

## Juvenile recurrent respiratory papillomatosis: A rare masquerade of asthma

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### Abstract

Juvenile recurrent respiratory papillomatosis (JRRP) is a rare condition. The varied presentation of this condition predisposes to misdiagnosis and potential life-threatening airway obstruction. In this paper, we have reported a case of JRRP presenting as severe respiratory distress and consequently mistreated as asthmatic attack culminating in a near fatal acute airway obstruction.

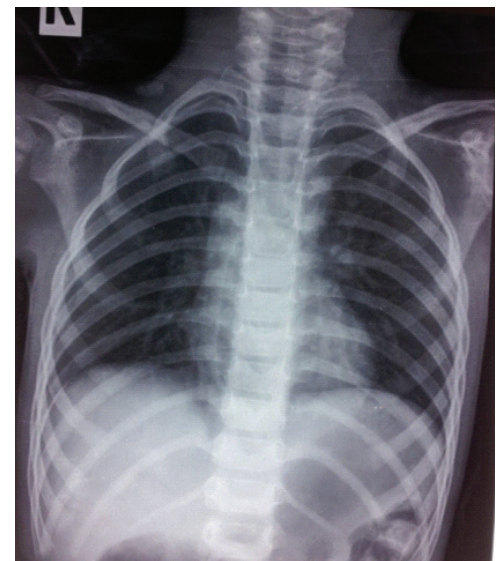
### Introduction

Recurrent respiratory papillomatosis (RRP) is a neoplastic disease of the aerodigestive airway characterised by exophytic squamous wart-like growth. This condition is caused by human papilloma virus (HPV), primarily of the subtypes 6 and 11, which constitute 90% of all RRP cases.<sup>1</sup> JRRP conventionally refers to the subset of RRP with onset of disease occurring at or below the age of 12 years.<sup>2</sup> Despite its rarity with an estimated incidence of 4.3/100,000, JRRP remains the most common benign neoplasm of the larynx in children.<sup>3,4</sup> JRRP has high recurrence rate with the mainstay of treatment involving repeated surgical excisions.<sup>4,5</sup> However, spontaneous remission may rarely occur during puberty.<sup>4,5</sup>

### Case report

A 4-year-old boy was brought by his mother to the emergency department (ED) with complaints of rapid breathing associated with 2-day history of afebrile cough and runny nose. The boy had no underlying medical condition with insignificant medical history except for an episode of rapid breathing 2 months ago, which was relieved by outpatient salbutamol nebulisation received at a private general practice. In addition, the mother also noticed that the boy had slight hoarseness of voice for the past 1 year. The boy had no dysphagia and no history suggestive of asthma or foreign body aspiration. Physical examination revealed the presence of tachypnea with marked intercostals, subcostal and suprasternal recession along with generalised rhonchi sounds in both lungs. Chest radiograph showed hyperinflated lungs

(Figure 1). Subsequently, the boy was treated for acute asthma attack with administration of oxygen, salbutamol nebulisation and intravenous corticosteroid before admission into the paediatric ward.



**Figure 1.** Chest radiograph showing hyperinflation with normal lung fields

Within 12 hours of presentation, the boy developed marked stridor and had a sudden acute respiratory collapse in the ward necessitating emergency endotracheal intubation performed by an anaesthetist. Urgent direct laryngoscopy under general anaesthesia performed by an otolaryngologist revealed papillomas at supraglottic level. Visualisation beyond the glottis was obscured by extensive papillomatous tissue. Endoscopic laryngeal microsurgery was carried out and subsequent tissue biopsy result showed the presence of moderate acanthotic

squamous epithelium with mild neutrophilic infiltrate but without stromal invasion or features of malignancy. The histopathology report was suggestive of benign squamous papilloma. Post-biopsy computed tomography (CT) of the neck and thorax showed an ill-defined enhancing homogenous soft tissue density lesion involving the supraglottis, vocal cord and base of tongue with significant luminal narrowing (Figure 2). Debulking surgery was subsequently carried out within a week of presentation. Since the diagnosis due to recurrence, the boy had undergone a total of three excision surgeries within a span of 1 year. Currently the boy is undergoing vocal rehabilitation and has shown satisfactory voice function. He is thriving well and remains under close follow-up at the otolaryngology clinic for surveillance of recurrence.



**Figure 2.** Computed tomography scans of head and neck showing mildly enhancing lesion (*red arrow*) and significant luminal narrowing of the trachea (*yellow arrow*)

JRRP is notorious for its wide spectrum of presentation. Approximately 75% of RRP cases are diagnosed in the first 5 years of life and almost all by the age of 7 years.<sup>3</sup> Classical symptoms include dysphonia as the most common initial complaint followed by obstructive symptoms such as dyspnea and stridor as the lesion proliferates.<sup>4,6</sup> More often than not, JRRP presents with non-specific symptoms such as cough, wheeze, dysphagia, failure to thrive, choking and even recurrent pneumonia rendering it a diagnostic challenge to clinicians.<sup>2,4</sup> A child presenting with respiratory distress requiring urgent intervention as in this case is rare.<sup>7</sup>

