Diagnostic Dilemma of Fine Needle Aspiration in Work-Up of p16+ OPSCC Unknown Primary Patients

Doreen Lam, BA [1,2]; Jalal Jalaly, MBBS, MS [3]; Devraj Basu, MD, PhD [2]; Steven B. Cannady, MD [2];
Ara A. Chalian, MD [2]; Karthik Rajasekaran, MD [2]; Gregory S. Weinstein, MD [2]; Robert M. Brody, MD [2]

[1]Perelman School of Medicine, University of Pennsylvania; [2]Department of Otorhinolaryngology-Head and Neck Surgery, University of Pennsylvania
[3]Department of Clinical Pathology and Laboratory Medicine, University of Pennsylvania

Introduction

Oropharyngeal squamous cell carcinoma (OPSCC) of unknown primaries present providers with a diagnostic dilemma. As with other suspected head and neck (H&N) cancers, fine needle aspiration (FNA) is the preferred method for initial work-up of suspicious lesions. While sensitivity of FNA for diagnosis of OPSCC can range from 80-92%, rates of nondiagnostic FNA results may be as high as 26.4%[1,2].

Morse et al., previously found that non-diagnostic FNA biopsies led to a delay in radiation initiation (mean delay = 58 days, p = 0.024)[2]. Delays in definitive treatment for p16+ OPSCC can lead to disease advancement and impaired prognosis. Brouha et al. estimated that a 30 day delay in leads to increased odd ratio of later stage (T3/4) disease (OR: 4.5; p = 0.01)[3]. To date, there have been no studies investigating the impact of non-diagnostic FNA biopsies on time to definitive surgical treatment in patients with OPSCC of unknown primaries.

In this study, we characterize sensitivity of FNAs in OPSCC diagnosis, review diagnostic methods in the work-up of unknown primaries, after nondiagnostic results and assess impact on time to treatment.

Methods

A retrospective cross-sectional study was performed on p16+ OPSCC of unknown primary patients treated with primary transoral robotic surgery (TORS) between October 2011 and June 2022 at the University of Pennsylvania Health System.

Patients were identified via CPT codes from the electronic medical record, and patients with p16+ SCC confirmed by pathology were included. Demographics, work-up details, surgical history and pathology results were abstracted via chart review. FNA results were categorized as "definitive SCC" diagnosis, "nondiagnostic or benign", or "suspicious but non-diagnostic". Analysis was performed in R Studio.

Results

137 patients met inclusion criteria (80% Male, 88% White). 121 (88%) patients underwent an initial FNA (Figure 1). Of those, 70 (58%) FNAs were positive for SCC, 34 (28%) suspicious but inconclusive, and 17 (14%) nondiagnostic. 41 (34%) underwent p16 staining.

SCC diagnosis after nondiagnostic or suspicious FNAs were made via excisional lymph node biopsy (49%), repeat FNA (29%) or core needle biopsy (10%). 10% underwent unknown primary TORS after suspicious FNA and PET findings without further biopsies. 2% were ultimately diagnosed with presumed HPV-associated OPSCC via positive circulating tumor HPV DNA assay after nondiagnostic FNA results and benign excisional biopsy pathology.

Kruskal-Wallis rank sum test showed nondiagnostic FNAs led to delayed first H&N surgeon appointment when compared to definitive or suspicious results (median = 58 vs 15, 19 days; p = < 0.001) and TORS (98 vs 38, 60; p = < 0.001), with no difference in time between H&N consultation and definitive surgery.

Figure 1: Diagnostic Methods of Unknown Primary SCC Diagnosis

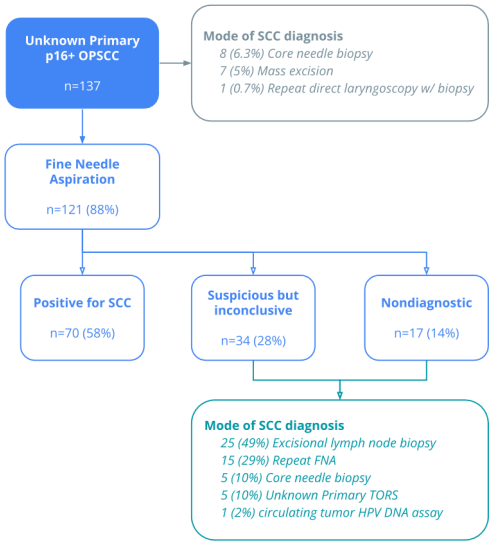

Table 1: Impact of Initial FNA Results on Time to SCC Diagnosis & Patient Care

	Positive	Suspicious but Nondiagnostic	Nondiagnostic	p-value
Days from FNA to first H&N appt	15 (9-22)	19 (9-55)	58 (27-79)	**<0.001**
Days from FNA to SCC diagnosis	—	29 (9-43)	33 (16-68)	**<0.001**
Days from FNA to first TORS	38 (26-50)	58 (32-90)	98 (47-127)	**<0.001**
Days from first H&N appt to TORS	22 (13-29)	19 (13-36)	32 (15-44)	0.3

Discussion

Obtaining definitive SCC diagnosis via FNA in patients with unknown primary tumors can be challenging, with 58% sensitivity observed in our study. Our review found excisional lymph node biopsy was the most common diagnostic method to confirm a SCC diagnosis following nondiagnostic or suspicious FNAs. Interestingly, compared to suspicious FNAs, nondiagnostic FNAs led to significant delays in H&N referral and TORS by an additional 39 and 38 days.

Because initial FNAs are often performed by general otolaryngologists, our findings highlight a need to identify and validate more sensitive methods of diagnosis, and to develop protocols for timely management of patients for whom clinicians have a high index of suspicion for OPSCC. Further studies are warranted to assess whether treatment delays have a clinically significant impact on patient prognosis or outcomes.

Contact
Doreen Lam, BA
Medical Student, Year 4
doreen.Lam@pennmedicine.upenn.edu

Affiliations
Department of Otorhinolaryngology—Head and Neck Surgery
Perelman School of Medicine
University of Pennsylvania, Philadelphia, PA, USA

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