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Hepatocellular Carcinoma Presenting with Tonsillar Metastasis: A Case Report with a Review of Literature

Annie Francis[1] Boben Thomas[1] Unni S. Pillai[1] Thomas Babu[1] Diya Jacob[2]

[1] Department of Medical Oncology, Caritas Hospital and Institute of Health Sciences, Kottayam, Kerala, India
[2] Department of Pathology, Caritas Hospital and Institute of Health Sciences, Kottayam, Kerala, India

Address for correspondence Annie Francis, MD, MBBS, Department of Medical Oncology, Caritas Hospital and Institute of Health Sciences, Thellakom P.O, Kottayam, Kerala, 686630, India (e-mail: anniefrancisg@gmail.com).

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Abstract

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy, with extrahepatic metastases occurring in approximately 5 to 15% of cases. Metastases to tonsils are exceedingly rare and can pose a considerable diagnostic challenge. We present a rare case of a 77-year-old male patient who presented with a tonsillar mass, which following tonsillectomy and histopathological analysis was identified as a metastatic lesion. Subsequent evaluation revealed multifocal HCC with extrahepatic spread to the tonsils and lymph nodes. The patient was initiated on immunotherapy and had an excellent treatment response. This case underscores the importance of considering metastatic disease in the differential diagnosis of atypical head and neck lesions in patients with risk factors for HCC. Early diagnosis and timely intervention can positively impact survival, even in cases of advanced malignancy with atypical presentations.

Keywords
- hepatocellular carcinoma
- tonsillar metastasis
- extrahepatic spread
- case report
- rare presentation

Introduction

The incidence of hepatocellular carcinoma (HCC) has been on the rise, making it the sixth most common cancer diagnosed globally and the third most common cause of cancer-related deaths.[1] HCC with a current prevalence of 2.27 per 100,000 population in India, represents a growing public health concern, particularly in the context of shifting etiological patterns and rising incidence and mortality rates across the country.[2] The risk factors for HCC include hepatitis B and C infection, aflatoxin exposure, heavy alcohol consumption, obesity, and type 2 diabetes mellitus.[1] HCC frequently metastasizes during the course of the disease. Patients with HCC might manifest both intra- and extrahepatic metastases (EHMs). About 5 to15% of patients presents with EHM at the time of diagnosis.[3] Among the various sites affected by extrahepatic spread of HCC, the lungs are the most frequently involved. However, rectum, spleen, esophagus, pancreas, and urinary bladder have also been described as rare sites of metastatic disease.[4] Less than 1% of cases show oral involvement, such metastases can involve both bone and the oral soft tissues.[3,4] Hence, in the differential diagnosis of malignant tumors of the oral cavity, it is important to consider both primary as well as metastatic lesions The prognosis of patients with HCC and EHM is generally poor, with median survival ranging between 7 and 15 months, even with systemic therapy.[5–7] However, recent advances in targeted therapy, particularly the combination of atezolizumab (programmed death-ligand 1 inhibitor) and bevacizumab (anti-vascular endothelial growth factor), have redefined management paradigms. This regimen, now a first-line option for advanced HCC, has shown promising results in prolonging overall survival and maintaining disease control.[8] Metastatic HCC to the tonsil is exceedingly rare and can present with

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nonspecific symptoms such as throat discomfort. Such atypical presentations often delay diagnosis and highlight the importance of maintaining clinical suspicion, especially in patients with underlying risk factors for liver disease. This report underscores the need for thorough evaluation of unusual oropharyngeal lesions and the role of systemic workup in identifying rare metastatic sites.

