

A Case of Stage I HPV-Mediated Oropharyngeal Squamous Cell Carcinoma Detected Using a Multi-Cancer Early Detection Test

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INTRODUCTION

- There are no routine screening tests for head and neck (H&N) cancers beyond self exam or findings noted through routine oral exams in dental offices¹
- Oropharyngeal cancer, a type of H&N cancer, is a less common cancer that occurs in ~2.9 per 100,000 people each year in the US²
 - The 5-year relative survival for localized, regional, and distant stage oropharyngeal cancer is 83.1%, 77.8%, and 48.7%, respectively,² underscoring the need for early detection to maximize chances for long-term survival
- Risk factors for oropharyngeal cancer include smoking and human papillomavirus (HPV) infection³
 - 40–60% of oropharyngeal cancer cases are linked to HPV⁴
- A multi-cancer early detection (MCED) test (Galleri[®],* GRAIL, LLC, Menlo Park, CA) is available as a complement to existing single-cancer screening tests and as a screening option for cancers that do not have USPSTF-recommended or other screening⁵⁻⁷
 - This MCED test detects a shared cancer signal from abnormal methylation patterns of tumor cell-free DNA in blood using a targeted methylation assay and machine learning algorithm
 - When a cancer signal is detected, a ‘cancer signal detected’ result (positive result) is reported with 1 or 2 predicted cancer signal origin(s) (CSO)
 - Importantly, this test may detect cancers at a late stage or not detect a cancer at all as sensitivity of cancer signal detection for this MCED test was 51.5% in the Circulating Cell-free Genome Atlas (CCGA) study (NCT02889978)⁷

OBJECTIVE

- Here, a case of oropharyngeal squamous cell carcinoma (SCC) is presented to demonstrate early detection using the MCED test in the real world and to review the CSO-guided diagnostic journey following a ‘cancer signal detected’ test result

KEY RESULTS: THE MCED TEST DETECTED A CANCER SIGNAL AND PREDICTED CSO TO DIRECT DIAGNOSTIC EVALUATION OF A STAGE I HPV-MEDIATED OROPHARYNGEAL SCC

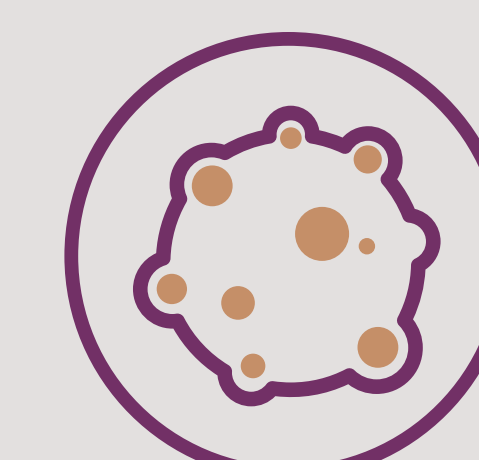
Asymptomatic, White Male
(Age, 74 y; BMI, 29.9 kg/m²)
With Cancer History



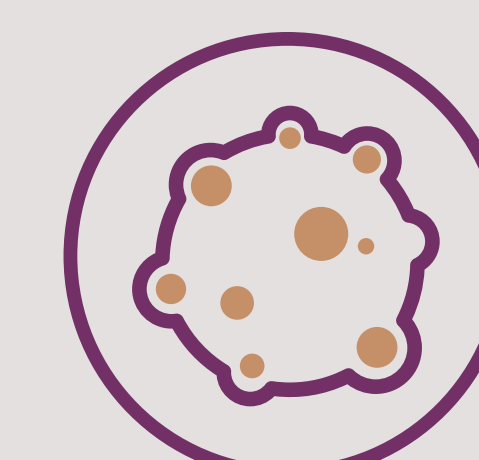
Asymptomatic Male



74 Years



CLL^a
(17 Years Prior)



Papillary Thyroid Cancer^b
(8 Years Prior)



Elevated PSA
(9–10 ng/mL)



