Laryngeal Paraganglioma - A Rare Entity

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ABSTRACT

Laryngeal paragangliomas are neural crest derived rare neuroendocrine tumors which originates from either superior or inferior laryngeal paraganglia. It arises most commonly in supraglottis with mean age of 44 years and it is three times more common in females.

This is a case of 39 years female who underwent endoscopic debulking and excision of tumor for histopathological examination which proved to be poorly differentiated squamous cell carcinoma and received a cycle of chemotherapy that probably resulted in complete resolution of initial mass which was confirmed in subsequent follow up. Futher immunohistochemistry examination diagnosed the case as Laryngeal paraganglioma. With this consideration, how effective is the role of chemotherapy in the management of proven case of Laryngeal paragangliomas?

KEY WORDS

Chemotherapy, Immunohistochemistry, Laryngeal paraganglioma

INTRODUCTION

Laryngeal paragangliomas are rare neuroendocrine tumors arising from neural crest-derived cells of parasympathetic nervous system. This entity was first described in literature in 1955.[1] Eighty one cases have been reported worldwide so far.[2] These tumours originate either from the superior or inferior paraganglia. Superior paraganglia are related to Superior laryngeal nerve and are located in the false vocal cords. Inferior paraganglia are related to Recurrent laryngeal nerve and are located near the lateral margin of cricoid cartilage.[3]

These tumours have female predisposition (3:1) with mean age of 44 years.[4] Site-specific distribution includes supraglottis (82%), subglottis (15%) and glottis (1%).[5] Patients commonly present with dysphonia, hoarseness, dysphagia, dyspnoea, and stridor. Chronic cough, plunging goiter are also reported in literature.[6,7] Diagnostic evaluation includes indirect and fiberoptic laryngoscopy, which reveals smooth, submucosal red-violet mass.[8] Imaging of the tumor requires Computed tomography and/or Magnetic resonance imaging. Surgical removal is the treatment of choice. Histopathological examination is the mainstay for diagnosis, and immunohistochemistry is required for differentiating it from other epithelial-derived and nonepithelial-derived neuroendocrine tumours.[3] We are presenting a case of laryngeal paraganglioma that initially was misdiagnosed as squamous cell carcinoma on histopathological examination.

CASE REPORT

A 39-year-old female presented to our Out-patient Department with complaint of hoarseness and dyspnoea for one year. She did not smoke or consume alcohol. Indirect and fiberoptic laryngoscopy examination revealed smooth, submucosal growth arising from ? posterior glottis, glottis itself could not be seen. Computed tomography (CT) scan of neck demonstrated well-defined lesion of 22x20 mm with significant homogeneous enhancement along the posterior wall of glottis with pedunculated inferior portion along the left true vocal cord, likely polyp ? neoplastic lesion (Fig. 1). Tracheostomy for lower airway protection followed

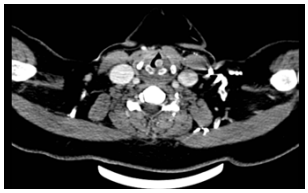

Figure 1. CT scan showing tumor mass arising from posterior-inferior aspect of vocal cord

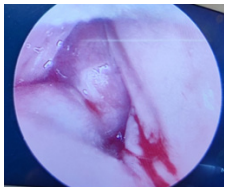

Figure 2. Pre-operative laryngoscopic picture of the mass

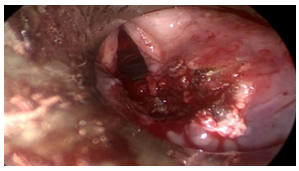

Figure 3. Hypervascular tumor and post excision picture

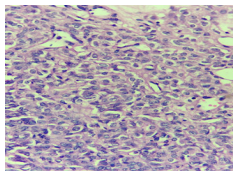

Figure 4. Histopathological image showing occasional Zellballen pattern

by endoscopic excision of the lesion, and assessment for postoperative surgical decannulation was planned. Under awake fibre-optic guided nasotracheal intubation with general anaesthesia, tracheostomy was done to secure the airway. Laryngoscopy with endoscopic guidance was done, followed by debulking of the tumour (Fig. 2). Due to the hypervascular nature of the mass, complete excision could not be done (Fig. 3). Hemostasis was achieved with the use of THUNDERBEATTM hybrid energy device. Histopathology reported polygonal tumor cells arranged in diffuse sheets with fibrocollagenous stroma, with morphology suggestive of poorly-differentiated Squamous cell carcinoma (SCC) (Fig. 4), and advised for Immunohistochemistry (IHC) for further evaluation. Patient was referred for Chemoradiotherapy to Cancer Hospital. Patient received 1 cycle of chemotherapy while awaiting the results of IHC. IHC however revealed tumour cells to be negative for Cytokeratin, CAM 5.2, P 40/ P 63, Human Melanoma Black (HMB) -45, and positive for Synaptophysin and CD-56, confirming the diagnosis as laryngeal paraganglioma (Fig. 5). Patient was called for follow-up and fiberoptic laryngoscopy revealed normal laryngeal findings (Fig. 6). She was then decannulated and kept on regular follow-up. There was no recurrence of growth for 6 months.