Case Report

Our patient is a 77-year-old male who presented to the otorhinolaryngology department with complaints of foreign body sensation of the throat. His past medical history included chronic liver disease. Clinical examination of the oropharynx revealed a soft tissue lesion in the left tonsil. Palpation of the neck and flexible nasolaryngoscopy did not reveal any other abnormal findings. Laboratory examinations demonstrated mild thrombocytopenia. Contrast-enhanced computed tomography (CT) scan of neck showed enlarged left tonsil with no enhancing cystic area, the differential diagnosis considered were chronic tonsillitis, tonsillar abscess, and primary tonsillar malignancy. He was planned for coblation-assisted tonsillectomy. In view of history of chronic liver disease, a gastroenterology opinion was sought for fitness and an ultrasound of abdomen was performed that revealed chronic liver disease with features of HCC and right portal vein thrombosis.

A contrast-enhanced CT scan of abdomen revealed multifocal HCC. He was referred to the department of oncology for further evaluation. He had an alpha-fetoprotein (AFP) value of 22 ng/mL and Child–Pugh score A, Barcelona Clinic Liver Cancer stage C disease. Hepatitis B surface antigen and hepatitis C was reported as nonreactive. Patient underwent left coblation-assisted tonsillectomy. Histopathology report was suggestive of infiltrating poorly differentiated malignant neoplasm (►**Fig. 1**), Immunohistochemistry showed hepatocyte paraffin 1 (HepPar 1) positivity, which was consistent with metastasis from HCC (►**Fig. 2**). Positron emission tomography (PET)-CT scan was performed, which confirmed multifocal HCC with tonsillar and pelvic nodal metastases (►**Fig. 3**). In view of metastatic multifocal HCC, patient was initiated on immunotherapy from December 2022 with atezolizumab 1200 mg and bevacizumab at 15 mg/kg dose every 3 weeks. His thrombocytopenia was attributed to hypersplenism secondary to chronic liver disease, which was managed conservatively along with serial monitoring of complete blood counts and liver function test during the course of therapy. He had completed 18 months of immunotherapy in May 2024. Reassessment PET-CT in June 2024 revealed stable disease. Due to a decline in performance status, comorbidities, and advanced age, his treatment was stopped, and he has been on supportive care since then. His disease is under control and is doing relatively well to date with a progression-free survival (PFS) of 30 months.

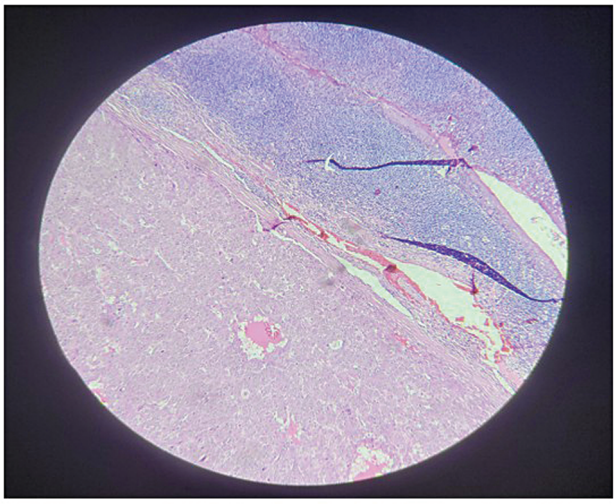

Fig. 1 Hematoxylin and eosin (H and E) stain—Diffuse infiltration of tonsil with malignant cells.

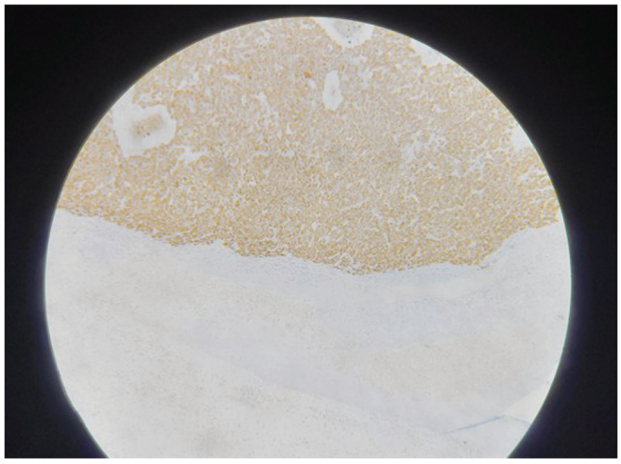

Fig. 2 Immunohistochemistry (IHC)—Hepatocyte paraffin 1 (HepPar 1) membrane positivity.

