

79127_Auto_Edited.docx

Solitary Hyoid Plasmacytoma with Unicentric Castleman Disease: A Case Report

Hyoid Plasmacytoma with Castleman Disease

Abstract**BACKGROUND**

Solitary plasmacytoma and unicentric Castleman disease are rare lymphoproliferative disorders characterized by monoclonal plasma cells and a single set of locally enlarged lymph nodes, respectively.

CASE SUMMARY

A 48-year-old Han Chinese man presented to our department with a neck mass and progressive foreign body sensation in his throat. ^{18}F -FDG PET revealed focally increased radioactivity centered around the hyoid, and CT revealed osteolytic lesions. Histopathology revealed Castleman-like features and CD138/CD38-positive mature plasma cells. Systemic work-up ruled out the possibility of POEMS syndrome, lymphoma, and multiple myeloma, leading to a final diagnosis of solitary hyoid plasmacytoma with unicentric Castleman disease. The patient underwent partial hyoid resection and selective neck dissection, followed by intensity-modulated radiotherapy. ^{99}Tc -MDP SPECT/CT reevaluation showed neither local recurrence nor distant bone metastasis at the 40-month follow-up.

CONCLUSION

The diagnostic process and differential diagnosis of this rare case provided valuable educational information to clinicians.

Key Words: ^{18}F -FDG, PET/CT, Plasmacytoma, Hyoid Bone, Castleman Disease

Zhang YH, He YF, Yue H, Zhang YN, Shi L, Jin B, Dong P. Solitary Hyoid Plasmacytoma with Unicentric Castleman Disease: A Case Report. *World J Clin Cases* 2022; In press

Core Tip: In this study, we described the clinical presentations, diagnosis and differential diagnosis, management, outcome, and relative long-term follow-up for a man simultaneously affected with solitary plasmacytoma of the hyoid bone and unicentric Castleman disease. To our knowledge, this is the first reported case presented with these two rare clinical entities. Besides the comprehensive histopathological examination, ^{18}F -FDG PET/CT and $^{99\text{mTc}}$ -MDP SPECT/CT were broadly used in our clinical practice of differential diagnosis, disease staging, and follow-up monitoring, highlighting the advantages of nuclear medicine and other imaging techniques in the management of solitary plasmacytoma in the head and neck. Additionally, the diagnostic process and differential diagnosis of this patient provided valuable educational information to clinicians.

INTRODUCTION

Solitary plasmacytoma (SP) is a rare disease characterized by abnormal proliferation of monoclonal plasma cells, with a cumulative incidence of 0.15/100000 [1,2]. Solitary bone plasmacytoma (SBP) is a subtype of SP that occurs primarily in the red-marrow-containing axial skeleton and long bones [3] and accounts for 70% of all SP cases [1]. SBP with minimal (<10%) bone marrow plasma cells progresses to multiple myeloma (MM) within 3 years in approximately 60% of patients [2, 4]. All SP are radiation-sensitive; therefore, radiotherapy (RT) is recommended as the first-line treatment strategy for the long-term disease control in these patients [3, 5].

Unicentric Castleman disease (UCD) is a rare lymphoproliferative disorder with unknown prevalence and belongs to a heterogeneous group of conditions characterized by similar histopathological features but has distinct pathological etiologies, clinical symptoms, management, and outcomes [6, 7]. For patients with resectable UCD, complete surgical excision is the optimal first-line treatment, with a 5-year overall survival of up to 90%; even after a 10-year follow-up, disease relapse is rare [6, 8].

Here, we report the case of a 48-year-old man with SBP of the hyoid and UCD along with the clinical diagnosis, management process, and follow-up. Moreover, we reviewed the literature of related SBP cases to provide a comparative experience in guiding the management of this rare disease.

CASE PRESENTATION

Chief complaints

A 48-year-old Han Chinese man presented with a neck mass and progressive foreign body sensation in his throat.

History of present illness

The patient reported no sore throat, dyspnea, or dysphagia during the course of the disease.

1

History of past illness

The patient had no history of past illness.

Personal and family history

The patient had no personal or family history.

Physical examination

Basic physical examination showed no obvious abnormalities.

