

Carcinoma of Unknown Primary: Improved Ways to Manage Patients

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Carcinoma of unknown primary (CUP) is a cervical lymph node metastasis without an identifiable mucosal malignancy. This disease was first described by Hayes Martin in 1944, and recently the incidence of CUP has increased in the past decade due to the rise of HPV-associated oropharyngeal malignancies. Most HPV-associated squamous cell carcinomas now present with a neck mass found to be a regional lymph node metastasis.¹ While many patients are treated with wide-field radiation, these individuals have the greatest potential benefit of deintensified treatment for their small mucosal malignancies. When a primary mucosal cancer is identified, people are frequently amenable to minimally invasive surgical excision and reduced adjuvant treatments.

Diagnostic Testing

- **Fine needle aspiration (FNA)** of the neck mass is the initial diagnostic procedure of choice to confirm tissue diagnosis. This is an efficient, minimally invasive, and cost-effective technique with negligible risk of seeding tumor cells along the needle track. Ultrasound-guided FNA is an alternative technique for cystic neck masses with inconclusive initial tissue samples.
- **Open cervical lymph node biopsy** should be reserved after failed attempts of FNA.
- **Contrast-enhanced anatomic imaging (CT or MRI)** is effective at detecting the extent of

cervical lymph node metastasis and possibly identifying occult mucosal primaries.

- **Positron Emission Tomography (PET)/CT** is a useful tool to aid in identifying hyper-metabolic areas in the aerodigestive track. PET/CT improves detection rates of mucosal primaries during endoscopy; however, PET/CT findings should be cautiously reviewed due to the high rate of false positives found in the palatine tonsils and base of tongue.

Surgical Diagnostic Tools

The initial goal of managing patients with the CUP is to identify the occult malignancy. Successful identification of the primary improves oncologic outcomes and reduces treatment-related side effects.

- Over 90 percent of primaries that are found originate in the tonsil and base of tongue. However, these oropharyngeal subsites are notoriously difficult to examine due to their cryptic structures.
- **Transoral robotic surgery (TORS)** has been successful in improving detection rates up to 80 percent.² Excisional biopsies of the palatine tonsil, glossotonsillar sulcus, and lingual tonsils are able to identify and excise small mucosal cancers. After surgery, patients are able to return home on an oral diet without the need for a feeding tube.

- During the same surgical session as the TORS procedure, the patient often undergoes a therapeutic neck dissection to remove the regional lymph node metastasis.

Improving Treatment-related Morbidity

Current treatment recommendations by the National Comprehensive Cancer Network (NCCN) for CUP advocates for radiation to at risk mucosal sites, which often results in wide-field radiation to the entire pharyngeal axis. This treatment given with concurrent chemotherapy frequently results in mucositis requiring stomach tube placement and esophageal strictures in as many as 59 percent of patients.³

However, the TORS-assisted approach to the CUP has shown significant improvement in identifying these occult cancers and potentially reducing treatment-related side effects. This novel approach has reduced the rate of radiation and chemotherapy for individuals presenting with this disease. Patients with a tiny cancer identified during TORS are frequently excellent candidates to undergo definitive resection of their cancer. The reported rates have found that among patients presenting with CUP:

- 25 percent avoid radiation and chemotherapy altogether
- 67 percent will not require chemotherapy

References

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