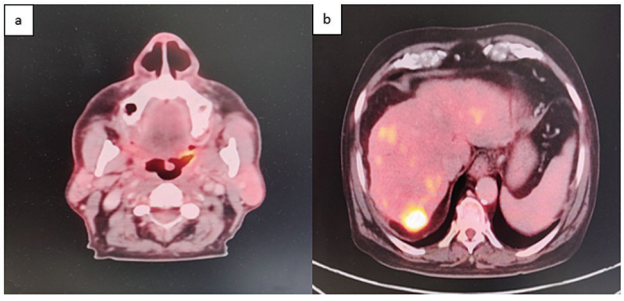

Fig. 3 Positron emission tomography-computed tomography (PET-CT) showing focal metabolic uptake in the left tonsillar region (**A**). Fluorodeoxyglucose (FDG)-avid right lobe liver lesion (**B**).

Discussion

Epidemiology and Global Burden

HCC is the leading type of liver cancer and ranks as the sixth most prevalent cancer globally.[1] HCC is the third most common cause of cancer-related deaths, with its incidence

Table 1 Showing summary of literature referenced in the discussion

Author	Year	Objective	Type of paper	Conclusion	Relevance to present case
Bray et al[1]	2024	To provide global cancer statistics including incidence and mortality	Epidemiological study	HCC is the 6th most common cancer globally and 3rd leading cause of cancer death	Contextualizes the global burden of HCC and the importance of recognizing all presentations, even rare ones like tonsillar metastasis
McGlynn et al[2]	2021	To discuss global trends and risk factors of HCC	Review article	Chronic HBV/HCV, alcohol, aflatoxin, obesity are key drivers; incidence rising globally	Demonstrates that tonsillar metastasis is extremely rare and not among the commonly reported sites
Katyal et al[6]	2000	To evaluate the pattern and frequency of extrahepatic metastases in HCC	Retrospective radiology study	EHM occurs in 5–15% of HCC cases; lungs, bones, and adrenal glands are the most frequent sites	Helps define the risk profile of the patient with chronic liver disease, a significant predisposing factor in our case
Greten et al[7]	2005	To assess survival in HCC patients with extrahepatic spread	Retrospective clinical study	Median survival for EHM patients is <12 months; survival depends on tumor burden and performance status	Highlights the unusual prolonged survival (30 months) in our case compared with typical outcomes
Hirshberg et al[9]	2008	To review 673 oral metastasis cases and identify primary origins	Systematic review	Liver metastases are extremely rare ($<1\%$); oral lesions may be the first sign of systemic malignancy	Confirms the rarity of oral metastasis from HCC; emphasizes diagnostic challenge
Seoane et al[22]	2009	To analyze oral metastasis survival patterns	Case series	EHM has poor prognosis; awareness of rare metastatic patterns is key for timely diagnosis	Similar to our patient whose tonsillar mass was the initial diagnostic clue for advanced HCC
Nadkarni et al[5]	2020	To present a rare case of buccal mucosal metastasis from undiagnosed HCC	Case report	Buccal lesion led to HCC diagnosis; underscores importance of considering metastasis in oral growths	Closely parallels our case in both presentation and the diagnostic pathway
Finn et al[6]	2020	To assess atezolizumab + bevacizumab for unresectable HCC	Randomized controlled trial	Immunotherapy combo significantly improves overall and progression-free survival over sorafenib	
Askland et al[16]	2010	To describe a case of tonsillar metastasis from HCC	Case report	HCC can metastasize to tonsil; requires biopsy and immunohistochemical confirmation for accurate diagnosis	Most similar case in literature; supports validity and uniqueness of our presentation
Kumar et al[17]	2018	To report another rare case of tonsillar metastasis	Case report	Presentation mimicked tonsillitis; tissue biopsy critical for diagnosis; HepPar-1 confirmed HCC origin	Diagnostic process mirrors ours, with foreign body sensation leading to tonsillectomy and biopsy confirmation
Cheng et al[9]	2023	To evaluate real-world outcomes of immunotherapy in HCC	Observational study	Real-world data confirm improved survival and tolerability of atezolizumab + bevacizumab combination	

