Synchronous malignant vagal paraganglioma with contralateral carotid body paraganglioma treated by radiation therapy

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Abstract

Paragangliomas are rare tumors and very few cases of malignant vagal paraganglioma with synchronous carotid body paraganglioma have been reported. We report a case of a 20-year old male who presented with slow growing bilateral neck masses of eight years duration. He had symptoms of dysphagia to solids, occasional mouth breathing and hoarseness of voice. Fine needle aspiration cytology (FNAC) performed where he lived showed a sinus histiocytosis and he was administered anti-tubercular treatment for six months without any improvement in his symptoms. His physical examination revealed pulsatile, soft to firm, non-tender swellings over the anterolateral neck confined to the upper-mid jugulo-diagastric region on both sides. Direct laryngoscopy examination revealed a bulge on the posterior pharyngeal wall and another over the right lateral pharyngeal wall. Magnetic resonance imaging (MRI), 99mTc-labeled octreotide scan and angiography diagnosed the swellings as carotid body paraganglioma, stage III on the right side with left-sided vagal malignant paraganglioma. Surgery was ruled out as a high morbidity with additional risk to life was expected due to the highly vascular nature of the tumor. The patient was treated with radiation therapy by image guided radiation to a dose of 5040cGy in 28 fractions. At a follow-up at 16 months, the tumors have regressed bilaterally and the patient can take solids with ease.

Case Report

We report a case of a 20-year old male who presented in June 2008 with complaints of slowly growing bilateral neck masses of eight years duration and pain over the right neck. It was associated with dysphagia to solids, occasional breathing and hoarseness of voice. He had taken anti-tubercular treatment for six months where he lived without any improvement in his neck swellings. No history of evening rise of temperature, hemoptysis, hematemesis, excessive sweating, hypertension, tachycardia, weight loss or chronic obstructive pulmonary disease was available.

Physical examination revealed pulsatile, soft to firm, non-tender swellings over the anterolateral neck, confined to upper-mid jugulo-diagastric region on both sides. The right-sided mass measured 8×6 cm size while the left-sided mass was 3×2 cm. Both the masses were vertically fixed and laterally mobile with the normal overlying skin. Direct laryngoscopy examination revealed a bulge on the posterior pharyngeal wall and another over the right lateral pharyngeal wall. Atrophy of the left side of the tongue with fibrillation was noted. No other cranial nerve deficit could be elicited and systemic examination was non-contributory. His reports from the previous hospital showed a cytopathological diagnosis of sinus histiocytosis (Rosai Dorfman disease).

Neck MRI showed large lobulated, intensely enhancing bilateral neck masses with the lesion on the right side splaying the right external carotid artery (ECA) and internal carotid artery (ICA) and engulfing the common carotid artery (CCA) and ICA (Figure 1). The right side lesion extended from the level of cricoid cartilage to the greater wing of the sphenoid. The lesion on the left side displaced the ICA and ECA anteriorly. It was higher up than the right sided lesion and extended from the level of the left common carotid bifurcation to the base of the skull, focally involving the dura at the level of the cerebellar tonsils. The lesion on the right side was compressing the oropharynx and hypopharynx. Bilateral level III and IV neck nodes were seen, the largest on the right side measuring 11.5 mm and on the left side measuring 11 mm. 99mTc-labeled octreotide scan showed regions of intense focal uptake in the neck bilaterally and a small satellite lesion with more intense uptake was seen just below the mass on the left side, most likely to be a lymph node (Figure 2). Twenty-four hour urinary metanephrine levels were not elevated.

All the above findings were suggestive of bilateral paraganglioma (carotid body tumor on right side, stage III according to Shamblin's classification[1] and malignant vagal paraganglioma on the left side with lymph node involvement).