JRRP has a tendency to masquerade as asthma. A case series by Zacharisen in 2006 reported strong predilection of misdiagnosis, with all cases of JRRP variably mistreated as croup, asthma, laryngeal haemangioma and tracheomalacia.<sup>3</sup> Harris et al. (2012) further confirmed the diagnostic intricacies by a report on seven cases of JRRP diagnosed in Leeds General Infirmary over the span of 12 years of which five cases (71%) had prior erroneous treatment as asthma.<sup>6</sup> Another landmark case report described JRRP masquerading as a glucocorticoid-dependent asthma in a 3-year-old child with a history of multiple visits to ED due to recurrent severe wheeze.<sup>5</sup> Patients with JRRP are frequently mistreated as asthma, often receiving multiple inhalers before definitive diagnosis by an otolaryngologist.<sup>6</sup>

The confusion with asthma is attributed to the fact that acute asthma exacerbation remains the most frequent inpatient diagnosis for paediatric populations.<sup>3</sup> Unfamiliarity with the disease has also been implicated as reason for delayed diagnosis.<sup>8</sup> As an important mimicker of asthma, a paramount caveat is that the classic stridor described in JRRP can be notably absent as exemplified by this case. This is because the mass of papillomas may be too soft to vibrate the air column.<sup>9</sup> Interestingly, the case series reported by Zacharisen were similarly void of the cardinal symptom of gradual progressive stridor leading to airway obstruction.<sup>3</sup> Even if it is present in JRRP, the biphasic stridor can be difficult to differentiate from the expiratory wheeze of asthma.<sup>6</sup> In this case, a higher index of suspicion for JRRP may have averted the near-fatal outcome. The presence of rhonchi in chest examination and a history of

relief with inhaled salbutamol nebulisation for a recent similar episode of respiratory distress distracted and obscured the diagnosis of JRRP. The inconspicuous history of dysphonia for the past 1 year should have been given a more central consideration in formulating the differential diagnosis. This is consistent with the finding in literature, which suggests that the diagnosis of JRRP is often established on an average of 1 year after the initial onset of symptoms.<sup>4</sup> Established risk factors for JRRP that may be elicited in history taking include firstborn and vaginally delivered infants, especially to mothers with genital condyloma.<sup>4</sup> Clinicians should also bear in mind that partial or transient relief of airway distress with inhaled beta agonist or corticosteroid is not uncommon in JRRP.<sup>5</sup>

Often misdiagnosed, JRRP may result in severe airway obstruction and death due to delayed diagnosis.<sup>1,6,8</sup> Misdiagnosis of JRRP as asthma resulting in sudden death due to acute respiratory obstruction has been reported in the literature.<sup>10</sup> Even in established diagnosis, sudden death secondary to upper airway obstructive papillomatosis can still occur reflecting the importance of timely diagnosis.<sup>11</sup>

This boy required three excision surgeries in the first year of diagnosis due to symptomatic recurrences marked by stridor and hoarseness. Typically, JRRP requires a mean of 4.4 surgeries in the first year of diagnosis due to high recurrences.<sup>12</sup> RRP is classified as aggressive when a patient requires 10 or more surgical procedures in total, three or more surgeries per year or if the disease spreads to the subglottic region.<sup>13</sup> As such, this boy is regarded to harbour the aggressive type of RRP.

Despite a reported low risk of malignant transformation in JRRP (<1%),<sup>1</sup> surveillance with repeated biopsy may still be warranted particularly if a change in growth pattern is observed.<sup>14</sup> The palliative role of surgical intervention in JRRP aims at preservation of airway patency and a serviceable voice.<sup>7,14</sup>

Research on adjunct therapies to prevent recurrence still lack robust clinical data with current modalities employed include photodynamic therapy, intralesional cidofovir injection, interferon alpha, indole-3-carbinol, acyclovir, ribavirin and numerous others.<sup>2,3</sup>

At present, this boy has shown good progress in voice quality through vocal rehabilitation. JRRP is notorious for its unpredictable and often protracted clinical course with some children requiring more than 100 lifetime surgical interventions to manage airway while others may achieve spontaneous remission.<sup>5,15</sup> As such, the prognosis for this boy is yet to be defined in time.

### Conclusion

Despite its rare occurrences, timely diagnosis of JRRP is crucial to prevent high morbidity and mortality. The diagnosis of JRRP may be challenging unless there is a high index of suspicion and awareness of the variable presentations. General practitioners should proceed with caution in any child with shortness of breath, in particular when associated with hoarseness of voice which warrants tertiary referral to rule out this potentially devastating disease.

### Conflict of interest

The authors declare that there is no conflict of interest.

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### Contribution of authors

Philip Rajan and Woi Hon Boo diagnosed and treated the patient. Siew Mooi Ching and Ping Yein Lee conceived the study. All of them participated in the interpretation and drafted the manuscript.

### How does this paper make a difference to general practice?

- Promote awareness among clinicians, especially general practitioners (GPs) regarding juvenile recurrent respiratory papillomatosis (JRRP) as a rare disease with varied presentation and tendency to masquerade as asthma
- Highlight the implications of high mortality and morbidity with delayed diagnosis and mismanagement of this rare disorder
- Emphasise the need for GPs to maintain high index of suspicion in ruling out this devastating disease when encountering any child with airway problem in particular the need to obtain relevant history of symptoms that may suggest JRRP

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