Non-Smoker

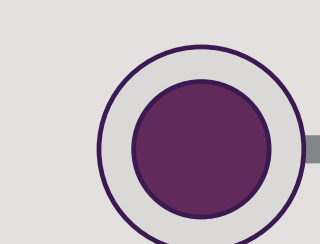


No Genetic Cancer Predisposition



CSO Prediction Was Correct

CSO1 = H&N
Diagnosis: Day 57
Oropharyngeal SCC

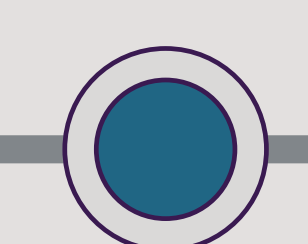


DAY 1

Cancer Signal Detected and Results Communicated

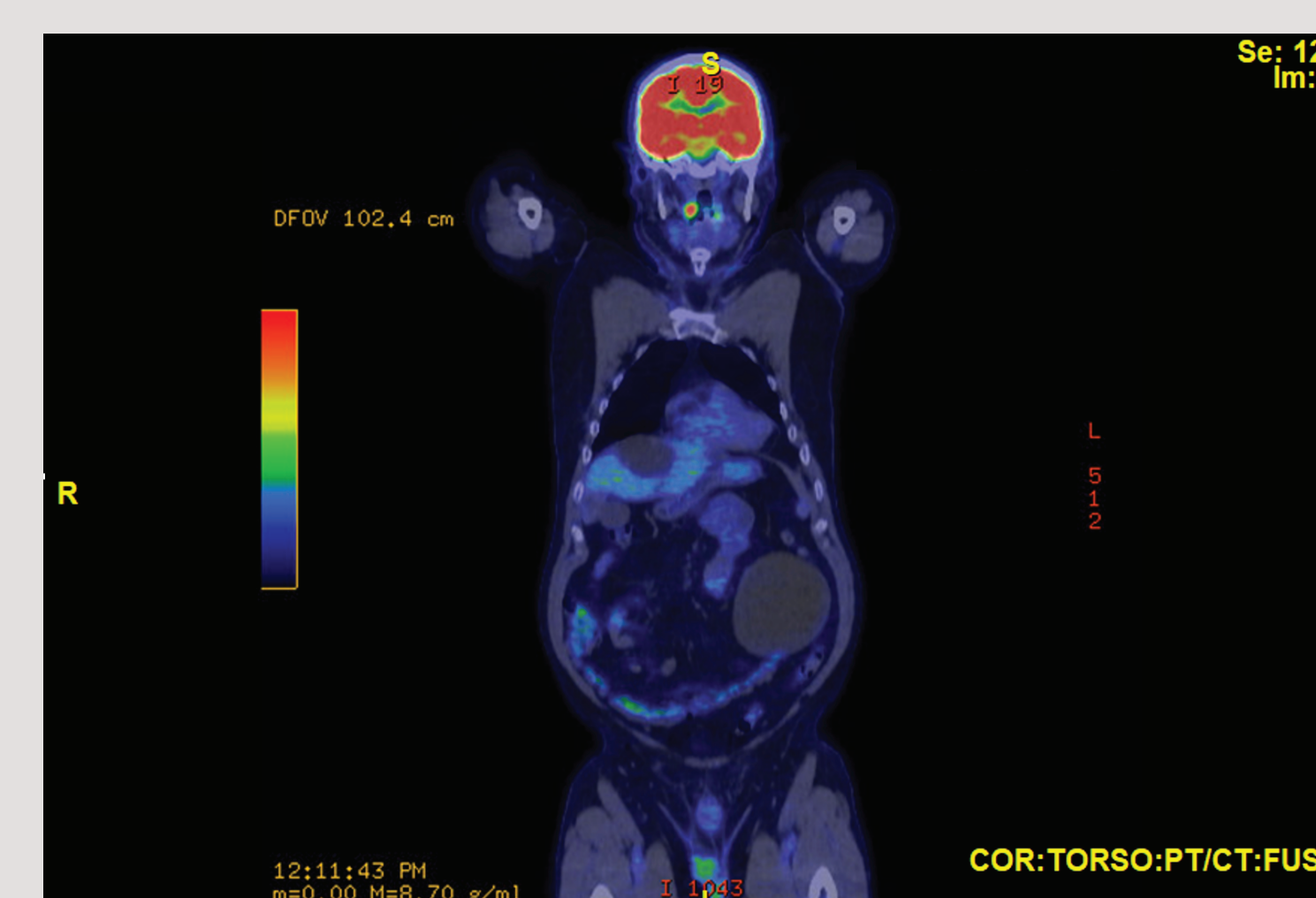


CSO1 = H&N



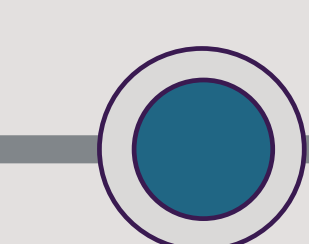
DAY 28

CBC/CMP and PET-CT



Clinical Notes

- Lab work showed elevated WBC count due to CLL
- PET-CT showed abnormal uptake in the right tonsil
- PET-CT considered as first confirmatory diagnostic test due to prior cancer history and elevated PSA



