Navigating Diagnostic pitfalls: Understanding Risks in Misclassifying Cystic Neck Masses in the Era of HPV-Associated Oropharyngeal Cancer-A Case Study.

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Introduction

The diagnostic landscape for HPV-associated oropharyngeal squamous cell carcinoma (SCC) has undergone transformative shifts, necessitating a critical evaluation of diagnostic protocols. This case study aims to explore the complexities surrounding the differentiation between cystic nodal metastases and benign branchial cleft cysts, highlighting the implications of misdiagnosis and emphasizing the need for enhanced diagnostic accuracy and adherence to existing national guidelines in management of cystic neck masses.

Significance/Uniqueness of the Case

Understanding the nuances of diagnosing HPV-related oropharyngeal SCC is pivotal, given its distinct clinical manifestations compared to traditional head and neck cancers. Misdiagnosis not only poses significant clinical challenges but also jeopardizes patient outcomes, leading to delayed interventions, disease progression, increased metastatic potential, and the risk of inadvertent tumour spillage. This study underscores the critical importance of accurate diagnostics in optimizing therapeutic strategies and improving patient prognosis.

Objectives/Hypothesis:

The primary objective of this study is to dissect cases of delayed HPV-OPC diagnosis after initial misdiagnoses of benign branchial cleft cyst or inconclusive evaluations. We hypothesize that HPV-OPC may manifest unique growth patterns and clinical trajectories, necessitating refined diagnostic protocols and enhance clinical vigilance.

Incidence:

In 2012, the GLOBOCAN estimates indicated approximately 142,387 new cases of “other pharyngeal” cancer worldwide, with varying rates across regions. The highest age-standardized rate (ASR[W]) for "other pharyngeal" cancer was observed in the WHO South-East Asia region (3.6 per 100,000) (Chi et al., 2015).

The American Cancer Society projected 45,780 new cases of oral cavity and pharyngeal cancer in 2015, with a median age at diagnosis of 62.0 years and an age-adjusted incidence of 11.0 per 100,000 (Chi et al., 2015).

Oropharyngeal cancer incidence has been increasing in numerous developed nations over recent decades. For instance, in the US, there was an annual percentage change (APC) of 3.0 for SEER 9 areas from 1999 through 2012 (Chi et al., 2015). Furthermore, studies have shown increasing prevalence rates over different time periods, indicating a rising trend in the incidence of OPSCC (Stein et al., 2014).

Etiology

Human papillomavirus (HPV) has emerged as a significant etiological factor for oropharyngeal squamous cell carcinoma (OPSCC). HPV, particularly types 16 and 18, has been implicated in a substantial proportion of oropharyngeal cancers globally (Wittekindt et al., 2019).

HPV-related OPSCC has distinct molecular and clinical features compared to HPV-negative tumors. Patients with HPV-associated OPSCC generally exhibit a better prognosis. However, the current treatment approach does not differentiate based on HPV status, prompting considerations for treatment de-escalation in clinical trials (Wittekindt et al., 2019; Chi et al., 2015).

Historically, risk factors for HNSCC, including OPSCC, were tobacco and alcohol use. However, the emergence of HPV as a causative agent indicates a shift, with HPV-positive OPSCC patients having different risk profiles such as multiple sexual partners and early age of sexual activity (Stein et al., 2014).

Rising OPSCC incidence in certain developed countries, especially among younger individuals, is attributed to changing sexual behaviours and HPV infections. The introduction of HPV vaccination for young females aims to reduce cervical cancer and could potentially lead to a decline in OPSCC incidence (Van Monsjou et al., 2010).

Case History

A 55-year-old male presented with right neck lump to his GP. Ultrasound reported 2nd Branchial cleft cyst. The GP assumed its benign with no further follow up required.

4-months later, patient presented again to the GP with increase in the lump size.

Patient was then referred to ENT with CT and PET scan performed. Findings demonstrated a right tonsillar mass (high uptake on PET scan) with right level II cystic lesion.

FNAB of the cystic lesion revealed a squamous cell carcinoma with positive P16.

Diagnosis of T2N1M0 oropharyngeal SSC was made. Patient was subsequently referred for radiotherapy and chemotherapy.