Laboratory examinations

Laboratory tests showed that the routine blood and urine results as well as blood biochemical indices, including serum calcium-albumin-creatinine, blood urea nitrogen, lactate dehydrogenase, $\beta 2$ microglobulin, and 24-hour urine for total protein, moreover, the results of serum immunoglobulin and complement assay (**Table S1**), were all within normal limits.

Imaging examinations

Electronic laryngoscopy and plain CT showed thickening of the left epiglottis (**Figure 1A, 1C**, arrows), arytenoid and aryepiglottic folds (**Figure 1B, 1D**, arrows), osteolytic lesions of the left hyoid (**Figure 1E**), and thyroid cartilage plate (**Figure 1F**). The left piriform fossa was occluded, and enlarged cervical and submandibular lymph nodes were observed bilaterally. The patient underwent selective neck dissection and partial hyoid resection to relieve neck compression, and a final diagnosis was made. ^{18}F -FDG PET/CT revealed focally increased radioactivity centered around the hyoid body and its left greater horn (arrows, $\text{SUV}_{\text{max}}=8.8$) and the left submandibular and submental soft tissue (arrowheads, $\text{SUV}_{\text{max}}=4.8$) exhibited on PET (**Figure 1G-1I**), CT (**Figure 1J-1L**), and PET/CT fusion (**Figure 1M-1O**). Osteolytic lesions were identified on the plain CT bone window. The MIP PET image (**Figure 1P**) showed no other sites with abnormal ^{18}F -FDG uptake, except for the perihyoid region. These findings were suggestive of a malignancy.

FURTHER DIAGNOSTIC WORK-UP

Histological results revealed angiofollicular lymph node hyperplasia of the hyaline-vascular type arranged in an onion-bulb appearance (**Figure 2A, 2B**, 200x and 400x), and the presence of mature plasma cells characterized by an oval shape, abundant basophilic cytoplasm, perinuclear halo, round eccentric nuclei, and indiscernible nucleoli [6, 7, 9] (**Figure 2C, 2D**, 200x and 400x). Histopathological results were positive for plasma cell markers (CD138 (**Figure 2E**), CD38 (**Figure 2F**), κ (**Figure 2G**) and λ

(**Figure 2H**) light chains, CD79 α (**Figure 2I**), IgG, IgM), and focal expression of T-cell markers (CD43 (**Figure 2J**), CD45), and CD56; however, deficiency of B-cell markers (CD20 (**Figure 2K**), CD19) was observed. The Ki-67 proliferation index was 3% (**Figure 2L**). No paraproteins and pathological elevation of κ and λ chains were detected by the SPEP and FLC assays [4, 10]. Bone marrow biopsy indicated normal trilineage hematopoiesis with only 0.2% plasma cells in all leukocytes [4]. Additionally, polyneuropathy and other minor symptoms were absent.

FINAL DIAGNOSIS

Systemic work-up ruled out the possibility of POEMS syndrome, lymphoma, and MM [4, 11, 12], thus leading to the diagnosis of SP of the hyoid, with UCD. Inflammatory factors, such as TNF α , IL-6, IL1 β , TGF β 1, and VEGF α (**Figure S1**), were increased, confirming the multiple cytokine-producing property of SBP [13, 14].

TREATMENT

The patient underwent intensity-modulated RT [5] for the hyoid bone and high-risk subclinical areas, with a total dose of 50.4 Gy, divided into 28 fractions [10].

OUTCOME AND FOLLOW-UP

No acute toxicity was observed during RT. After 3 mo, CECT revealed a slightly shrunken tumor boundary. The patient underwent CT and ^{18}F -FDG PET/CT or $^{99\text{mTc}}$ -MDP SPECT/CT examinations at 6 and 12 mo, respectively. Recent $^{99\text{mTc}}$ -MDP SPECT/CT reevaluation showed a slight increase in radioactivity around the hyoid, considering postoperative changes rather than local recurrence on SPECT (**Figure 3A**), CT (**Figure 3B**), and SPECT/CT fusion (**Figure 3C**). Focal bone destruction and secondary hyperosteogeny were also observed in the CT bone window (**Figure 3D**). Whole-body SPECT revealed no evidence of distant bone metastasis (**Figure 3E** and **3F**). The patient was symptomatic and progression-free at the 40-month follow-up visit.

