A Novel Case of Oropharyngeal Squamous Cell Carcinoma with Hypercalcemia of Malignancy

Ahmad Abdelhadi, BS[1]; Hallie R. Wilson, BS[1]; David Z. Allen, MD[2]; Kunal S. Jain, MD[2]

[1]The University of Texas Health Science Center At Houston, McGovern Medical School, Houston, TX

[2]Department of Otorhinolaryngology-Head and Neck Surgery, The University of Texas Health Science Center At Houston, Houston, TX

Introduction

- Humoral hypercalcemia of malignancy (HHM) is a paraneoplastic syndrome caused by tumor secretion of parathyroid hormone-related peptide (PTHrP), occurring in 2-30% of cancer patients with advanced disease[1,2]
- Most commonly seen in lung, kidney, and breast malignancies; in head and neck cancers documented in nasal cavity, oral cavity, larynx, and hypopharyngeal SCC[1]
- Clinical presentation: hypercalcemia, hypophosphatemia, normal-low PTH, elevated PTHrP with symptoms of fatigue, polyuria, polydipsia, and altered mental status[2]
- Poor prognosis: median survival of weeks to months despite aggressive treatment[2]
- We present the first documented case of PTHrP-mediated HHM in tonsillar SCC

Case Summary

Patient & History:

- Mid-60s male with tobacco history
- Stage IVB (cT3N3M0) p16-positive OPSCC treated with induction chemotherapy + concurrent chemoradiotherapy 11 months prior
- Complete clinical response at 5 months post-treatment

Initial ED Presentation (Recurrence):

- Progressive dysphagia, left-sided neck pain, visible neck mass
- CT/PET confirmed recurrent disease with 4.1 cm tonsillar lesion causing airway compromise
- Required emergent tracheostomy and gastrostomy tube placement

Laboratory Findings - First Admission:

- Hypercalcemia: serum Ca^{2+} 11.8 mg/dL, ionized Ca^{2+} 1.55 mmol/L
- Hypophosphatemia: phosphorous 2.3 mg/dL
- Normal PTH: 10.7 pg/mL
- Responded to IV hydration and phosphate supplementation

Second Admission (2 months later):

- Symptomatic severe hypercalcemia: serum Ca^{2+} 17.3 mg/dL, ionized Ca^{2+} 2.00 mmol/L
- Symptoms: muscle cramps, body aches, constipation, polyuria
- PTHrP markedly elevated at 3.2 pmol/L, confirming HHM diagnosis
- Suppressed PTH: 8.8 pg/mL

Treatment Course:

- IV hydration + calcitonin 200 units q12h → transient improvement
- One cycle carboplatin/paclitaxel (second cycle deferred due to bacteremia)
- Zoledronic acid 4 mg IV → temporary calcium reduction to 8.9-10.6 mg/dL\
- Refractory hypercalcemia persisted: ionized Ca^{2+} 1.90 mmol/L, PTHrP 2.9 pmol/L
- Denosumab 120 mg SC administered for treatment-resistant disease

Outcome:

- Persistent refractory hypercalcemia prevented effective cancer therapy
- Fatal hemorrhagic event from tumor bleeding one day post-denosumab
- Death attributed to inability to treat advancing underlying malignancy due to refractory HHM

Table 1. Treatment response and laboratory values demonstrating refractory hypercalcemia despite escalating anti-resorptive therapy. Red values = elevated.

