Synchronous Squamous Cell Carcinoma of Tongue and Unicentric Cervical Castleman's Disease Clinically Mimicking a Stage IV Disease: A Rare Association or Coincidence?

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Abstract Malignancy in a setting of hyaline vascular type of Castleman's disease (HVCD) is an exceptional occurrence. Herein, we report an extremely rare case of synchronous unicentric cervical HVCD and squamous cell carcinoma (SCC) of tongue mimicking stage IV disease. A 32-year-old gentleman presented with an ulcerated mass on the right tongue border and ipsilateral cervical nodal mass. As the clinical stage was IVB (T₁N₃M₀), an anterior two-third glossectomy with bilateral modified neck dissection was performed. On gross examination, an ulcerated mass on the right lateral border was identified. In addition, an 8 cm large nodal mass at right level III–V was seen. Microscopy from the ulcerated growth in the tongue revealed an invasive well differentiated squamous cell carcinoma. However, the right cervical nodal mass yielded surprise histology of Castleman's disease, hyaline-vascular type. Final tumor pathological staging was revised to pT1N0M0. This case reveals that HVCD can rarely be associated with an epithelial malignancy wherein it can clinically mimic nodal metastasis. Whether such a phenomenon occurs due to underlying immune aberrations or is a rare co-incidence remains unclear.

Keywords Hyaline vascular Castleman's disease · Squamous cell carcinoma tongue · Synchronous

Introduction

Castleman's disease (CD) is a rare lymphoproliferative disorder which is histologically subdivided into a hyaline vascular (HVCD) and plasma cell (PCCD) types, with mixed variants [1] and clinically into localized and multicentric types. The HVCD occurs much more frequently than the PCCD and is usually localized to the mediastinum or pulmonary hilum. The latter involves lymph nodes separately or in aggregations and often displays multicentricity with systemic symptoms including autoimmune phenomena and aggressive course. Small hyalinized and hypervascular germinal centers with hypervascular interfollicular stroma and sinus effacement are common features of the HVCD, whereas hyperplastic germinal centers with plasma cell aggregates in lymph node paracortex and partially spared sinuses are characteristic features of the PCCD [2]. A key event in the pathogenesis of CD has been recently suggested to be an abnormal production of a B cell growth factor, such as IL-6, leading to lymphoid cell proliferation and plasma cell differentiation [3, 4].

Malignancies arising in the setting of CD are rare. PCCD has been uncommonly associated with malignancies such as Kaposi's sarcoma, B cell non-Hodgkin lymphomas and Hodgkin lymphoma, and with POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes) syndrome [5]. Malignancy in the setting of HVCD is rather rare and the most common malignancy that occurs in such an eventuality is a follicular dendritic cell sarcoma (FDSC) [6]. Association or coexistence of an epithelial malignancy with a HVCD is an

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exceptional occurrence. Herein, we report an extremely rare case that presented with a synchronous squamous cell carcinoma (SCC) of tongue and cervical HVCD and clinically simulated a nodal metastatic disease.

Case Report

A 32-year-old male pharmacist by occupation and a chronic tobacco chewer presented with complaints of non healing ulcer at right lateral border of tongue along with a gradually enlarging right neck mass, both noted 2 years ago. Physical examination of the patient revealed good general condition. The vitals were within the normal limits. On local examination, an ulceroinfiltrative growth measuring 2×1 cm was noted on the right lateral border of tongue. There was a right cervical nodal mass, 8 cm in largest dimension, mobile, non tender, deep to the supraclavicular muscle in the submandibular region. Chest was clear to auscultation. The remainder of systemic examination was normal with no generalized lymphadenopathy and hepatosplenomegaly.

The laboratory findings were significant for following values: WBC count 5,160/uL (range 4.0–10.0 $\times 10^3$ /uL) (neutrophils-55%, lymphocytes-33%, eosinophils-04%, monocytes-08%), haemoglobin-11.5 g/dL (range 11.0–15.0 g/dL). The biochemical evaluation values and the coagulation profile were within normal limits. Human immunodeficiency virus and hepatitis virus (B and C) titers were not indicative of any recent or remote infections. The chest radiograph was normal. The computerized tomography (CT) of neck and thorax revealed right cervical mass and a solitary left cervical node measuring 1.3×1.2 cm. A tongue biopsy was performed and diagnosed as SCC. Clinically, the disease was staged as stage IVB. Subsequently, right hemiglossectomy with bilateral modified neck dissection was done. On gross examination, a $2 \times 1 \times 0.9$ cm ulceroproliferative growth was present on the right lateral border of tongue. In addition, a large right cervical mass measuring $8 \times 5 \times 4$ cm was seen. The outer surface was nodular and cut surface was homogenous, tan colored (Fig. 1). Microscopic examination of the right lateral border tongue growth in the resected specimen showed a well differentiated SCC (Fig. 2). Histology of the right cervical mass revealed enlarged lymph node with prominent mantle zones comprised of small, mature lymphocytes arrayed in concentric 'onion skin' layers surrounding atrophic germinal centers penetrated by hyalinised vessels (Fig. 3). Prominent endothelial cells were seen in the vessels extending into the adjacent interfollicular area. There was no interfollicular plasma cell infiltrate. There was no evidence of metastasis. On microscopy, although histology was characteristic of HVCD and no lymphoma was suspected. However, a panel