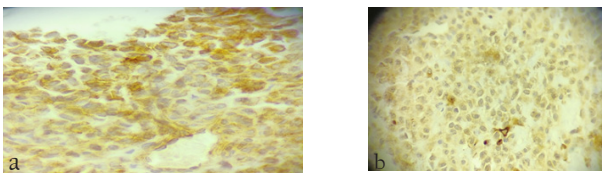

Figure 5. Immunohistochemistry images a. A-Positive for Synaptophysin, b. Negative for Cytokeratin

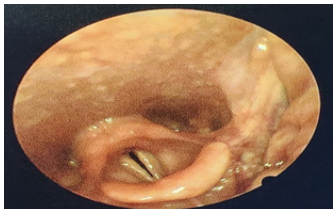

Figure 6. Post chemotherapy follow-up image showing complete resolution of mass

DISCUSSION

Laryngeal neuroendocrine tumours are classified based on their origin into Epithelial (typical carcinoid, atypical carcinoid, small cell) and Neural (paraganglioma).[9] The first case of laryngeal paraganglioma was reported by Blanchard and Saunders.[1]

Laryngeal paragangliomas are more common in females, and tend to occur during fourth to sixth decade of life. They are predominantly located in the right side.[10] However, Konowitz et al. reported approximately equal sexual incidence.[11] Majority of these are supraglottic in location. These arise from superior laryngeal paraganglia near superior edge of thyroid cartilage.[5] Our patient was 39 year old female with left supraglottic paraganglioma. Left sided lesion was also reported earlier by Jain et al.[12]

These benign tumours are slow growing with symptoms resembling squamous cell carcinoma.[10] Growth rate is 0.83 mm per year with a doubling time of 10 years.[2] Symptoms are determined by the location and size of the tumour. Supraglottic lesions impair vocal cord vibration resulting in the commonest complaint of hoarseness. With increasing size of the lesions, compressive symptomatology of dyspnoea, stridor, and dysphagia may develop.[3] Our case also presented with hoarseness and dyspnoea. Subglottic lesions may present with wheezing, and have higher chances of airway obstruction.[13]

Examination typically reveals red or blue, smooth, lobulated, submucosal mass. They are not often accompanied by neck masses. The lesion was also submucosal, lobulated and reddish in our case. Contrast enhanced computed tomography reveals the vascular nature of the tumour signified by the post-contrast enhancement. Preoperative angiography permits diagnosis, defines the tumour blood supply, detects synchronous head and neck paragangliomas, and also permits selective embolization of the tumour.[14] The primary feeding vessel is Superior thyroid artery and embolization creates bloodless operative field.[3] The diagnostic imaging modality of choice is Gadolinium enhanced MRI due to the evaluation of adjacent soft tissues and vascular structures along with the primary tumours.[15]

Role of preoperative biopsy is controversial due to the highly vascular nature of the lesion that often necessitates airway intervention, and also the need of deeper biopsies due to the submucosal location and to increase the diagnostic yield.[11,14] These lesions pose a diagnostic challenge to the pathologist.[11] These tumors are firm and rubbery in consistency, with red or brown cut surface, with areas of hemorrhage. The gross appearance of the tumour in our case was similar. Microscopic appearance consists of chief cells with or without interspersed sustentacular cells arranged in a typical “Zellballen pattern” with a delicate stroma containing numerous vascular channels. Mitoses, necrosis and vascular invasion are infrequent. There is lack of glandular structures and mucin.[16] In our case,

histopathological evaluation revealed polygonal tumor cells with moderate eosinophilic cytoplasm, hyperchromatic to vesicular nuclei arranged in sheets, with some areas of tumour cells nests separated by fibrous vascularized septa.

Mitosis was also seen. It was reported positive for malignancy with possibility of poorly differentiated squamous cell carcinoma, and IHC was also advised. The "Zellballen" pattern is not diagnostic or unique to paraganglioma.[16] Differentiation from epithelial-derived and other neuroendocrine tumours is a must, due to differences in prognosis, outcome and treatment.[17] Initial histologic misdiagnosis was reported in upto 26% cases, like SCC, adenocarcinoma, melanoma etc.[11] Immunohistochemistry has diagnostic implication with positivity to general neuroendocrine markers like neuron-specific enolase, chromogranin, and synaptophysin. Also, these lesions stain negative for epithelial markers like cytokeratin (CK), carcinoembryonic antigen (CEA) and Epithelial membrane antigen. Cytokeratin reactivity has not been reported so far in laryngeal paraganglioma. Sustentacular cells of paraganglioma stain strongly for S-100 protein.[17] In our case, CK and CAM 5.2 markers were negative. Synaptophysin and CD-56 was positive. The major differential diagnosis is atypical carcinoid, which is more frequent in males (3:1), with a mean age of 61 years, presenting with a submucosal mass with predilection to supraglottis. Microscopic pseudo-Zellballen pattern is frequent with positivity to neuroendocrine markers mimicing paraganglioma, however these almost always stain positive with epithelial marker CK. These are aggressive tumours with metastatic disease.[17]

Surgical resection is preferred modality of treatment, with organ preservation partial laryngectomy procedures becoming the standard protocol.[16] Endoscopic excision is limited due to profuse hemorrhage, that often requires need for open surgeries or causes recurrence.[16,19] Lateral pharyngotomy is preferred based on the extent and site of tumour.[16,19] Endoscopic excision of the tumour could not be achieved in our case too due to excessive intraoperative hemorrhage, and change to lateral pharyngotomy approach was not attempted due to patient party's unwillingness for transcervical surgery.

Literature provides no role for radiotherapy or chemotherapy in the management of laryngeal paraganglioma.[20] Due to the histologic misdiagnosis in our case, the patient received a single cycle of chemotherapy which resolved the remnant tumour in the larynx. Further studies to assess the role of chemotherapeutic agents in laryngeal paraganglioma may be needed.

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