

# Pediatric Laryngeal Malignancies: Current Management Protocols and Review of Literature

Sudhir M Naik, A Nanjundappa, H Srihariprasad, Rajshekar Halkud, Purshottam Chavan, Sumit Gupta

## ABSTRACT

**Background:** Malignant lesions of the larynx are very rare in pediatric population as it accounts for less than 0.1% of all head and neck malignancies in childhood. Apart from human papilloma virus infection, adult risk factors like laryngeal papilloma, gastroesophageal reflux, human immunodeficiency virus (HIV) infection, immunosuppressive therapy, smoking, alcohol abuse, poor oral hygiene and a family history of cancer also play a role in pediatric laryngeal cancers.

**Case report:** A 14-year-old boy presented to us with hoarseness of voice since 8 months. He was treated for laryngitis and subacute bacterial laryngitis and later referred to us. He complained of mild dysphagia and the hoarseness of voice. An ulceroproliferative lesion in the left arytenoids and aryepiglottic fold was seen with retroarytenoid extension in the left arytenoids and the left hemilarynx was fixed. The left level II node was enlarged 2 × 2 cm and a staged as carcinoma supraglottis T3/4N1Mx. The node aspiration biopsy revealed metastatic squamous cell carcinoma.

**Intervention:** The case was posted for wide field laryngectomy, under ASA grade II. The direct laryngoscopic examination revealed the extent of the tumor, and the frozen sections of biopsy revealed squamous cell carcinoma of the larynx. The surgery was done with the classical Gluck Sorenson incision and the patient was given postoperative radiotherapy.

**Conclusion:** Pediatric laryngeal cancers are very rare and studies about the etiology, biology of the tumor, diagnostic and management protocols are not standardized. Formulating a protocol for childhood laryngeal cancers management which includes early diagnosis and accurate treatment is essential.

**Keywords:** Squamous cell carcinoma, Hoarseness, Total laryngectomy, External beam radiation, Human papilloma virus.

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## INTRODUCTION

Malignant lesions of the larynx are very rare in pediatric population as it accounts for less than 0.1% of all head and neck malignancies in childhood.<sup>1,2</sup> Rehn in 1868 first reported a case of laryngeal cancers in a 3-year-old child.<sup>3</sup> Extensive literature search revealed that overall 91 cases of laryngeal cancers have been reported with 28 cases below 10 years and 63 cases below 15 years.<sup>1,4</sup> Male predominance is not seen as in adults.<sup>5</sup>

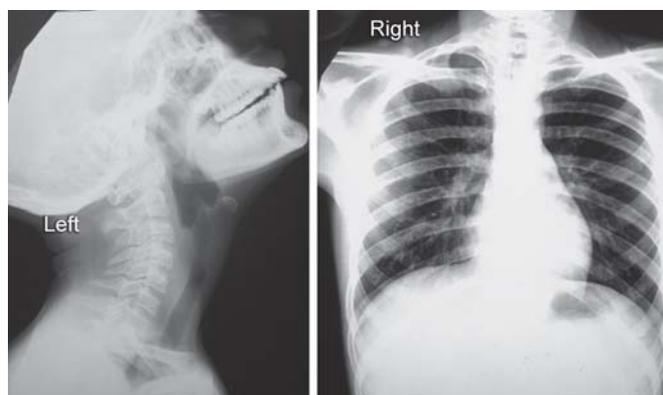
Zahidul et al reported literature research of 98 cases of carcinoma of the larynx in patients less than 20 years of age, which have about 20 cases in the age group less than 12 years.<sup>2</sup> So a remote differential diagnosis should be in mind as laryngeal cancers in pediatric population accounts for less than 0.1% of all head and neck malignancies.<sup>6-8</sup> Incidence in female are nearly equal to male in pediatric laryngeal cancer (female 40% in pediatric, 10% in adult cancer).<sup>3</sup> Risk factor include previous irradiation of papilloma, papillomatosis, malnutrition and human papilloma virus (HPV) infection.<sup>3</sup>

Immunologic and genetic factor which drastically modify the common risk factors, such as tobacco use, previous radiation and chemical carcinogens into definite etiologies also play a role in pediatric patients.<sup>9,10</sup> Juvenile papillomatosis show malignant degeneration after irradiation and so irradiation as treatment is abandoned.<sup>2</sup> Adult risk factors like laryngeal papilloma, gastroesophageal reflux, human immunodeficiency virus (HIV) infection, immunosuppressive therapy, exposure to drug use during pregnancy, both active and passive smoking, exposure to certain chemicals (e.g. asbestos), alcohol use, poor oral hygiene and a family history of cancer also play a role in pediatric laryngeal cancers.<sup>11</sup> Long history of progressive airway obstruction, dysphagia or dysphonia are seen in children but lesions are only diagnosed by a laryngologist by routine mirror or fiber-optic airway examination.<sup>3</sup> The scarcity of cases, attempt to preserve anatomy and function of larynx and for avoidance of complications impedes establishment of treatment protocols in children.<sup>3</sup> The rarity of case has made treatment protocols difficult while workup is similar to that in adults.<sup>12,13</sup> No literature on organ preservation strategies, prognosis, survival rates are reported.<sup>3</sup>

We present a case of squamous cell carcinoma (SCC) in a 15-year-old male, presenting in the advanced stage with laryngeal function compromised and underwent wide field laryngectomy with postoperative concurrent chemoradiotherapy.