Fig. 1 Well-differentiated squamous cell carcinoma of the right lateral border of tongue (Haematoxylin and eosin, $\times 400$)

Fig. 2 Gross appearance of the right cervical mass

Fig. 3 Histology of cervical mass reveals hyaline vascular type castlemans disease (Haematoxylin and eosin, $\times 200$)

Fig. 4 Classical ‘lollipop’ vessel penetrating abortive follicle (Haematoxylin and eosin, $\times 400$)

of immunohistochemistry that included CD20, CD3, CD43, CD5, CD23, CD10, bcl-2, kappa and lambda light chains and cyclinD1 was performed to exclude a low grade lymphoma, namely, marginal zone lymphoma, mantle lymphoma and follicular lymphoma. Morphologic features and Immunohistochemistry results showed no abnormal haematolymphoid population and were labeled as HVCD. The left cervical nodes were reactive. The final diagnosis was a synchronous SCC of tongue and a cervical HVCD with non metastatic regional nodes; TNM (6th edition) pT1N0M0. Post operative course was unremarkable. Patient was well for 1 year after surgery and was subsequently lost to follow up (Fig. 4).

Discussion

Castleman’s disease is a benign lympho-proliferative disorder characterized by enlarged hyperplastic lymph nodes. The earliest description of Castleman’s disease dates back to 1954 [1]. Histologically, three variants are recognized: hyaline vascular, plasma cell type, and mixed type [2]. Hyaline-vascular type is the commonest type and is usually localized to mediastinum or pulmonary hilum; while only 6% of all cases of CD present as primary cervical lymphadenopathy [7].

Association of Castleman’s disease with malignancy is known, albeit rare. The predominant association of various malignancies i.e. Kaposi’s sarcoma, B cell non Hodgkin lymphoma and Hodgkin lymphoma is with the PCCD histologic subtype [5]. Uncommonly, FDCS has been reported to arise in the background of HVCD [6]. Occurrence of an epithelial malignancy in the setting of CD is an exceptional phenomenon. Previously, two case reports observe synchronous occurrence of carcinoma, namely

thymic carcinoma and pulmonary SCC in association with HVCD [8, 9]. There is a solitary case reported in literature of a synchronous SCC of tongue and a mediastinal HVCD [10]. To the best of our knowledge, present case is the first report of a synchronous SCC of tongue and a unicentric HVCD in the cervical region. Present case was clinically stage IVB due the 8 cm neck nodal mass preoperatively and following the histopathological examination, the stage was revised to pT1N0M0.

The exact pathogenesis of concurrent occurrence of either hematolymphoid malignancy or an epithelial malignancy with CD still remains to be unraveled. Aberrations in follicular dendritic cell (FDC) networks as well as FDC dysplasia observed in some follicles in HVCD which later evolve into a full blown FDCS maybe a plausible basis for HVCD’s association with FDCS. On the other hand, in the case of thymic carcinoma associated with the mediastinal CD, the authors hypothesize that the carcinoma cells release cytokines (IL-6 like) which stimulate development of HVCD [6]. Key role of IL-6, a potent, pleiotropic pro-inflammatory cytokine in the etio-pathogenesis of CD is already well known [4]. Interestingly, significantly elevated serum IL-6 levels have been documented in head and neck squamous cell carcinomas (HNSCC) [11] and IL-6 over expression has been associated with tumor aggressiveness, immune unresponsiveness and distant metastasis [8]. Under such circumstances, IL-6 remains as one of the potential synergistic mediators that maybe involved in cross-talk between two spatially and pathologically distinct lesions occurring simultaneously. Given the extreme paucity of similar instances in literature, the current deliberation, although conjectural, is a tempting and exciting possibility. Unfortunately, serum or tumor tissue IL-6 levels were not available in the present case to explore the hypothesis further.

In conclusion, we report an extremely rare case of synchronous unicentric cervical HVCD and SCC of tongue clinically simulating a stage IVB disease. Whether such an association is due to underlying immune phenomenon involving mediators such as IL-6 or is a rare co-incidence remains to be established.

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