The case was discussed by the tumor board made up of cardiothoracic surgeons, head and neck surgeons, radiologist, nuclear medicine specialist, pathologist and radiation oncologist. Surgery was ruled out as the bilateral two stage procedure would have involved internal carotid shunting resulting in multiple cranial nerve deficits with additional risk to life. The vascular surgeon did not agree to sclerosis of the feeder vessels as the tumors were bilateral and the possibility of active surgical intervention for complete resection even after sclerosis appeared remote. The final decision was to offer external beam radiation to this large lesion with the intent of reducing its vascularity by causing radiation induced endarteritis obiliterans and to consider surgical intervention 12-18 months after radiotherapy for residual disease.

Informed written consent for radiation therapy was obtained. After performing a planning CT-scan, target volumes and organs at risk were contoured on a Tomocom work-station. Bilateral gross disease including visible lymph nodes were contoured as gross tumor volume (GTV). The clinical target volume (CTV) was contoured by giving a 1.5 cm margin to GTV. A margin of 3 mm from CTV was enlarged for planning target volume (PTV). Planning was performed on a Precise treatment planning system and a dose of 5040cGy in 28 fractions was prescribed to PTV. Isocentric coplanar intensity modulated treatment (IMRT) plan with 8 portals and 31 segments was generated and D95% of 4700cGy was obtained surrounding the PTV (Figure 3). After plan evaluation, radiation was delivered by image guided radiation therapy technique (IGRT) from 24th July to 30th August 2008 on an Elekta Synergy linear accelerator. The patient tolerated radiation

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Key words: bilateral paraganglioma, malignant vagal paraganglioma, radiotherapy.

Contributions: KT, conception, design, interpretation of data and final approval. BSS, drafting the article, revision, analysis of data. MS, drafting the article, analysis of data. AA, drafting the article, revision. PS and CD, interpretation of data/imaging.

Conflict of interest: the authors report no conflicts of interest.

Received for publication: 12 September 2009.
Revision received: 25 February 2010.
Accepted for publication: 26 February 2010.

Rare Tumors 2010; 2:e21
doi:10.4081/rt.2010.e21

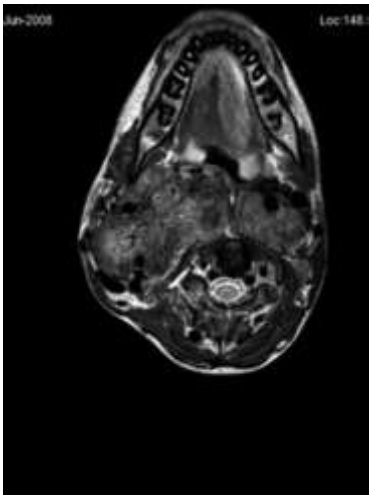

Figure 1. Pre-treatment neck MRI showing splaying of ICA, ECA on the right side by CBP where as the vessels are pushed anteriorly on the left side by vagal paraganglioma.

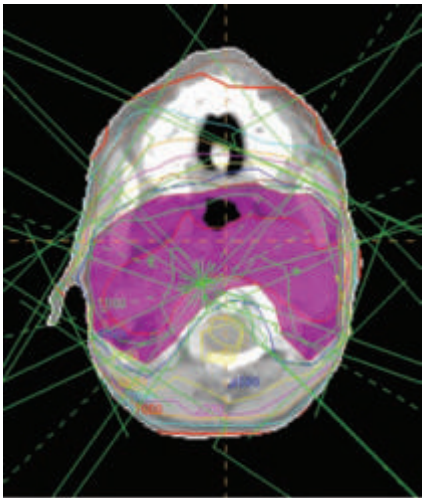

Figure 3. Irradiation portals with dose distribution showing 8 isocentrically placed beams and coverage of PTV by 95% isodose (color wash).

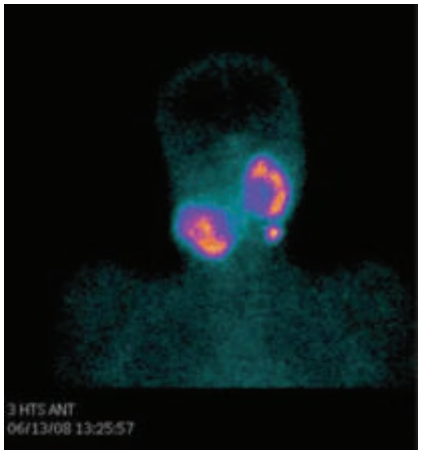

Figure 2. Pre-treatment 99mTc-labeled octreotide scan.