## CASE REPORT

A 14-year-old boy presented to us with hoarseness of voice since 8 months. He was treated at various hospitals for laryngitis and subacute bacterial laryngitis and later referred to us for further evaluation. He also complained of mild



**Fig. 1:** Chest X-ray being normal and lateral X-ray of the neck showing no subglottic extension



**Fig. 2:** Post wide field laryngectomy and radiotherapy stoma

dysphagia and the hoarseness of voice was slowly progressive in type. On indirect laryngoscopic examination revealed an ulceroproliferative lesion in the left arytenoids and aryepiglottic fold. There was a retroarytenoid extension in the left arytenoids and the left hemilarynx was fixed. The left level II node was enlarged  $2 \times 2$  cm and the lesion was staged as carcinoma supraglottis T3/4N1Mx (Fig. 1).

The fine needle aspiration biopsy revealed metastatic SCC. With the clinical lesion with metastasis to the neck, staged with computed tomographic (CT) scan, the patient was posted for wide field laryngectomy. The patient was posted for total laryngectomy, as the larynx was functionally compromised and cartilage infiltration seen. The case was posted for wide field laryngectomy, under ASA grade II. The direct laryngoscopic examination revealed the extent of the tumor, and the frozen sections of biopsy revealed SCC of the larynx. The postoperative period was uneventful and recovery was uneventful.

Postoperative histopathological examination revealed SCC grade II, with the tumor extending to the cartilage, all the cartilages free, and the tracheal cut margins free. Pre-epiglottic and paraglottic space involvement was present. Three nodes in level 2a had metastatic spread without extracapsular spread, while all the left level 2b, level 3, level 4 nodes had no metastasis. All the right-sided nodes were reactive. Left sided hemithyroidectomy specimen was free of tumor. The patient had postoperative concurrent chemoradiotherapy with 4 cycles of radical CDDP weekly with external beam radiotherapy of 54 grays. The patient is being followed up with 18 months of disease free survival. The patient is trained for electrolarynx as the patient could not afford the costs of voice prosthesis and second surgical intervention of trachea esophageal puncture (Fig. 2).

## DISCUSSION

Laryngeal cancers are malignancies of old age, common in males and usually present in the 5 and 6th decade of life.<sup>3</sup>

Laryngeal papillomatosis is the commonest laryngeal neoplasm in children and supraglottic carcinoma is common laryngeal carcinoma among the literature reported so far.<sup>3</sup>

Manish et al in literature search on 71 cases found increased female incidences, 10% in 0 to 5 years, 23% in 5 to 10 years and 63% in 10 to 15 years age group.<sup>5</sup> The lesions were common in glottis 78%, while in supraglottis was 17% and 5% in subglottis.<sup>5,14</sup> Early and advanced cases were equally seen in these laryngeal subsites.<sup>5</sup> Most of the cases were SCC while adenocarcinoma, mucoepidermoid carcinoma, adenoid cystic carcinoma and clear cell carcinoma, metastasis to larynx were also reported.<sup>15-18</sup> SCC with neck nodes metastasis have been reported in one case.<sup>15-18</sup> All the patients had prolonged symptoms of hoarseness or upper airway obstruction and often overlooked as voice changes during puberty, recurrent upper respiratory tract infection (URTI) or vocal abuse.<sup>15-18</sup>

Difficulty in eliciting history examination, clinical and imaging studies added to the woes of the surgeon.<sup>5</sup> Most common predisposing factor in most of the cases were irradiation of benign lesions of the head and neck, especially juvenile laryngeal papilloma.<sup>8,19,20</sup> As the condition resembles benign lesions and possibility of it included as differential diagnosis is rare and difficulty in clinical examination due to recurrent respiratory tract infection, or asthma, vocal abuse makes the disease more advanced at presentation.<sup>9,10</sup>

Etiologies included are irradiation for recurrent respiratory papillomatosis and HPV infection.<sup>11,21</sup> Spontaneous malignant changes in the recurrent respiratory papillomatosis is also reported in the laryngotracheal and bronchoalveolar regions with an incidence rate of 2.3%.<sup>22</sup>