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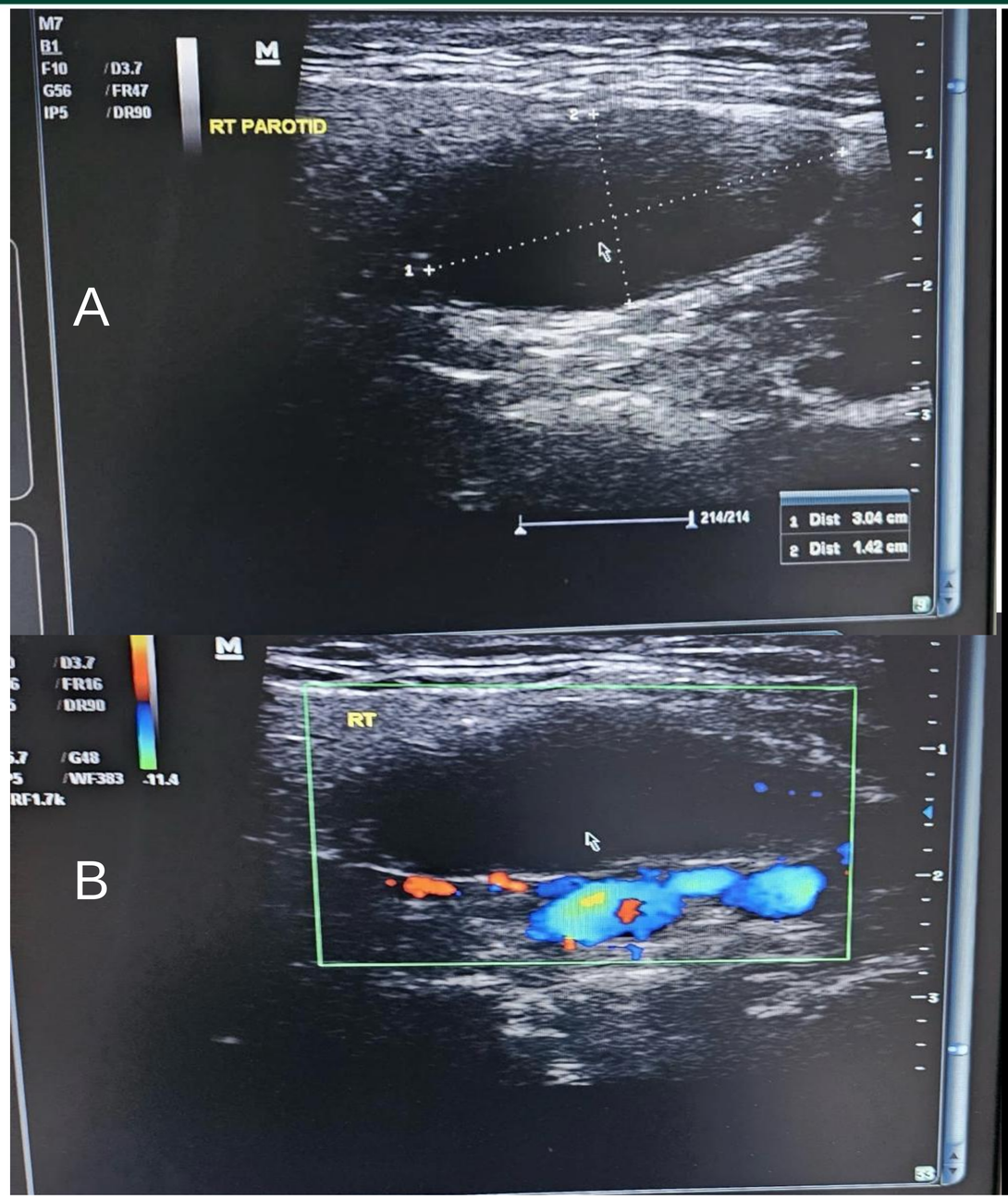