Abbreviations: EHM, extrahepatic metastasis; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus.

varying widely across regions due to risk factors like chronic hepatitis B and C infections, aflatoxin exposure, alcohol-related liver damage, obesity, and metabolic syndrome. EHMs are identified in approximately 5 to 15% of cases at the time of diagnosis, with detection rates rising due to advancements in imaging and prolonged survival. The lungs are the most frequently involved site (55–60%), followed by bones (30–40%), lymph nodes, and adrenal glands.[2–5]

Pathophysiology of Extrahepatic Spread

HCC spreads beyond the liver through hematogenous routes, lymphatic dissemination, and direct extension. Besides more common sites, HCC can metastasize to rare sites like the rectum, spleen, esophagus, pancreas, and urinary bladder.

Improvements in imaging (CT, magnetic resonance imaging, PET-CT) have enhanced detection of small-volume EHM and atypical sites, prompting reassessment of their true incidence.[6,7,9,10] EHMs of HCC have been reported to occur in 5 to 15% of patients. The presence of metastases beyond the liver generally indicates a poor outcome, with median survival typically falling below 1 year.[3,7,8]

Oropharyngeal Metastases: An Atypical Presentation

Metastatic involvement of the oral cavity and oropharynx from primary cancers elsewhere in the body is extremely rare, contributing to only 1 to 2% of all oral malignancies. In men, such secondary tumors most commonly originate from the lungs, kidneys, or prostate, while in women, they typically arise from the breast or female reproductive organs. The mechanism of most oral/oropharyngeal metastases is through hematogenous dissemination.[9] Studies have shown that one-fourth of the oral metastases had been found before the primary tumors diagnosis.[11] Clinically, such lesions may mimic benign conditions presenting as soft tissue masses, ulcerations, or symptoms like foreign body sensation, pain, bleeding, and dysphagia. In nearly 25% of cases, the oral lesion precedes the diagnosis of the primary tumor (►**Table 1**).[7,9,12,13]

Diagnostic Challenges

Diagnosing tonsillar metastasis is challenging due to nonspecific symptoms and resemblance to benign tonsillar pathology (e.g., hypertrophy, infection, abscess). Definitive diagnosis relies on tissue biopsy. Histologically, metastatic HCC often presents as poorly differentiated malignant cells with trabecular architecture. Immunohistochemical (IHC) markers including HepPar-1, glypican-3, arginase-1, and AFP expression support hepatic origin.[13–15] Although tonsillar metastasis from HCC is exceedingly rare, one possible mechanism involves the opening of portosystemic anastomoses in advanced liver disease. These shunts, particularly connections to Batson's venous plexus, can allow hematogenous spread of tumor cells to the head and neck region, bypassing the pulmonary circulation. This hypothesis has been proposed in a few case reports that describe similar pathways leading to tonsillar involvement in HCC patients.[16–18]

Clinical Relevance

Prognosis for EHM in HCC remains generally poor, with median overall survival of 5 to 12 months.[4,6,7] And the survival is influenced by performance status, tumor burden, portal vein thrombosis, AFP levels, and therapeutic interventions.[5,6]

Our patient, a 77-year-old male with known chronic liver disease, presented with a seemingly benign symptom—foreign body sensation in the throat. The left tonsillar lesion, initially suspected to be an inflammatory or infectious pathology, was ultimately confirmed to be a metastatic deposit of poorly differentiated HCC, as evidenced by histopathology and strong HepPar-1 immunopositivity. This highlights the importance of considering a wide range of possible diagnoses when evaluating unusual lesions in the oropharynx, particularly in individuals with a history of liver disease or existing hepatic tumors.