DISCUSSION

Plasma cell disease comprises a heterogeneous group of disorders characterized by an increase in the number of monoclonal plasma cells [4]. Abnormally proliferative cells can secrete a large quantity of monoclonal Ig and invade and damage various tissues or organs, such as the bones, bone marrow, kidneys, hearts, lungs, and immune system. Precision clinical intervention is needed for the accurate diagnosis of these diseases. In the present study, the histology of the neck mass showed Castleman's lesion, such as vitreous degeneration with an "onion skin" appearance, and monoclonal proliferation of plasma cells, resembling the typical features of Castleman disease (CD) variant of POEMS syndrome. However, the patient did not meet the other major or minor criteria required for a definite diagnosis of POEMS syndrome or MM [4, 11, 12]; therefore, led to a final diagnosed with SBP of the hyoid and UCD. The NCCN recommends using primary RT of a total dose of 40–50 Gy in 1.8–2.0 Gy per fraction over 4 wk, for patients with SP in whom the surgery is depended on clinical necessity [10]; in addition, for patients with UCD, excisional surgery is the optimal strategy with the benefit of long-term disease control [6, 8]. The patient received intensity-modulated RT according to the guidelines after extended dissection of the neoplastic mass adjoining the primary lesion. The hyoid bone is an atypical location and is extremely rare for the growth of SP; to the best of our knowledge, only three cases have been reported [15–17]. Goel *et al* presented the first case of local RT followed by chemotherapy, and the hyoid swelling was significantly reduced in size during the 18-month follow-up [15]. Danaci *et al* described the second case of a 60-year-old man. This patient underwent total excision of the hyoid mass but was not subsequently treated with RT or chemotherapy and was alive and progression-free during the 24-month follow-up period [16]. The third patient was diagnosed with non-secretory MM stage IIIA and presented with plasma cell infiltration into the hyoid bone. This patient received chemotherapy and antihypercalcemic therapy; however, the prognosis was not referred to in the report [17].

SP can be divided into SBP and solitary extramedullary plasmacytoma (SEMP) based on its origin from the bone marrow or soft tissue organs [4]. Abnormal monoclonal plasma

cells and bone marrow stromal cells (BMSCs) in SBP strongly express multiple cytokines and their corresponding receptors that promote the growth and survival of tumor cells or angiogenesis through autocrine and paracrine mechanisms [13, 14]. Plasma cell-derived matrix metalloproteinases participate in the degradation of the extracellular matrix and basement membrane, leading to chronic inflammation and bone-destructive lesions [18]. Abnormal plasma cells also induce local angiogenesis and stimulate neovascularization depending on secreted cytokines, such as ANG-1, CXCL12, and VEGF α , which supply nutrition for tumor cell growth [19-21]. Cytokine homeostasis, particularly that secreted by BMSCs, acts as a regulatory mechanism for tumor growth [22]. Some reports indicate that aberrant activation of gp130-dependent and NOTCH signaling may provide strong advantages for the growth of plasmacytomas [19, 23-25]. CD and POEMS syndrome are also associated with the elevation of several classical cytokines in serum, such as IL-6, VEGF α , TNF α , IL1 β , and TGF β 1 secreted by proinflammatory cells, as found in SBP. CD and SP can present independently, concurrently, or sequentially with POEMS [26-28]. Patients with CD and/or POEMS syndrome usually have an upregulation of serum VEGF α and IL-6 mediated cytokine storm, which might impair cerebral vessels, resulting in vasculopathy of the central nervous system and an increased risk of cerebral infarction [26, 29, 30].

2 Recently, with the development of high-throughput sequencing (HTS) technology, genetic analyses have been broadly applied to reveal the molecular mechanisms of UCD and idiopathic multicentric Castleman disease (iMCD) [31-35]. Overall, two recurrent hotspot somatic mutations, *PDGFRB* (NM_002609.4, c.1997A>G, p.N666S) and *NCOA4* (NM_005437.4, c.781>T, p.L261F), were identified in 17% and 18% of the tested UCD and iMCD cases, respectively [33, 34]. In a patient with iMCD accompanied by severe peripheral neuropathy, somatic alterations were identified in genes related to neuronal development, such as *PDLIM5*, *SEC24B*, *ZFHX3*, and *PACRG* [36]. Another patient harbored a somatic *JAK1* missense mutation, but normal serum IL-6 had a complete response rate to the IL-6 antibody siltuximab, implicating the essential roles of the IL-6/IL-6R/JAK1/STAT pathway and its mutations in the pathogenesis of iMCD [37].