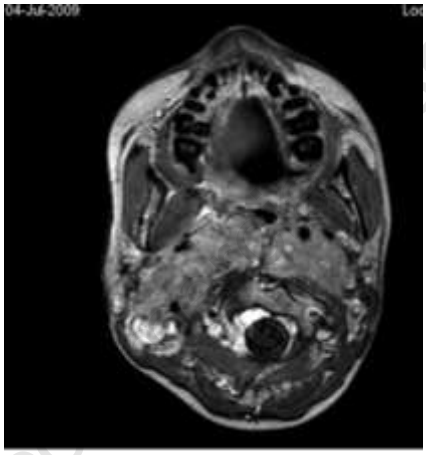

Figure 4. Neck MRI nine months post treatment.

well with grade II mucositis in oropharynx that was managed with topical analgesics.

At first follow-up at three months, the patient reported only minimal relief in his symptoms. On examination there was mild regression in the bilateral neck masses. On MRI, the mass on the left side measured 4.5 cm (transverse) × 2.8 cm (AP) × 6.6 cm (CC) and the right-sided mass was 7.4 cm (Transverse) × 5.6 cm (AP) × 9 cm (CC), suggestive of stable disease according to RECIST criteria.[2] On second follow-up in June 2009, there was significant subjective improvement in symptoms of dysphagia, hoarseness and mouth breathing. Neck examination showed a decrease in the right-sided neck mass with fullness on the left side of the neck without any discrete palpable lesion. MRI showed mass on the right side of 7.5 cm (Tr.) × 5.7cm (AP) × 8.9 cm (CC) and on the left side it was 3.9 cm (Transverse) × 3.4 cm (AP) × 6.2 cm (CC). This was evaluated as stable disease on both sides (Figure 4). On 99mTc-labeled octreotide scan, intensity was less in the bilateral neck masses and the lymph node was much less prominent.

At 16 months post treatment, the patient is able to take solids with ease and clinically no external masses are palpable in the neck. Oropharyngeal examination shows a healthy mucosa with no para-pharyngeal bulge.

Discussion

Paraganglia are part of the diffuse neuroendocrine system which are widely dispersed aggregates of neuroendocrine tissues located near nerves and vessels.[3] They arise from neural crest progenitor cells and migrate along the branchial mesoderm in head and neck. Paraganglioma or tumors of paraganglia arise from this specialized tissue. Within the head and neck, common sites are carotid body at CCA bifurcation, jugular foramen along the vagus nerve and within the middle ear.[4] Paragangliomas of head and neck are rare tumors, accounting for only 0.012% of all head neck tumors[5] of which the carotid body is the most common site. Vagal paraganglioma represent less than 5% of all the cases.[6] Bilateral paragangliomas are much less common and malignancy in paraganglioma is even rarer (3-6%).[7] Few cases of synchronous bilateral carotid body and vagal paraganglioma have been reported in literature but we were not able to find synchronous bilateral carotid body paragangliona (CBP) and malignant vagal paraganglioma managed by radiation therapy.

CBP commonly arise along the posteromedial wall at the CCA bifurcation but may also be located along either the ECA or ICA.[4] They are slow growing tumors with a mean growth rate of 5 mm/year[8] and a mean doubling time of 4.2 years. Vagal body paraganglioma most commonly arise from the inferior (nodose) ganglion but may also arise from superior and middle ganglion and are typically more cephalad than carotid body tumors.[6] Most authorities regard extension to regional lymphnode or distant metastasis as the only reliable indicators of malignancy[9] as histopathological examination of the tumor is unreliable for establishing a malignant diagnosis.