The present case report adds to the limited but growing body of evidence on rare metastatic presentations of HCC, similar study stated the diagnostic challenge and the vital role of IHC staining with HepPar-1 to confirm hepatic origin.[18] In another study, a foreign body sensation led to tonsillectomy and subsequent diagnosis of HCC metastasis, with the lesion initially mimicking benign tonsillitis.[19] These case reports parallel our patient's presentation, in whom a left tonsillar lesion was the first clinical sign of advanced HCC, again confirmed via HepPar-1 positivity on IHC. Together, these cases emphasize the importance of including metastatic disease in the differential diagnosis of atypical oropharyngeal masses, particularly in elderly patients with chronic liver disease. Similarly, other studies presented a case where the patient's symptoms mimicked benign tonsillitis, with the final diagnosis of HCC confirmed post-tonsillectomy through immunohistochemistry. These parallels with our current study.[20–22] The rarity of metastasis to uncommon oral sites may lead clinicians to misidentify metastatic lesions as primary oral tumors, potentially delaying accurate diagnosis and timely treatment. Therefore, in oral/oropharyngeal growth, the remote possibility of secondaries from primaries elsewhere has to be considered as a differential diagnosis, thereby helping in to focus and identify the uncommon metastasis sites for patient's overall well-being and timely treatment.

Strengths and Limitations

The strength of this case lies in documenting an exceptionally rare site of metastasis from HCC, adding to the very limited published literature on tonsillar involvement. It highlights the diagnostic challenge when atypical oropharyngeal lesions mimic benign or primary head-and-neck pathologies. However, as with all case reports, the limitation is that findings are based on a single patient and cannot be generalized to all individuals with HCC. Lack of genetic or molecular profiling in this patient further limits mechanistic understanding of unusual metastatic patterns.

Generalizability

Although this is a single case, the report emphasizes the clinical relevance of considering primary or metastatic malignancy in elderly patients with chronic liver disease presenting with atypical oropharyngeal masses. The principle of maintaining diagnostic suspicion and the role of histopathology and immunohistochemistry can be generalized to similar clinical settings.

Future Research Directions

Further multi-institutional case series and registries are warranted to document rare metastatic sites of HCC. Studies

integrating genomic and molecular analyses could provide insights into pathways enabling unusual metastatic spread, such as to the tonsils. Additionally, long-term evaluation of systemic immunotherapy in patients with atypical metastatic presentations could help refine treatment protocols.

Gray Areas for Further Study

The exact mechanisms underlying tonsillar metastasis from HCC remain unclear. Whether vascular shunts (e.g., through Batson's plexus) or other pathways contribute predominantly requires further exploration. Moreover, optimal surveillance strategies for early detection of atypical metastatic sites remain undefined. Clarifying these gray areas could improve patient outcomes by guiding earlier diagnosis and tailored therapy.

Conclusion

Our case demonstrates an atypical presentation of HCC as tonsillar mass in a patient with chronic liver disease. We highlight the importance to rule out EHM at uncommon sites. Despite unusual presentation, our patient was able to receive a timely diagnosis and early treatment with an excellent PFS.

Data Availability Statement

The data for the current study are available from the corresponding author on reasonable request.

Authors' Contributions

A.F.: Concept, data collection, and manuscript writing. B.T.: Case management, review, and editing. U.S.P.: Conceptual guidance and manuscript review. T.B.: Oncology input and literature review. D.J.: Histopathology and immunohistochemistry analysis.

Patient's Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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None.

Conflict of Interest

None declared.

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