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CASE REPORT

Simultaneous Triple Primary Head and Neck Malignancies: A Rare Case Report

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Abstract The occurrences of multiple primary malignant tumours in the head and neck region are reported as simultaneous, synchronous, or metachronous based on their chronology of presentation. Lymphoid malignancies presenting in association with squamous cell carcinoma in the head and neck region are extremely rare. We report a case of a 71 year old male patient with simultaneous triple primary malignancies of different histologic origin, involving larynx (squamous cell carcinoma), thyroid (papillary thyroid carcinoma) and lymph nodes (non-Hodgkin's lymphoma).

Keywords Simultaneous · Triple primary malignancies · Head and neck malignancies

Introduction

The occurrences of multiple primary malignant tumours of the head and neck region are reported as simultaneous, synchronous, or metachronous based on their chronology of presentation. Patients with head and neck squamous cell carcinoma are at increased risk of developing a second primary malignancy, most commonly in the upper aero-digestive tract, with incidence varying from 17 to 30 % and annual risk of 3–10 % [1]. There are reported small series of thyroid malignancy presenting with laryngeal squamous cell carcinoma. However, lymphoid malignancies presenting with head and neck squamous cell carcinoma are rare [2]. The incidences of three head and neck primary malignancies of different histologic origin are extremely rare. Among head and neck sub-sites, nasopharynx, larynx, and hypopharynx show increased propensity for triplicate malignancies [3]. The incidence of multiple primary malignant neoplasms increases with age. They are diagnosed more frequently now-a-days due to improvement in imaging and other diagnostic tools [4].

Here we report a case of a 71 year old male patient, with simultaneous triple primary malignancies of the head and neck region: squamous cell carcinoma of larynx co-existing with papillary thyroid carcinoma and non-Hodgkin's lymphoma.

Case Report

A 71 year old male patient, non-smoker, non-alcoholic, without any co-mobidities, presented with a history of change in voice for 6 months duration. This was progressive and associated with respiratory difficulty. There was no history of dysphagia. No member in the family was ever diagnosed with malignancy. Fiber-optic laryngoscopy showed ulcerative growth involving the left true vocal cord, left false vocal cord, anterior commissure, and right true vocal cord. Left vocal cord was fixed. The rest of the larynx, hypopharynx, valeculla, and base of tongue were normal. Laryngeal crepitus was present. Small lymph nodes of size 1 cm were palpable in left level II and III. Multiple nodes were also palpated in both axillae and groins. Complete blood count, liver function test, renal function test, coagulation profile, and thyroid function tests were within normal range. Contrast enhanced computed

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tomography (CECT) of neck revealed bulky asymmetrical soft tissue lesion involving left hemi-larynx with erosion of thyroid cartilage and extra-laryngeal spread to the strap muscles. Multiple enlarged neck nodes were found on both sides. Multiple heterogeneous nodules with dystrophic calcification were also seen within both thyroid lobes (Fig. 1a). CECT thorax revealed no evidence of lung metastasis or primary lung lesion. However, significant lymphadenopathy was seen in both axillae and retroperitoneum.

Direct laryngoscopy and biopsy from the laryngeal growth showed invasive keratinizing squamous cell carcinoma. Biopsy from axillary lymph node showed nodal marginal zone lymphoma with plasmacytic differentiation, positive for CD20 and CD138, and negative for CD10, CD5, CD23, and CD3. These immunohistochemical markers ruled out small lymphoblastic lymphoma, mantle cell lymphoma, follicular lymphoma, and other low grade B cell non-Hodgkin's lymphomas. Bone marrow biopsy revealed B Cell lymphoproliferative disorder. Serum protein electrophoresis revealed 'M-band' in gamma region. He underwent total laryngectomy with total thyroidectomy and bilateral selective neck dissection (level II–IV). Postoperative histopathology of Larynx specimen showed invasive keratinizing squamous cell carcinoma, moderately differentiated (p T4a) (Fig. 1b). Histopathology of thyroid specimen showed papillary architecture, follicular cells with optically clear nuclear inclusions, grooving and nuclear overlapping suggesting diagnosis of papillary thyroid carcinoma classical variant, involving both lobes, p T1 (m) (Fig. 1c, d). Neck dissection specimen showed bilateral level II, III, and IV lymph nodes involved by nodal marginal zone lymphoma with plasmacytic differentiation. There was near total effacement of lymph nodal architecture by small, monomorphic neoplastic cells. These cells had round to irregular nuclei, indistinct nucleoli, and abundant pale to clear cytoplasm, with distinct cell border (Fig. 2a). Immunohistochemical profile was same as described earlier. Paracortical zone shows few T-Cell nodules positive for CD5 (Fig. 2b–d).

