Uncommon Sites of Hepatocellular Carcinoma Metastasis: A Systematic Review of Salivary Gland Involvement

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INTRODUCTION / BACKGROUND

Hepatocellular carcinoma (HCC) is a leading cause of cancer-related mortality. While liver transplantation offers curative potential, recurrence occurs in up to 20% of recipients, typically within two years and often involving the lungs, bone, or lymph nodes. Metastasis to the salivary glands—especially the parotid—is exceedingly rare and may mimic benign tumors, delaying diagnosis. Diagnostic tools like FNAB are often inconclusive, and surveillance strategies rarely include the head and neck. This systematic review synthesizes all known cases of salivary gland metastasis from HCC and presents the first reported case in a liver transplant recipient.

OBJECTIVES / AIMS

- Review published cases of HCC metastasis to salivary glands.
- Describe clinical presentation, diagnostics, treatment, and outcomes.
- Highlight the first reported case of parotid metastasis following liver transplantation.

RESULTS

Figure 1. PRISMA Diagram

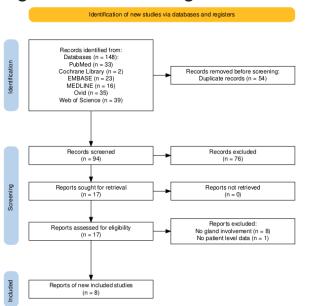


Table 1. Summary of Cases

Findings:

- Total studies included: 9 (1991–2025)
- All patients were male; median age: 64 (range: 36-82)
- Most common gland involved: Parotid (8/9 cases)
- Most common symptom: Nontender swelling or mass (6/9)
- Median time to metastasis (metachronous cases): 2.5 years
- FNAB was diagnostic in only 2 of 8 cases
- Surgical resection performed in 6 of 9 cases
- Median survival: 6 months; 1-year survival: 33%

| Author | Gland | Metastasis Timing | Symptoms | Surgical Treatment | Outcome |
|------------------|---------------|---------------------------|--------------------|---------------------------|-------------------|
| Morada (2025) | Parotid | Metachronous (2.5 Years) | Tender swelling | Parotidectomy | 13 mo (mortality) |
| Deng (2021) | Submandibular | Metachronous (8 Years) | Tender swelling | Resection + Flap | 6 mo (mortality) |
| Aiyer (2019) | Parotid | Synchronous | Nontender mass | None | Not Reported |
| Elzouki (2014) | Parotid | Synchronous | Tender swelling | None | 2 mo (mortality) |
| Yu (2013) | Parotid | Metachronous (0.66 Years) | Nontender swelling | Parotidectomy | 12 mo (survival) |
| Zhang (2017) | Parotid | Synchronous | Nontender mass | Parotidectomy | 10 mo (survival) |
| Zeng (2012) | Parotid | Synchronous | Nontender mass | Superficial Parotidectomy | 24 mo (survival) |
| Dardick (1991) | Parotid | Synchronous | Nontender swelling | Parotidectomy | 8 mo (mortality) |
| Yamashita (1991) | Parotid | Synchronous | Tender mass | Parotidectomy | 10 mo (survival) |

METHODS

Systematic review conducted in Nov 2024 per PRISMA quidelines. Databases: PubMed, EMBASE, MEDLINE, Cochrane, Web of Science, and Ovid. Inclusion: human studies reporting HCC metastasis to salivary glands. Two independent reviewers screened abstracts and full texts; discrepancies were resolved by consensus. Data extracted included demographics, presentation, diagnostics, treatment, and outcomes. Risk of bias assessed qualitatively due to case-based design.

CONCLUSIONS

Among the 9 cases reviewed, parotid gland metastasis was predominant, often presenting as painless swelling. FNAB frequently yielded inconclusive results, delaying diagnosis. Metachronous metastases showed slightly longer survival, especially when treated with surgery.

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