Case Report

Metastatic large cell neuroendocrine carcinoma of larynx: Individualizing tumor biology by dual tracer positron emission tomography/computed tomography (^{68}Ga-DOTATATE and ^{18}F-fluorodeoxyglucose) molecular imaging and disease stabilization following ^{177}Lu-DOTATATE peptide receptor radionuclide therapy after initial progression on chemoradiotherapy

ABSTRACT

Debate exists on the disease biology and course of primary large cell neuroendocrine carcinoma (LCNEC) of larynx, being classified as a variant of atypical carcinoid by the World Health Organisation-2005 classification, while literature of its aggressive behavior indicating poorly differentiated neuroendocrine carcinoma (akin to pulmonary LCNEC) exists. The utility of dual tracer positron emission tomography/computed tomography (^{68}Ga-DOTATATE and ^{18}F-fluorodeoxyglucose) in deciphering the dynamic tumor biology and feasibility of peptide receptor radionuclide therapy (PRRT) is illustrated in metastatic LCNEC of epiglottis after disease progression following conventional chemoradiotherapy. Relatively, atypical sites of soft-tissue metastases (subcutaneous tissue of arm, scrotal sac, peritoneum, and lamina of thyroid cartilage) and xiphisternum and disease stabilization following ^{177} Lu-DOTATATE PRRT were other noteworthy unique aspects of this report.

Keywords: ^{177}Lu-DOTATATE, ^{18}F-fluorodeoxyglucose, ^{68}Ga-DOTATATE, carcinoma larynx, dual tracer positron emission tomography-computed tomography, large cell neuroendocrine carcinoma, peptide receptor radionuclide therapy

INTRODUCTION

The disease management and prognosis of the neuroendocrine tumors (NETs) is dependent on the histological subtype (determining tumor biology), site, and stage of the disease. Laryngeal NETs are the most common primary site among head and neck NETs, though comprising <1% of all laryngeal neoplasms.[1] We herein describe a 60-year-old man of primary large cell neuroendocrine carcinoma (LCNEC) of epiglottis with atypical sites of metastases, who initially demonstrated progressive disease on conventional chemoradiotherapy, but subsequently showed disease stabilization following peptide receptor radionuclide therapy (PRRT) with^{177} Lu-DOTATATE.

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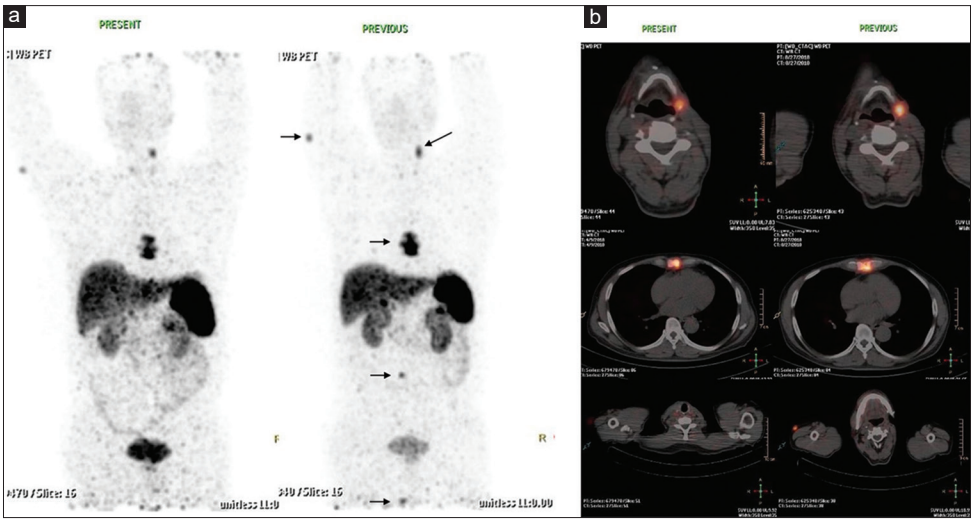

Figure 1: ^{68}Ga-DOTATATE baseline and recent (post 2 cycles of peptide receptor radionuclide therapy) maximum intensity projection images (a) and fused transaxial images (b) of 3 prominent lesions

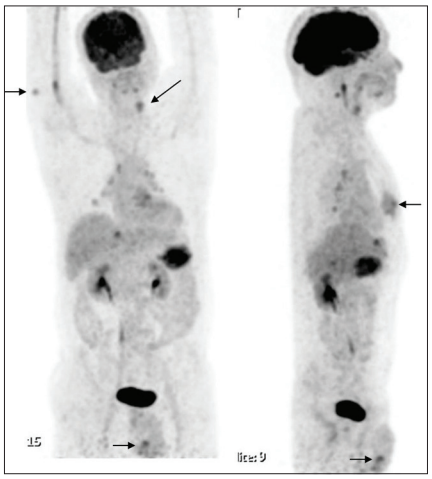

Figure 2: Recent fluorodeoxyglucose-positron emission tomography [Figure 2] and the last ^{177}Lu-DOTATATE posttreatment scan [Figure 3] demonstrating lesions at the xiphisternum, lamina of thyroid cartilage subcutaneous tissue of the right arm, scrotal sac, and peritoneum