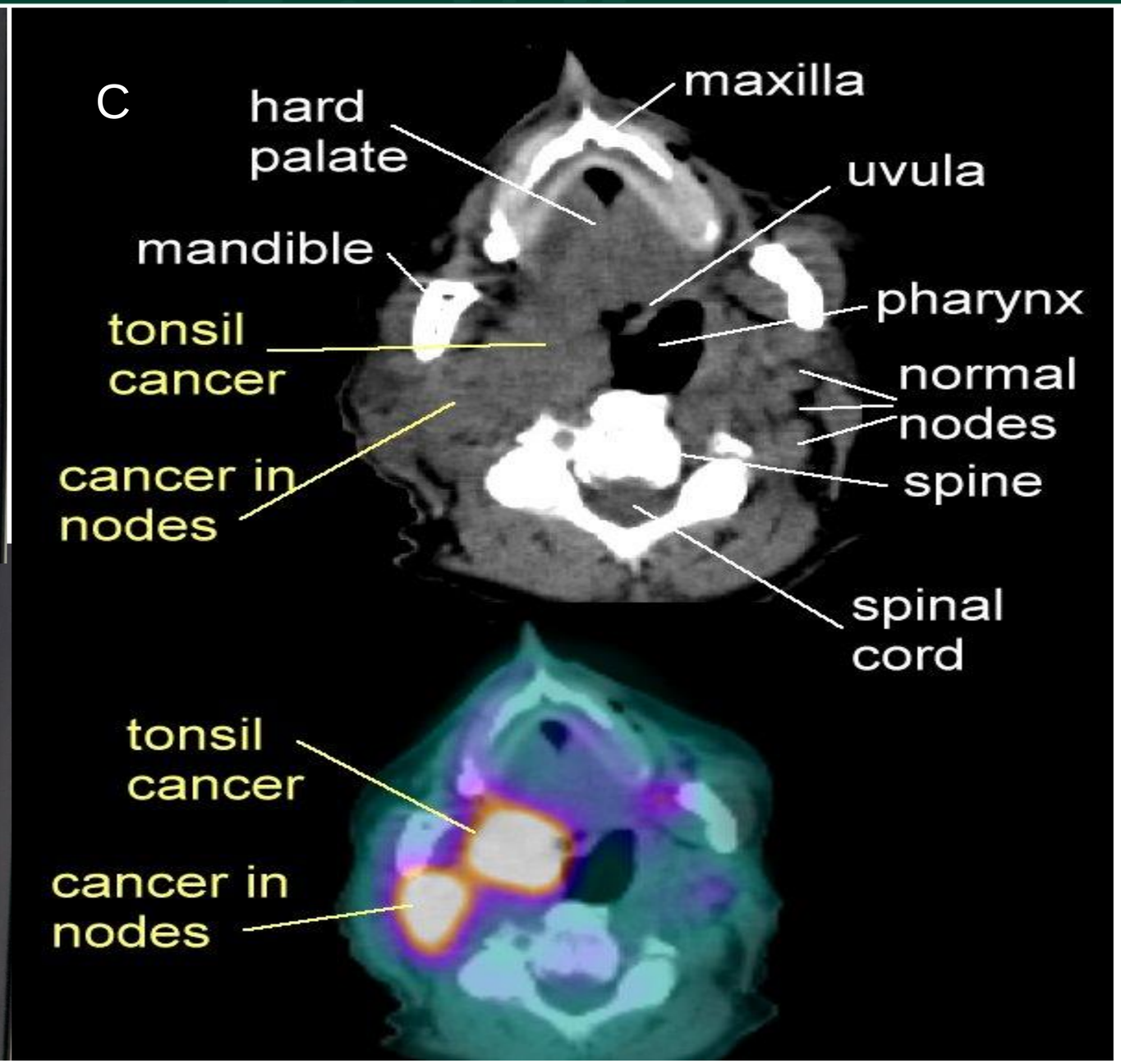

Fig. A and B: Ultrasound sections of the right neck Level II cystic lesion, appearing oval, thin walled and avascular. Small area of the parotid gland seen adjacent. C: Online image (PET and CT Scans (aboutcancer.com)) PET obtained for the purpose of this presentation; high uptake noted within the tonsil and the cervical node.

Discussion

In the context of HPV-associated oropharyngeal cancer, misclassifying cystic neck masses introduces significant diagnostic challenges that can adversely impact patient outcomes, leading to detrimental delays in treatment, further disease progression, and an increased potential for metastatic spread (Goyal et al., 2012; Pietarinen-Runtti et al., 2010). Notably, distinct demographic patterns emerge between branchial cleft cysts, commonly observed in younger adults, and cystic nodal metastases, which predominantly manifest after the age of 40, where 44% are malignant (Goyal et al., 2012; Pietarinen-Runtti et al., 2010). While CT serves as a cornerstone for diagnosis, its limitations in discerning benign from malignant cystic lesions due to overlapping radiological features are evident (Pietarinen-Runtti et al., 2010).

Amidst these challenges, FNAB cytology offers a diagnostic avenue, albeit fraught with limitations, particularly for cystic lesions where reported sensitivities fluctuate between 33% to 55%, accompanied by a concerning false-negative rate (Gourin & Johnson, 2000; Pisharodi, 1997). Despite its drawbacks, advancements in molecular analysis, including the detection of HPV DNA and thyroglobulin within aspirates, provide promising avenues for enhancing diagnostic precision, especially in discerning HPV-related oropharyngeal SCC and thyroid cancer (Zhang et al., 2008; Li et al., 2013). Given these intricacies, a holistic diagnostic strategy integrating CT, FNAB, and specialist consultations emerges as imperative for optimizing diagnostic accuracy and patient outcomes.

Conclusion

The diagnostic landscape for HPV-associated oropharyngeal squamous cell carcinoma (SCC) underscores the critical need for meticulous evaluation and adherence to national guidelines. This case study illuminates the complexities in distinguishing between benign branchial cleft cysts and cystic nodal metastases, emphasizing the grave consequences of misdiagnosis. With the rising incidence of HPV-related OPSCC and its distinct clinical manifestations, there's an imperative shift toward refining diagnostic protocols. The presented case highlights the potential pitfalls of relying solely on ultrasound and underscores the value of integrating CT scans, FNAB cytology, and molecular analyses for optimal diagnostic accuracy. Enhancing diagnostic precision is paramount, not only to ensure timely therapeutic interventions but also to improve patient outcomes and prognosis in the evolving landscape of oropharyngeal cancers.

References

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