Patient developed pharyngocutaneous fistula in postoperative period which was managed conservatively and fistula healed well. He received adjuvant radiation therapy to the tumour bed and bilateral level II, III, and IV, 60 Gy in 30 fractions, which was started on 6th week following surgery. This was followed by radioactive iodine ablation

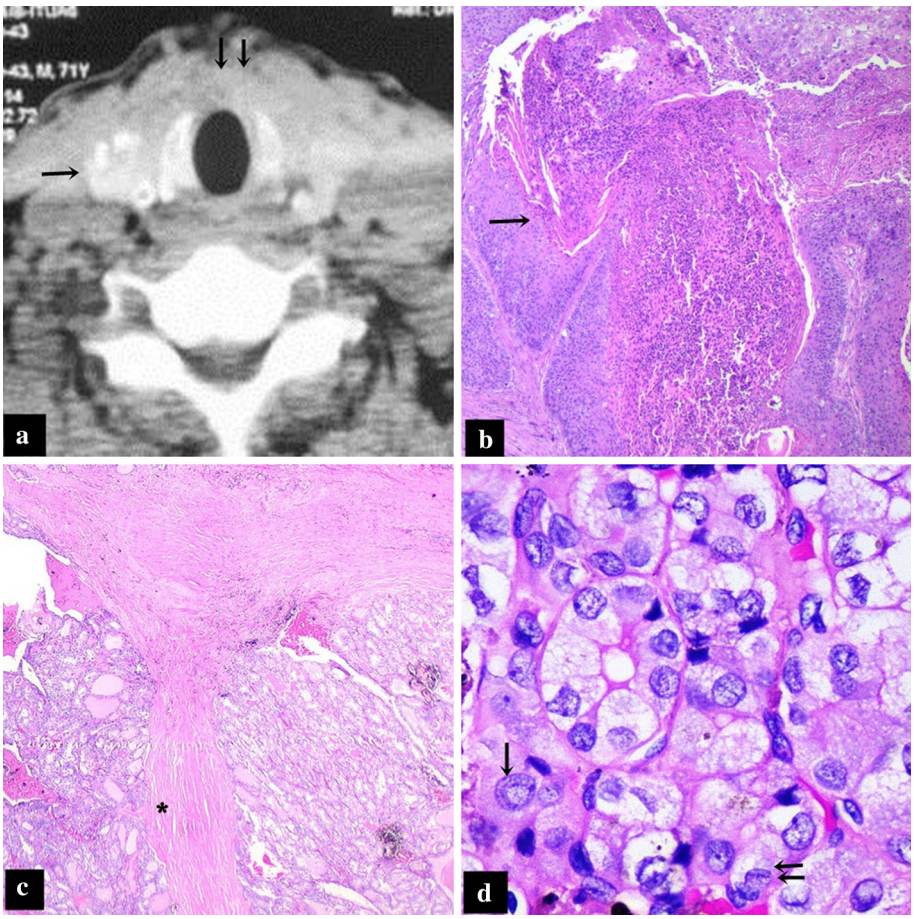

Fig. 1 **a** CECT of the neck showing right side thyroid nodule (*single black arrow*); there is extralaryngeal spread of squamous carcinoma of larynx with involvement of strap muscle (*double black arrows*); **b** Histopathology of larynx specimen showing invasive squamous cell carcinoma; **c** Histopathology of thyroid specimen (low power field, 2.5X) showing papillary architecture (*asterisk*); **d** Histopathology of thyroid specimen (high power field, 40X) showing follicular cells with enlarged nucleus, optically clear nuclear inclusion, grooving (*single black arrow*); overlapping of nuclei (*double black arrows*)

