



British Paediatric Orphan Lung Diseases (BPOLD)

Recurrent Respiratory Papillomatosis - [Dr Michael D Shields](#)

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Definition

Recurrent Respiratory Papillomatosis (RRP) is characterised by the growth of papillomas (wart like lesions) in the respiratory tract which have a propensity to recur after removal. Although RRP is the most common benign neoplasm of the airway it is still a rare disease with an estimated incidence in the USA of 4.3 per 100,000 children < 14 years. Three quarters of children are diagnosed by 5 years.

Causes

Vertical transmission of the human papilloma virus (HPV) occurs at birth as the newborn passes through an infected birth canal. Two thirds of mothers are positive for genital warts compared to <5% mothers of uninfected children. The HPV can be detected for several weeks in the oropharynx of infants born to mothers with genital warts. It has been estimated that 1:500 infants born vaginally to a mother with genital warts will develop RRP. However, not all cases are born to mothers with genital warts and it has been suggested that sexual abuse should be considered in such cases.

The replicating HPV, most commonly types 6 and 11, causes the wart like overgrowths of squamous epithelial cells. The papillomata are multiple projections each with a connective tissue stalk covered by well differentiated stratified squamous epithelium. Viral genome is detectable in surrounding normal appearing tissue suggesting that the infection is more widespread than is clinically apparent. This explains why treatment is so frustrating with recurrences coming after seemingly complete removal.

Clinical Presentations

Symptoms usually appear in children 2 to 4 years of age with 25% presenting in infancy. Symptoms reflect the site of involvement with the laryngeal area being most common. The wart like lesions typically grow out from the anterior portion of the true vocal cords, false cords and the laryngeal surface of the epiglottis. Children usually present with hoarseness, croupy cough, weak cry or dysphonia / aphonia. The degree of airway obstruction can be life threatening.

Diagnosis and investigations

The diagnosis can be made by visual inspection at laryngoscopy or bronchoscopy HPV subtyping may be useful in predicting aggressiveness of disease. Type 11 is more likely associated with need for a tracheostomy and types 11, 16 and 18 have a higher oncogenic potential.

Course

During childhood the pattern is typically of papillomas recurring early after removal during periods of activity interspersed with more quiescent periods. The disease, for unknown reasons, usually enters remission when puberty is reached. Rarely, spontaneous



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malignant transformation of benign papillomas into squamous cell carcinomas occurs (in < 5% RRP cases).

While the papillomas are recurrent in the majority of cases they remain isolated to the larynx and immediate subglottic area. However, between 6 and 12% of cases spread occurs to the distal trachea and in a smaller number this involves the lung tissue. Tracheostomy is associated with tracheobronchial seeding and spread. Within the lung papillomata grow and both obstruct airways and destroy tissue resulting in multiple nodular and cystic lesions which can be seen on CT scan. The lesions enlarge and cavitate overtime destroying healthy lung tissue. Although there is little published literature regarding pulmonary RRP it has been considered to be associated with a poor prognosis.

Treatment

Currently there is no cure for RRP and management is aimed at maintaining airway patency and adequate voice.

Surgery: surgical procedures aim to remove the papillomas while avoiding damage to surrounding normal tissue. Tracheostomy should be avoided if possible. Younger children may require surgical debulking initially on a two weekly basis. CO₂ laser vaporization of papillomas is performed using direct laryngoscopy and a surgical microscope or the microdebrider is used. Surgical resection for the rare isolated lung disease may be possible.

Adjuvant therapy: aims to reduce the frequency that surgical debulking is required. There are no large RCTs showing sustained benefit from any adjuvant therapy and there are no standard criteria for adding adjuvant therapy. Some recommend that it should be started if surgery is needed more than 4-5 times per year.

Interferon (α -2- β) has occasionally produced dramatic results, but with dose reduction or cessation exuberant regrowth can occur. Potentially new antiviral therapies are under evaluation (eg intralesional injection of cidofir).

Because pulmonary metastasis from RRP (demonstrated by CT Scan) carries a poor prognosis often with malignant transformation more aggressive adjuvant therapy has been recommended (see reference 4).

Recent advances using 'virus like particles' to develop vaccines may allow strategies to be put in place for primary prevention

Useful references:

Predictors of remission in juvenile-onset recurrent respiratory papillomatosis.

S Ruparelia et al.

Arch Otolaryngology Head Neck Surg. 2003; 129: 1275-1278.

American Society of Pediatric Otolaryngology Member's experience with recurrent respiratory papillomatosis and the use of adjuvant therapy.

S Schraff et al.

Arch Otolaryngology Head Neck Surg. 2004; 130: 1039-1042

Current status of antiviral therapy for juvenile-

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onset recurrent respiratory papillomatosis.

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63: 141-151.

Diagnosis and management of pulmonary metastasis from recurrent respiratory papillomatosis.

RD Silver et al.

Otolaryngol Head Neck Surg 2003; 129: 622-629.

Web links:

<http://www.rspf.org/>

<http://wwwrrpwebsite.org/>