CBP almost always presents as palpable antero-lateral neck mass, located at or superior to carotid bifurcation and deep to the sternomastoid muscle[10] and some cases may present with a pain in the mass. Incisional biopsy is contraindicated due to the risk of hemorrhage.[11] MRI is superior to CT for soft tissue details, dura and neural involvement.[12] CBP causes splaying of the common carotid bifurcation and displaces the ICA posteriorly and laterally. On T2-weighted images, the classical "salt and pepper" appearance is seen.[13] Octreotide scintigraphy is a non-invasive modality which demonstrates an accuracy of 90%, sensitivity of 94% and specificity of 75%.[14] Vagal paraganglioma also presents as slow growing asymptomatic upper neck mass and may involve the following nerves in decreasing frequency: vagal, hypoglossal, spinal accessory nerve. Sign and symptoms include hoarseness, dysphagia, atrophy of the hemitongue, vocal cord palsy. The progression of symptoms is helpful in differentiating vagal paraganglioma from other head neck paraganglioma.[15] Our patient had symptoms of dysphagia, hoarseness and atrophy of left half of the tongue.

Surgical resection has been the mainstay of the treatment for paraganglioma but surgery is

relatively contraindicated in extensive skull base involvement and bilateral or multiple paraganglioma that may result in unacceptable post-operative morbidity and mortality. Lower cranial nerve dysfunction is a common complication of surgical resection of head neck paraganglioma and bilateral lower cranial nerve palsies represent a severe life-threatening situation. Permanent cranial nerve deficit of 13% to 40%[16,17] has been reported. Radiation therapy is an effective therapeutic option especially in the management of unresectable paraganglioma or if the surgery would result in significant debility requiring long-term rehabilitation.[18] There is rarely total resolution of the tumor after radiation therapy hence local control usually means stability of tumor size and non-progression of neurological symptoms.

In the last 40 years, most of the patients have been treated with wedge pair or parallel-opposed field setups but with the advent of conformal techniques, IMRT and fractionated stereotactic radiotherapy (SRT) have become preferred treatment methods. There seems to be no significant difference among the radiation treatment modalities in terms of tumor control[19] but the conformal techniques can exclude as many normal structures as possible resulting in lesser side effects. Kim *et al.,* demonstrated that optimal dose appeared to be greater than 40 Gy as local failure was 1% versus 25% for patients receiving more than 40Gy versus less than 40 Gy, respectively.[20] Hinerman *et al.* demonstrated that the probability of tumor control with radiation does not appear to depend on tumor size, at least when treated to the recommended dose of 45Gy. We delivered a dose of 5040cGy over 28 fractions with conformal planning.

In a review comparing results of radiation with surgery, local control rates were comparable to surgery, 72% versus 78%, although more advanced lesions were treated with radiotherapy.[21] In a retrospective study by Chino *et al.* of 31 patients of paraganglioma (14 after surgical resection) treated between 1963 to 2005 with a mean dose of 54Gy (38Gy-65Gy), the local control (LC) at five, ten and 15 years was 96%, 90% and 90%, respectively. There was no difference in LC between salvage radiation used after surgical failure and definitive radiation therapy, and there were no late radiation toxicities greater than grade 2.[22] Russel *et al.* shared a 35-year experience of definitive radiotherapy in 104 patients with 121 paragangliomas treated between 1968 and 2004 where 89 paragangliomas were treated with conventional megavoltage techniques, 15 paragangliomas with stereotactic fractionated radiation therapy, 6 paragangliomas with SRT and 11 paragangliomas with IMRT. There were 6 local recurrences and the actuarial local control and cause-specific survival rates at ten years were 94% and 95% where as the overall control rate for all 121 lesions was 95% and the incidence of treatment related complication was low.[19] Acute radiation complications usually seen are loss of taste, dryness of mouth, dysphagia, odynophagia and dermatitis which are usually well tolerated with minimal long-term toxicities like subcutaneous fibrosis, xerostomia, and hypothyroidism.

Conclusions

Clinicians should have a high index of suspicion when a patient presents with pulsatile neck mass and biopsy should not be attempted. For unresectable tumors or high-risk cases, radiation therapy is a good alternative with acceptable acute side effects and minimal late complications.

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