluded from analysis and values included in colleagues responses were adjusted to reflect the experience of consultants within the same department.

3. Results

A total of 41 paediatric otolaryngology consultants from 27 departments responded to the survey. Not all consultants responded to all of the questions in the survey, with two departments not providing any numbers of patients treated. The response indicated that 26 consultants from 18 departments are currently treating patients with RRP. The distribution is shown in Fig. 1 with a total of 103 patients, resulting in a median of 5 patients per department.

There were three departments in which more then one consultant responded to the survey.

Five departments, treating 49 patients (47.5%) have a total of 13 patients (12.6%) treated with adjuvant medical therapy, see Fig. 2.

The most commonly used adjuvant therapies were cidofovir (n = 10), interferon (n = 4), and indole 3 carbinol (n = 1). Two of the patients received sequentially cidofovir followed up by interferon. Unfortunately most of the respondents were unable to provide any detailed information on the use of the adjuvant medical therapies and could not reliably rate their efficacy.

Eight departments are treating 27 (26.2%) patients with distal spread of the disease in the trachea (18), trachea and bronchi (5), trachea, bronchi, and lung parenchyma (4). Two of those are treated with surgery alone, whereas six have surgery and adjuvant therapy (cidofovir, interferon and indole 3 carbinol).

Different types of laser are the preferred means for surgical removal of laryngeal RRP, with CO₂ used by 12 (46.1%) respondents, KTP by 5 (19.2%), and...
It relied on accurate documentation by the surveyed consultants regarding the management of RRP in their departments. Considering the methodology, this survey has obvious limitations and is open to selection (membership, nonrespondent) and ‘best estimate’ biases. There may be consultants in the UK that manage paediatric patients with RRP and not are members of BAPO. Also the response rate of 39.4% is way under the required 80% that would eliminate nonrespondent bias. Most of the surveyed consultants were unable to provide detailed data on the use of cidofovir and rate its efficacy as an adjuvant therapy. On two occasions there were no estimates on the number of patients treated. On three occasions more than one consultant from the same department responded to the survey. All data was analysed on an individual (i.e. per consultant) or departmental basis.

Analysing the data each responding department in the UK manages a median of five paediatric patients with RRP. This is less than the nine reported by the ASPO survey [8]. In the UK surgery represents the mainstay of treatment for RRP. Three types of laser account for the majority of procedures, with CO2 laser accounting for 46.1%; this is close to the 42% rate reported in the ASPO survey [8]. Interestingly our survey found that the KTP laser is used by 19.2% of the consultants, whereas there is no report about its usage in the ASPO survey. In one department the pulsed dye diode laser is used. The CO2 laser has stood the test of time as one of the preferred surgical methods but is not without its problems, related to expense, risk of airway fire, delayed and collateral local tissue damage and the potential for HPV DNA particles aerosolization during the procedure [9,10]. The 585 nm pulsed dye laser has been reported as a safer alternative [11]. The microdebrider is used by 38.5% of the respondents, much less when compared with the 53% usage by the ASPO members. The microdebrider is just as precise as the CO2, it is easier to use, involves shorter procedure times and results in better voice quality and reduced costs [12]. A number of the consultants used more than one surgical method.

### Table 1  Method of surgical removal of RRP

<table>
<thead>
<tr>
<th>Surgical method</th>
<th>Number of surgeons</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO2 laser</td>
<td>12</td>
</tr>
<tr>
<td>KTP laser</td>
<td>5</td>
</tr>
<tr>
<td>Diode laser</td>
<td>1</td>
</tr>
<tr>
<td>Microdebrider</td>
<td>10</td>
</tr>
<tr>
<td>Endolaryngeal microsurgery</td>
<td>2</td>
</tr>
<tr>
<td>Cold steel</td>
<td>1</td>
</tr>
</tbody>
</table>

When questioned regarding anaesthesia management during laryngeal papilloma surgery, 17 (65.3%) consultants prefer spontaneous ventilation, 6 (23%) endotracheal intubation, 2 a combination of the above, and 1 jet ventilation.

In six departments, there were 6 (5.8%) deaths due to progressive RRP disease. Of these, three died from progressive pulmonary failure, two from asphyxiation and one from malignant squamous cell carcinoma transformation. CT scanning to monitor for pulmonary spread is used by only seven consultants, two every 3 months, three every 6 months, and two on a yearly basis.

The vast majority of the respondents 20 (76.9%) do not routinely place their patients on antireflux medication, but 2 (7.7%) do so.

When asked about routine HPV typing (i.e. 6 and 11) of their RRP patients, 9 (34.6%) do so, but 14 (53.8%) do not. After the initial biopsy, a change in growth pattern was the most common cause for re-biopsy (73%), followed by clinical symptoms (2 consultants), on a yearly basis (1 consultant), and with every surgery (1 consultant).

### 4. Discussion

This survey aimed to determine the current treatment strategies of paediatric RRP in the UK among the consultant members of BAPO. In order to do this,
The treatment is recommended for 6 months and can result in eradication of disease or a reduction in the tumour burden. Unfortunately, the disease can recur after 6 months and the toxicity associated with its use (leukopaenia, spastic diplegia) has limited its use to severe recalcitrant RRP disease [16]. A more recent study, looking at both paediatric and adult populations, suggested longer treatment regimens (>6 months) in HPV 6 positive patients provide good long term results [17].

Our survey identified 6 (6.5%) deaths from progressive RRP disease. This compares with the 4% rate reported in the ASPO survey.

Only 7.7% of responding consultants reported the use of antireflux medication, compared with 15% in the ASPO survey, despite studies showing beneficial effects in reducing the rate of disease recurrence and soft tissue complications [18].

Only 7 (26.9%) consultants routinely use CT scans to monitor the development or spreading of pulmonary disease. Out of these, 28.6% do so every 3 months, 42.8% every 6 months and 28.6% on a yearly basis. This is the opposite of the results reported in the ASPO survey.

HPV subtyping can be useful in predicting the aggressiveness of the RRP disease. Only 34.6% of the respondents obtain HPV typing (i.e. 6 and 11) of their patients. This compares with the 45% reported by the ASPO survey.

There is still controversy regarding the need to perform a re-biopsy of the papilloma at subsequent surgical interventions. From our survey, 73% of the respondents do it if there is a change in the growth pattern.

What conclusions can we draw from this survey?

Firstly, there is an urgent need for the establishment of a centralized national base to which all treating consultants can report their cases. This will eliminate some of the biases in this survey.

Secondly, the time has come for national multicenter controlled trials on the use of adjuvant interventions – particularly cidofovir – for the treatment of both severe and less severe RRP disease. These can be organized under the umbrella of BAPO.

Thirdly, treatment trends are largely similar on both sides of the Atlantic.

Recurrent respiratory papillomatosis is a benign disease with significant morbidity and potential mortality. Treatment continues to be difficult and involves both surgical and medical modalities. Both modalities are continuously evolving in search of a ‘cure’ with decreased side effects. Only further research and international cooperation can potentially achieve these aims.

References