Time Point	Treatment Administered	Serum Ca2+	Ionized Ca2+	PTHrP	Clinical Response
Initial Admission	**IV Hydration + Phosphate**	**11.8**	**1.55**	Not measured	Stable, discharged
2 Months Later	**IV Hydration + Calcitonin 200u q12h**	**17.3**	**2.00**	**3.2**	Transient improvement
3 Weeks Later	**Zoledronic Acid 4mg IV**	**14.4**	**1.90**	**2.9**	Temporary reduction
2 Weeks Post-Zoledronic	—	8.9-10.6	—	—	Brief normalization
1 Month Later	**Denosumab 120mg SC**	**10.5-13.6**	**1.67-1.87**	—	Refractory disease

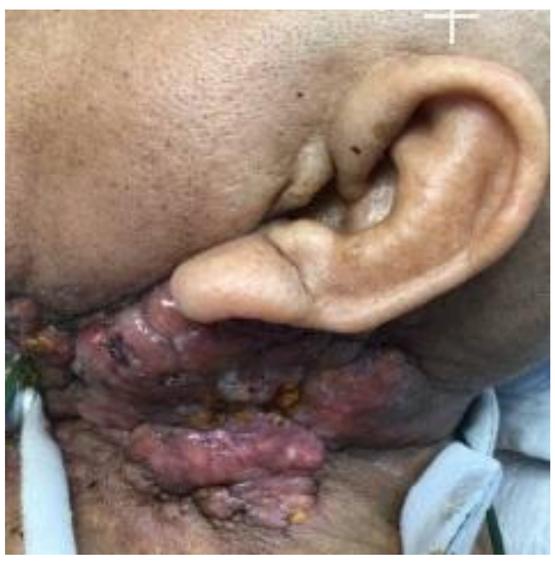

Figure 1. Extensive recurrent tonsillar SCC with external extension

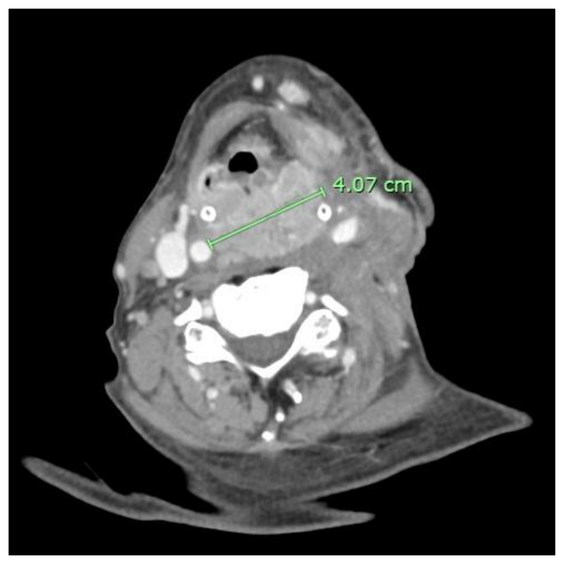

Figure 2. Axial CT showing 4.1 cm recurrent tonsillar lesion

Discussion

- First reported case of PTHrP-mediated HHM in tonsillar SCC - while HHM is documented in other head and neck SCCs (oral cavity 4.1% incidence, base of tongue), tonsillar occurrence not previously established[3]
- Stage IVB presentation aligns with established patterns; HHM cases arise with advanced disease, reflecting tumor burden required for clinically significant PTHrP production[4]
- Refractory hypercalcemia disrupts oncologic management - anticancer therapy discontinuation occurs in 26.9% of hypercalcemic vs. 4.3% of normocalcemic patients[5]
- Patient survival of 4 months from HHM diagnosis exceeds typical median (<2 months) but demonstrates tonsillar SCC follows same aggressive pattern as other head and neck subsites[6,7]
- HHM secondary to advanced malignancy became the primary clinical factor dictating treatment options and survival in this case

Conclusion

- This case represents the first documented case of HHM in tonsillar SCC
- Paraneoplastic manifestations such as HHM likely to occur with advanced disease course. Further investigation needed to determine prevalence.

Contact

Kunal S. Jain, MD
Department of Otorhinolaryngology - Head and Neck Surgery
UTHealth Houston - McGovern Medical School
6431 Fannin Street, Houston, TX 77030
Kunal.S.Jain@uth.tmc.edu | 713-500-5332

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