Role of primary and adjuvant radiotherapy in the management of laryngeal paraganglioma: report of two cases and review of literature

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Abstract

Introduction: We present the second reported case of a paraganglioma of the larynx treated with radiotherapy.
Methodology: We present two cases and a literature review of paraganglioma of the larynx.
Case number one: A 68-year-old woman, with hoarseness, dyspnoea and supraglottic mass. Biopsy showed laryngeal paraganglioma, excised by transhyoid approach with laryngofissure. Histopathology confirmed tumour completely excised with close margins (less than 5mm). 45 Gy of adjuvant radiotherapy was added. She is doing well on ninth year clinic follow up.
Cases number two: A 77-year-old woman with change in voice, progressive dyspnoea and supraglottic mass. Biopsy revealed a Laryngeal Paraganglioma. CT scan and carotid angiogram are in keeping with the histological diagnosis. She was offered primary radiotherapy giving her age and additional co-morbidities. Now on her seventh-year clinic follow up. Larynx stable and no concerns clinically.
Conclusion: There is very limited data on the role of radiotherapy. This is the second reported case of primary radiotherapy in the English literature. It is pertinent to appreciate the role and future of radiotherapy in the treatment of paraganglioma of the larynx.
Keywords: Paraganglioma; Larynx; Radiotherapy

Introduction

Head and Neck paragangliomas are rare, slow-growing, vascular, submucosal neuroendocrine tumours originating from the parasympathetic nervous system.[1,2] Carotid body is the commonest site then jugulotympanic and vagal paragangliomas.[3] It rarely occurs in the larynx. Surgery has been the mainstay of treatment of laryngeal paragangliomas. Although external beam radiotherapy has been used as

primary and adjuvant treatment of paragangliomas of carotid body and jugulotympanicum, its use in laryngeal paragangliomas is not widely published.[4]

Case No. 1

Ms H.K. is a 68-year-old woman, who presented to the Accident and Emergency department with hoarseness of two years duration, six weeks history of progressive dyspnoea and foreign body sensation in the throat for one month duration. Flexible laryngoscopy revealed a smooth right supraglottic mass. Excisional biopsy was attended with torrential bleeding. Hence, the procedure was abandoned and the patient was tracheostomised and decanulated five days later. Histopathology report showed a well-circumscribed, reddish-brown, submucosal masses consisting of chief and sustentacular cells in keeping with a laryngeal paraganglioma (Fig 1). A month later, she presented to the emergency department in acute upper airway obstruction necessitating emergency tracheostomy. Subsequent Panendoscopy revealed a supraglottic mass with right parapharyngeal extension. Neck computed tomography (CT) scans showed tumour in the right supraglottis and paraglottis (Fig. 2). Carotid CT angiogram revealed major feeding vessels arising from the right thyrocervical trunk and several small feeders from the ipsilateral external carotid artery. Twenty four hour urinary vanillyl mandelic acid (VMA) was not raised. An impression of laryngeal paraganglioma was made and it was excised via laryngofissure. Histopathology confirmed tumour completely excised with close margins (less than 5mm). Following head and neck multidisciplinary (MDT) discussion, 45 Gy of adjuvant radiotherapy was added. She is currently doing well on regular ENT and radio-oncology clinics follow up appointments for nine years.

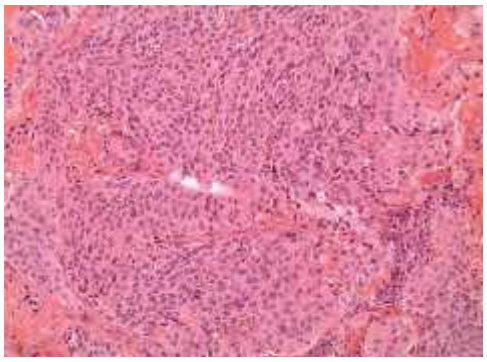

Figure 1: Photomicrograph of the tumour showing polygonal cells in a typical nested or ‘Zellballen’ arrangement. (H&E; ×200)

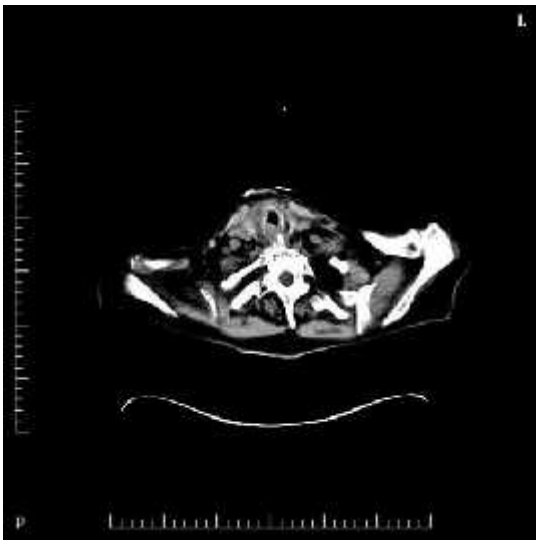

Figure 2: Axial computed tomography scan showing a right-sided, supraglottic, soft tissue mass. L= left; P = posterior