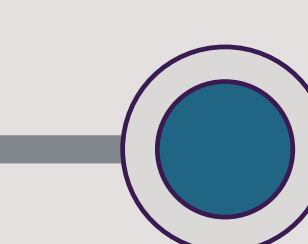
DAY 54

ENT Referral and Right Lymph Node Biopsy



Clinical Notes

- The biopsy showed presence of malignant cells



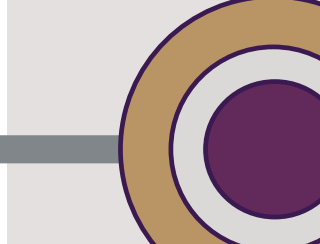
DAY 57

Right Tonsillectomy and Lymph Node Dissection



Clinical Notes

- Pathology report showed invasive moderately differentiated SCC, non-keratinizing, forming a 3x2.1x1.2 cm mass
- The surgical margins were negative for invasive or in situ carcinoma
- Distance from invasive tumor to closest margin: 5 mm
- 1 out of 27 lymph nodes involved
- The lymph node involved by tumor measured 3.2 cm (near totally replaced by the tumor)
- No extracapsular extension



DAY 57

Diagnosis

Diagnosis

HPV-mediated Oropharyngeal SCC, p16+, pT2, pN1, cMO (Stage I)

Treatment and Status

- No chemotherapy or radiation was required due to the early stage of detection
- Patient is currently at stable weight and is active (8 months follow-up)

BMI, body mass index; CBC, complete blood count; CMP, comprehensive metabolic panel; CSO1, top-predicted CSO; CLL, chronic lymphocytic leukemia; ENT, ear, nose, and throat; PET-CT, positron emission tomography–computed tomography; WBC, white blood cell; PSA, prostate-specific antigen.
^aRai stage 0; 13q, CD38, and ZAP-70 negative; no treatment was needed; monitored annually. ^bStage IVa; pT3N1bMO; thyroidectomy and radiation therapy; no recurrence.

SUPPORTING INFORMATION

Supporting Data

- In the CCGA study, an observational, multicenter, case-control study, sensitivity of cancer signal detection was 63.2% in stage I H&N cancer⁷ (Table S1)

Table S1. Sensitivity of Cancer Signal Detection in H&N Cancer by Stage

Clinical stage	Total	Test positive	Sensitivity (95% CI)
All	105	90	85.7% (77.8%–91.1%)
I	19	12	63.2% (41.0%–80.9%)
II	17	14	82.4% (59.0%–93.8%)
III	19	16	84.2% (62.4%–94.5%)
IV	50	48	96.0% (86.5%–98.9%)

CONCLUSIONS

- The MCED test detected a cancer signal and predicted an accurate CSO for an asymptomatic individual with stage I HPV-mediated oropharyngeal SCC
 - H&N cancer does not have USPSTF-recommended or other routine screening;¹ without the MCED test, this cancer may not have been detected until clinical presentation

- Notably, despite a history of CLL and thyroid cancer, and an elevated PSA level, the test accurately predicted CSO
 - This led to a directed workup diagnosing asymptomatic cancer in less than 2 months, while the cancer was still at stage I
- The use of this MCED test led to early detection of cancer and treatment (surgery without complications and without chemotherapy or radiation) with curative intent
 - Detection of a less common cancer in the real world by the MCED test is notable

References

- <https://www.cancer.org/cancer/oral-cavity-and-oropharyngeal-cancer/detection-diagnosis-staging/detection.html>
 - SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute. Accessed at <https://seer.cancer.gov/explorer/> on March 14, 2023.
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*The Galleri[®] test was developed and its performance characteristics were determined by GRAIL, LLC. The Galleri[®] test has not been cleared or approved by the Food and Drug Administration. GRAIL's clinical laboratory is regulated under Clinical Laboratory Improvement Amendments to perform high-complexity testing. The Galleri[®] test is intended for clinical purposes.