Stephen et al reported HPV 16, is a causative agent for 25% of head and neck SCC, including laryngeal squamous cell cancer (LSCC).<sup>23</sup> They reported no correlation of better survival of HPV-positive oropharyngeal tumors when compared to laryngeal lesions.<sup>23</sup> First, Zahidul et al reported

that HPV 11 had been linked to the malignant transformation of juvenile-onset recurrent respiratory papillomatosis.<sup>24</sup> Malignant transformations of papillomatosis were 14% (6 of 43 irradiated cases) below 30 whereas no transformation was reported in 58 cases treated with surgery alone.<sup>25</sup>

Torrente et al reported detection of HPV DNA in benign (papillomatosis), indolent (verrucous carcinoma) and malignant (SCC) lesions of the larynx.<sup>26</sup> HPV types associated with laryngeal papillomatosis include low-risk HPV types 6 and 11, with high-risk HPV types 16 and 18 more commonly present in neoplastic lesions (verrucous carcinoma and SCC).<sup>26</sup> A total of 25% of laryngeal SCCs harbor HPV infections on meta-analysis, with common involvement of high-risk HPV types 16 (highest frequency) and 18.<sup>26</sup> High-risk HPV infections seem to be biologically relevant in laryngeal carcinogenesis, manifested as having viral DNA integration in the cancer cell genome and increased expression of the p16 protein.<sup>26</sup> The clinical significance of these infections and the implications on disease management are unclear and require active research.<sup>26</sup>

With the analysis of the nearly 100 cases in literature a working guidelines has been drawn where supraglottic lesions behaves aggressively and so should be treated radically.<sup>5</sup> Laryngeal preservation can be thought of in glottis lesions as they have a favorable outcome.<sup>5</sup> The treatment options are individualized according to the institutional policies and facilities available as no evidence-based management guidelines are available.<sup>5</sup> Commonly surgery have been the main treatment protocol, while the role of radiotherapy and chemotherapy are not yet defined.<sup>5</sup> Radiotherapy can cause significant growth retardation of both soft tissue and bone with consequent deformity and dysfunction and long-term complications like facial growth retardation, neuroendocrine dysfunction, visual problems, dental abnormalities and hypothyroidism.<sup>5</sup> Locoregionally late side effects after a decade after radiotherapy include chondronecrosis, esophageal stenosis, second malignancy and brain hemorrhage.<sup>27</sup>

Gindhart et al reviewed 17 cases of childhood laryngeal SCC and found that seven had fatal course before definitive treatment, 10 cases operated, or with radiotherapy or postoperative radiotherapy had disease free survival of 20 months.<sup>1</sup> They reviewed 13 glottic lesions where stripping was done in two, partial laryngectomy in three, total laryngectomy in two, radiotherapy in three, total laryngectomy plus radiotherapy in one and chemotherapy plus radiotherapy in two.<sup>2,28</sup> Though long-term follow-up is not reported for all these cases, local recurrence was seen in only two patients, both of which were successfully

salvaged.<sup>1,29</sup> The four cases of supraglottic primaries, two died from rapidly progressive disease and two were irradiated.<sup>6,30,31</sup>

Mayo clinic in their study on 101 cases of laryngeal papilloma reported six of the 43 cases (14%) irradiated and developed SCC before 30 years, while the rest operated did not show malignant degeneration.<sup>25</sup> Other etiologies include infection with HPV 18 and 33, active and passive smoking and exposure to chemical agents like asbestos and a rare chromosomal translocation 15:19 associated with supraglottic tumors.<sup>4</sup> Patients in the age group 12 to 17 years with laryngeal cancers have tobacco smoking and chewing as principal risk factors.<sup>9</sup>

## CONCLUSION

Pediatric laryngeal cancers are very rare and studies about the etiology, biology of the tumor, diagnostic and management protocols are not standardized. Diagnosis should be thought of in cases with hoarseness of long duration, cough or upper airway disease not being controlled with aggressive medical treatment and associated with risk factors. Formulating a protocol for childhood laryngeal cancers management which includes early diagnosis and accurate treatment is essential.

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## ABOUT THE AUTHORS

### Sudhir M Naik (Corresponding Author)

Fellow, Department of Head and Neck Oncosurgery, Kidwai Memorial Institute of Oncology, Bengaluru, Karnataka, India, e-mail: sud223@gmail.com

### A Nanjundappa

Professor, Department of Head and Neck Oncosurgery, Kidwai Memorial Institute of Oncology, Bengaluru, Karnataka, India

### H Srihariprasad

Resident Medical Officer, Department of Head and Neck Oncosurgery Kidwai Memorial Institute of Oncology, Bengaluru, Karnataka, India

### Rajshekar Halkud

Associate Professor, Department of Head and Neck Oncosurgery Kidwai Memorial Institute of Oncology, Bengaluru, Karnataka, India

### Purshottam Chavan

Assistant Professor, Department of Head and Neck Oncosurgery Kidwai Memorial Institute of Oncology, Bengaluru, Karnataka, India

### Sumit Gupta

Fellow, Department of Head and Neck Oncosurgery, Kidwai Memorial Institute of Oncology, Bengaluru, Karnataka, India