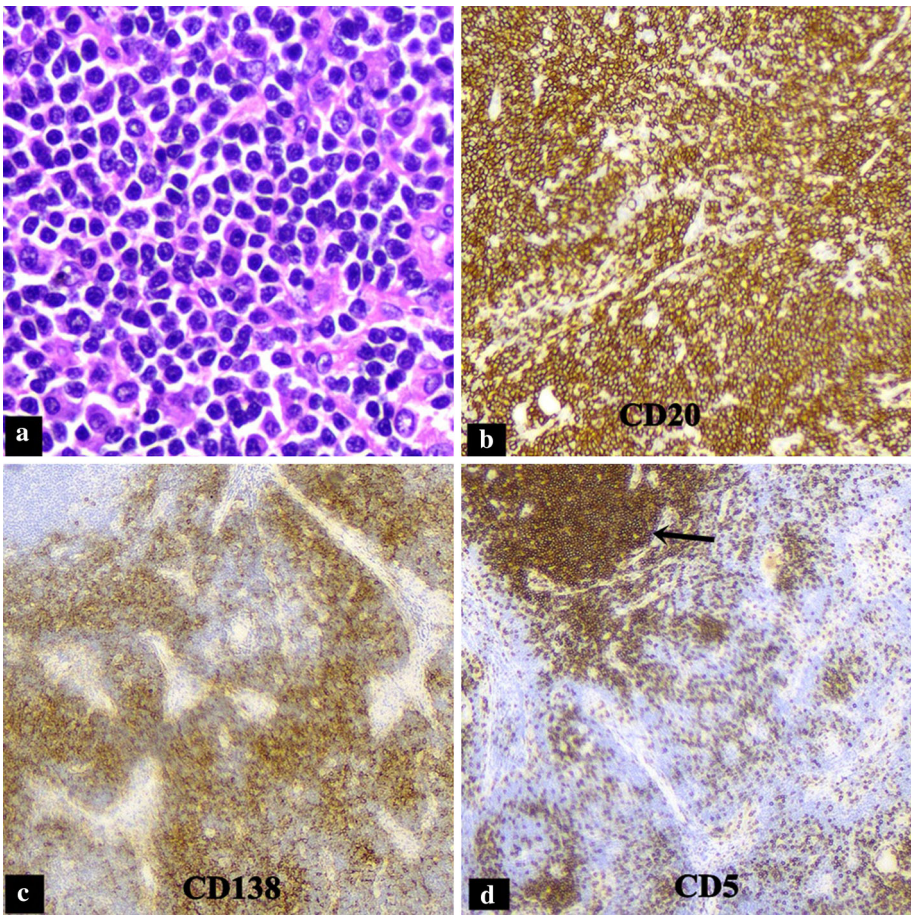

Fig. 2 Histopathology of lymph nodes showing nodal marginal zone lymphoma with plasmacytic differentiation. **a** Effacement of lymph nodal architecture by small, monomorphic neoplastic cells with round to irregular nuclei, indistinct nucleoli, abundant pale to clear cytoplasm and distinct border; **b** Showing neoplastic cells positive for CD20; **c** Plasmacytoid cells staining for CD138; **d** Neoplastic cells negative for CD5, while paracortical T-Cell nodule staining for CD5 (*single black arrow*)

with 150 milli curie (mCi) I^{131}. Post-ablation whole body scintigraphy revealed no residual functioning thyroid tissue in the neck and no distant metastatic lesions were noted. He also received chemotherapy (Cyclophosphamide and Dexamethasone) for lymphoma over a period of 6 months. He is on regular follow up since 1 year and doing well.

Discussion

Squamous cell carcinoma of the upper aerodigestive tract has high propensity to develop second primary malignancy. Explanation for this was proposed by Slaughter, who gave the concept of 'condemned mucosa' developing after chronic carcinogenic exposure [5]. Carey has countered that 'field cancerization' may be monoclonal with second tumours developing from micrometastatic deposits from original primary [6]. The majority of these second tumours develop in the upper aerodigestive tract, with lung cancer as the most frequently diagnosed malignancy [7]. However, simultaneous three primary malignancies of different histologic origin (as in the present case) in the head neck region may not be explained by these proposed theories. A possible relation may be genetic and/or immunologic alterations.

The present case is extremely rare, as simultaneous presentation of squamous cell carcinoma of larynx, papillary thyroid carcinoma, and non-Hodgkin's lymphoma, has not been reported in literature. However, there are reported small case series of head and neck squamous carcinoma presenting with papillary thyroid carcinoma [8, 9] and head and neck squamous carcinoma presenting with lymphoma [2, 10].

The effect of the first tumour on the second primary or vice versa is still not fully understood and needs to be explored. The second primary tumour is usually more aggressive, more treatment resistant, and metastasizes early, requiring a more aggressive treatment strategy. The prognosis of synchronous tumours is significantly poorer when compared to metachronus malignancies. The early implementation of aggressive treatment methods for second primaries may be successful in terms of survival [11].

A triple presentation of laryngeal, thyroid, and lymph node malignancies of different histology in the same patient simultaneously is very unique and to our knowledge no such case has been reported in the literature. It

emphasizes the need for vigilant, meticulous examination of such patients along with appropriate imaging and biopsy techniques. However, etiologic origin of such multiple primary tumours and their impact on survival needs to be explored.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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