Case No. 2

Ms K.G is a 77-year-old woman who presented to her General practitioner (GP) with a six month history of change in voice and two weeks history of progressive difficulty with breathing against a background hypertension and diabetes mellitus. Flexible laryngoscopy revealed a smooth supraglottic laryngeal swelling obscuring the laryngeal inlet (Fig. 3). She had panendoscopy and biopsy from the lesion revealed a Laryngeal Paraganglioma (Fig. 4 and 5). CT scan carotid angiogram revealed an intensely vascular lesion in keeping with the histological diagnosis (Fig. 6). She was discussed at the head and neck multidisciplinary meeting of St George's hospital and the decision was to offer her primary radiotherapy giving her age and additional co-morbidities. She received 50 Gy of radiotherapy which she tolerated very well with no complications. She is now on her seventh-year of regular follow up at ENT and radio-oncology clinics. Laryngeal swelling has remained stable and no concerns clinically.

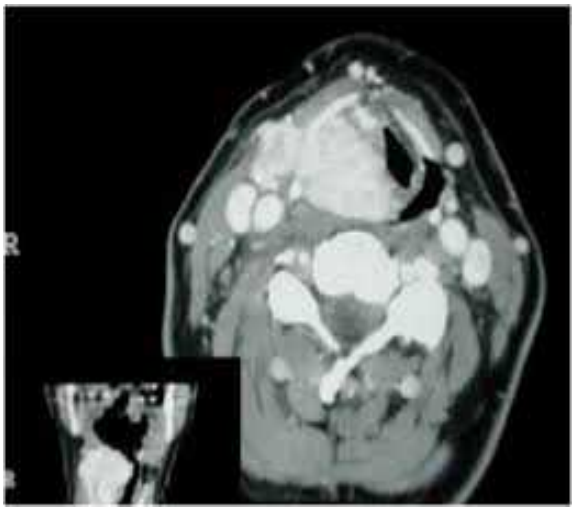

Figure 3: Axial computed tomography scan showing a right-sided, smooth supraglottic mass obscuring laryngeal inlet

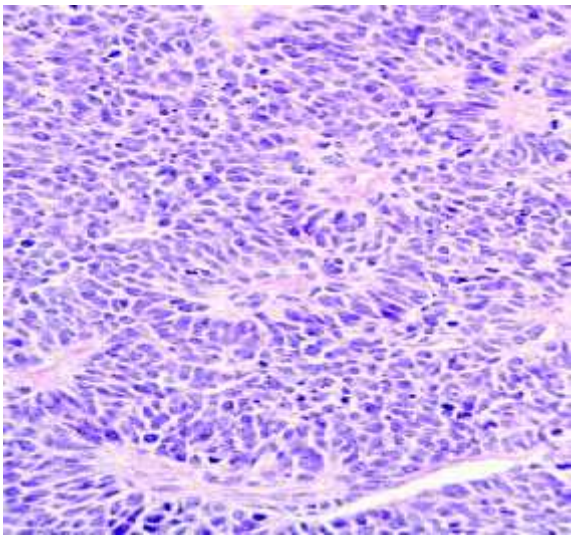

Figure 4: Photomicrograph of the tumour showing typical nesting or 'Zellballen' arrangement. (H&E; ×200)

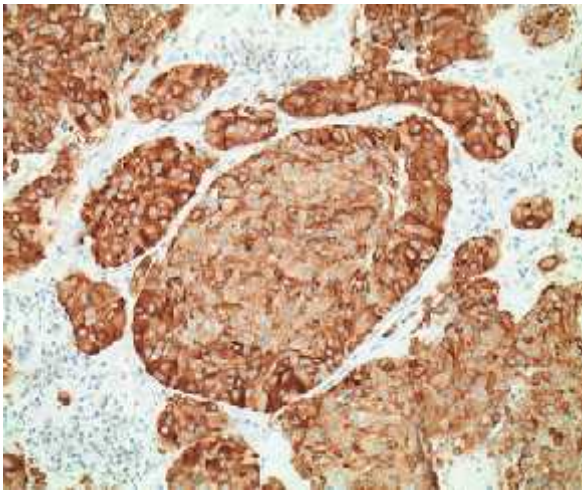

Figure 5: Photomicrograph showing central chief cells stained for chromogranin.

(×200).