CASE REPORT

A 60-year-old man with a diagnosis of LCNEC of epiglottis with cervical nodal metastases (was staged as T2N1M0), underwent CO_2 laser excision along with Left MND Type III). He received concurrent chemoradiotherapy (60 Gy/30#) and remained disease free for 20 months. Following relapsed with nodal metastasis, he was rechallanged with chemotherapy carboplatin and etoposide. The positron emission tomography-computed tomography (PET-CT) demonstrated stable disease post 6 cycles and was put on observation. Four months later, he presented with retrosternal pain and showed disease progression with a new lesion in sternum and was treated with 5 cycles of topotecan. At this time, he was considered for PRRT and underwent dual-tracer PET/CT with ^{68}Ga-DOTATATE and fluorodeoxyglucose (FDG) for the same; ^{68}Ga-DOTATATE PET-CT demonstrated high ^{68}Ga-DOTATATE and low FDG uptake in the metastatic lesions, (i) sternum (maximum standardized uptake value [SUVmax] 58.13; 4.32), (ii) soft-tissue nodule over left lamina of thyroid cartilage (SUVmax 27.91; 4.89), (iii) subcutaneous nodule in right arm (SUVmax 15.32; 3.32), (iv) sub cm-sized nodule in the right scrotal sac, and (v) peritoneal deposit (SUV max 49.41; 12.35). He received PRRT with ^{177}Lu-DOTATATE and following 2 cycles (cumulative dose: 12.506 GBq), he had a stable disease at 9 months and was worked up for 3rd cycle [Figures 1a, b, 2 and 3].

DISCUSSION

According to the 2005 World Health Organization (WHO) classification of head and neck tumors, NET of the larynx is divided into five histologic subtypes – typical carcinoid (TC), atypical carcinoid (AC), small cell NEC (SCNEC), combined small cell with non-small cell carcinoma, and paraganglioma.[2] In the same classification system, primary laryngeal LCNEC had been considered as a variant of AC in contrast to the well-known pulmonary LCNEC which is categorized as poorly differentiated NECs.[2] On the other hand, reports exist on its poor outcome emphasizing reclassification of LCNEC as variants of small cell carcinoma (poorly differentiated NEC).[3,4] In one report, patients of AC more often presented with Stage I and II disease while those with LCNEC presented with Stage III and IV disease.[4] In the same meta-analysis, the 5-year disease-specific survival was found to be 100% for TC, 53% for AC, 19% for SCNEC, and 15% for LCNEC.[4] Other authors have reported a favorable outcome of LCNEC indicating the possibility of a variant in LCNEC with comparatively slower disease course.[5] Hence, there is a need for further exploring and studying its biology.[5]

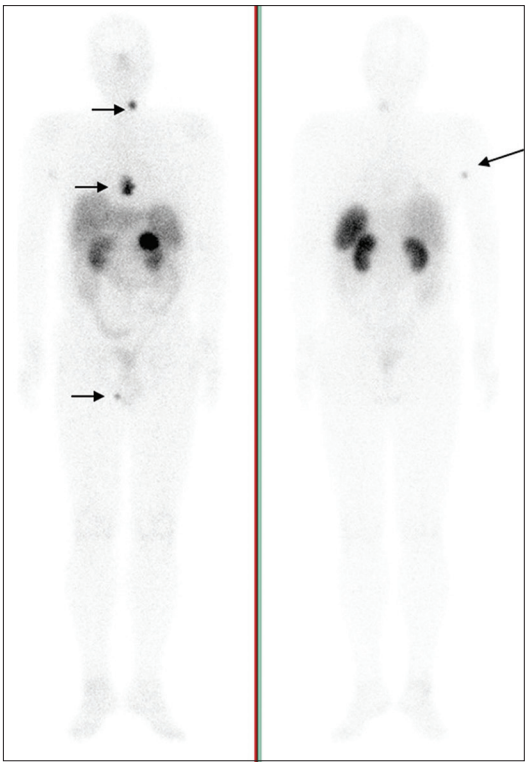

Figure 3: The peritoneal deposit was not evident in the follow-up diagnostic scans [Figure 1 and 3] and the posttreatment scans [Figure 3] indicating complete metabolic response

In the present case, interestingly, dual-tracer PET-CT demonstrated high-grade uptake on ^{68}Ga-DOTATATE and low uptake on FDG commensurate with the WHO-2005 classification of LCNEC as a variant of AC. High avidity observed on ^{68}Ga-DOTATATE (Krenning score-3) made ^{177}Lu-DOTATATE-based PRRT a feasible treatment option, which resulted in disease stabilization of most of the lesions (complete response of peritoneal deposit) and no disease progression at the timing of writing this report at 9 months.

CONCLUSION

The described case underscores the potential role of dual tracer PET-CT molecular imaging in assessing the disease biology of metastatic lesions in LCNEC including indicating the feasibility of PRRT. SSTR-targeted ^{68}Ga-DOTATATE PET-CT is a useful investigation in assessment, deciding on the feasibility of PRRT and follow-up akin to other NETs, while FDG uptake helps in prognosticating the disease. PRRT, in addition to concurrent chemo-radiotherapy, offers another potential therapeutic approach in receptor-positive cases of metastatic LCNEC and may result in longer survival.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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