Somatic mutations were prone to enrichment in the mitogen-activated protein kinase and interleukin pathways in UCD and iMCD; however, genes affecting chromatin remodeling were solely enriched in iMCD [38]. Moreover, patients with iMCD have a high prevalence of germline *MEFV* variants that modify their clinical phenotypes and treatment responses [39, 40]. Transcriptome profiling also revealed that UCD and MCD are involved in unique genes, pathways, and cell types [35].

¹⁸F-FDG PET/CT exhibits superior sensitivity and specificity for SBP lesions. It can detect minimal residual disease inside and outside the bone marrow at the same time in one examination, which cannot be identified by X-ray and MRI [41, 42]. In the early stages of patients with SBP after radiotherapy, ¹⁸F-FDG PET/CT performs poorly in disease staging; however, a high SUV_{max} value is a regular prognostic indicator for progression [43]. ^{99m}Tc-MDP scintigraphy shows a relatively low sensitivity to detect bone lesions of SBP due to the suppressed differentiation of osteoblasts [44] and can be more applicable for evaluating the complications of SBP [45]. ^{99m}Tc MIBI scintigraphy shows the same sensitivity and specificity as ¹⁸F-FDG PET/CT in the detection of SBP lesions [46] and even better performance in the detection of diffuse bone marrow involvement, but it is inefficient in the detection of focal lesions [47]. ¹⁸F-FDG PET/CT has the ability to simultaneously collect anatomical structure and metabolic information and can be used for the initial staging and response monitoring of CD [48]. It has high specificity and sensitivity for the identification of lymph node lesions in patients with CD [49] and is an important imaging marker for judging the severity and prognosis of the disease. A variety of metabolic parameters in ¹⁸F-FDG PET/CT, including SUV_{max}, SUV_{mean}, SUV_{peak}, metabolic tumor volume (MTV), and total lesion glycolysis (TLG), can be used for the differential diagnosis of UCD and other diseases [50].

CONCLUSION

To our knowledge, this is the first reported case presented with these two rare clinical entities (SP of the hyoid bone and UCD). In addition to comprehensive histopathological analysis, ¹⁸F-FDG PET/CT and ^{99m}Tc-MDP SPECT/CT are routinely

used in the clinical practice of differential diagnosis, disease staging, and follow-up monitoring, highlighting the advantages of nuclear medical and other imaging techniques in the management of SP in the head and neck. In addition, the diagnostic and management processes provided valuable educational information to clinicians.

ACKNOWLEDGEMENTS

We sincerely thank Dr. Ya-Qiong Ren and Yu-Qi Shen at the ⁵Chinese Academy of Medical Sciences & Peking Union Medical College (CAMS&PUMC) for staining of inflammatory factors of SBP and their independent figure combination and optimization.

4%

SIMILARITY INDEX

PRIMARY SOURCES

- 1

Hao Bai, Zi-Rui Meng, Bin-Wu Ying, Xue-Rong Chen. "Pulmonary alveolar proteinosis complicated with tuberculosis: A case report", World Journal of Clinical Cases, 2021
Crossref

28 words — 1%
- 2

www.ncbi.nlm.nih.gov
Internet

28 words — 1%
- 3

f6publishing.blob.core.windows.net
Internet

14 words — 1%
- 4

Hong-Jin Shi, Zhi-Nan Fan, Jin-Song Zhang, Bo-Bo Xiong, Hai-Feng Wang, Jian-Song Wang. "Small-cell carcinoma of the prostate with negative CD56, NSE, Syn, and CgA indicators: A case report", World Journal of Clinical Cases, 2022
Crossref

12 words — < 1%
- 5

onlinelibrary.wiley.com
Internet

12 words — < 1%
- 6

www.frontiersin.org
Internet

12 words — < 1%

EXCLUDE BIBLIOGRAPHY ON

EXCLUDE MATCHES

< 12 WORDS