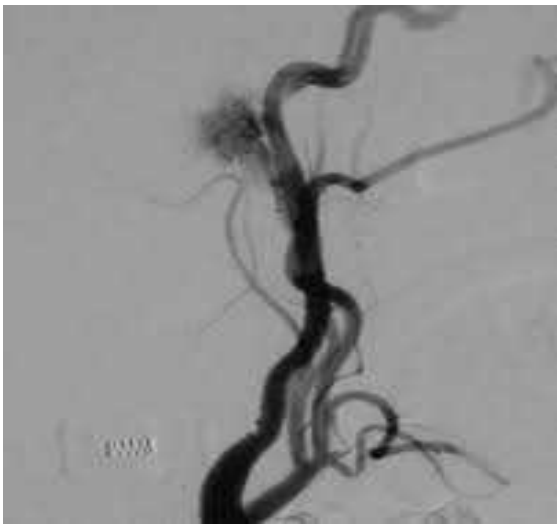

Figure 6: Angiogram demonstrating intense vascular supply from branches of the carotid artery

Discussion

There are two main groups of neuroendocrine neoplasms of the larynx. Those of epithelial origin (typical carcinoid, atypical carcinoid and small cell neuroendocrine carcinoma) and those of neural type (paraganglioma).[5] Paragangliomas are uncommon, slow-growing, generally benign tumor, arising from paraganglion cells derived from the neural crest as part of the diffuse neuroendocrine system. Most frequently found in the head and neck with the commonest site being carotid bifurcation and jugulotympanic area. The larynx is a much less involved site and supraglottis is the commonest.[6]

The first documented case of laryngeal paraganglioma was reported by Blanchard and Saunders[7] in 1955. Since then, there have been fewer than 90 cases reported in the literature. Typically, laryngeal paraganglioma show slight female preponderance with a male: female ratio of 1:3 and is commonest around the fourth to sixth decade of life.[8,9] The youngest patient diagnosed was aged 5 years.[10] Superior laryngeal artery provides the blood supply to most laryngeal paragangliomas.[11] Depending on the site and size, patients presents with hoarseness, dyspnea, stridor, foreign body sensation or dysphasia. Wheezing, cough and vocal fold paralysis have been reported.[12]

Typical appearance on laryngoscopy is a red or blue, lobulated, smooth submucosal mass.[8] It is important to differentiate laryngeal paraganglioma from other neuroendocrine tumours such as; malignant melanoma; metastatic renal cell carcinoma, medullary carcinoma of the thyroid gland and atypical carcinoid because of the higher malignant potential and differences in treatment.[13]

Laryngeal paragangliomas grossly appear well-circumscribed, tan, brown or reddish-brown, submucosal masses.[14] Histopathologically, they consist of two cell types – chief cells and sustentacular cells – in a Zellballen pattern which is typical, but not diagnostic of paraganglioma. This pattern can also be found in carcinoid tumours, melanomas and medullary carcinomas of the thyroid.[15] The chief cells are polygonal with abundant, granular cytoplasm and round nuclei with 'salt and pepper' chromatin. Nuclear pleomorphism may be present, but mitotic figures are rare and tumour necrosis is absent. The sustentacular cells are spindled cells at the periphery of the nest, which are apparent on immunostaining with S-100.[11,15] Magnetic Resonance Imaging (MRI) with gadolinium enhancement is the diagnostic imaging modality of choice.[9,16] Myssiorek *et. al.* reported using MRI with ^{111}In pentetreotide to determine tumor extent and multifocality and found it as effectively as angiography.[8,12,17] CT scan is reserved for suspicion of cartilage destruction.[18] Some investigators have tried angiography which offers an advantage of selective embolization.[9,19] Diagnosis is made from clinical history, examination and preoperative biopsy for histopathology is recommended. However, these patients do bleed excessively when biopsied and often

require some form of airway intervention as was the case in our index patient.

Surgery is the goal standard of treatment. Previously, Cryosurgery was attempted, but subsequent requirement of laryngofissure[22] and endoscopic resection resulted in higher recurrence. Microlaryngoscopy with laser excision yielded mixed results.[10,16] More successful open surgical approaches includes supraglottic laryngectomy,[8] total laryngectomy,[24] laryngofissure and lateral thyrotomy.[8] There is very limited data on the role of radiotherapy in the treatment of laryngeal paraganglioma,[10] although, it has been used with good results in the treatment of carotid body and jugulotympanic paraganglioma to limits its growth and reduce its size.[22,26] Pharm T *et. al.* reported a case of laryngeal paraganglioma presenting three months after radical radiotherapy for squamous cell carcinoma (SCC), hence questioned the effectiveness of radiotherapy as a treatment modality for laryngeal paraganglioma.[4] Smolarz *et. al.* reported successful tumour size reduction to 2 mm with external beam radiotherapy, in which the patient has remained symptoms free at five-year follow up.[27] In our report, the first patient has been successfully treated with adjuvant radiotherapy and has remained symptom-free on her ninth-year of follow up. The second patient has been successfully treated with primary radiotherapy. She has been symptom-free on her seventh-year follow up. Therefore, we think she will make the second case reported in the literature.

Conclusion

Although surgery is the traditional gold standard of treatment in Laryngeal paraganglioma, there is very limited data on the role of radiotherapy as a whole. This is the second reported case of primary radiotherapy in the English literature. It is pertinent to appreciate the role and future of radiotherapy in the treatment of paraganglioma of the larynx.

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