

## Carcinoma of Unknown Primary-Where Does PET-CT Stand

Manas Kumar Sahoo<sup>1\*</sup> and Mudalsha Ravina<sup>2</sup>

<sup>1</sup>Division of Nuclear Medicine, Thyroid Care & PET/CT, Add Annex Health Care Pvt. Ltd, India

<sup>2</sup>SRIMS FIMC, India

**\*Corresponding author:** Manas Kumar Sahoo, Division of Nuclear Medicine, Thyroid Care & PET/CT Centre, Add Annex Health Care Pvt. Ltd, College Square, Cuttack, Odisha-753003, India, Tel: +91-9013590865; Email: drmkshoo@gmail.com

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# Medical Case Reports and Images

Carcinoma unknown primary (CUP) at times referred to as CUP syndrome has always been a diagnostic challenge to the oncologist. In view of ever increasing clinical applications of PET-CT in oncology, there is a need of discussing, role of PET-CT in occult primary. Cancer of unknown primary sites, (CUP) or occult primary tumors, is not rare, accounting for approximately 2% of all malignancies diagnosed in the United States to the seventh to eighth most frequently occurring cancer in the world. Most of the CUP cases are limited to epithelial and undifferentiated malignancies. The cases have been on an increasing trend since the past decade, due to increasing awareness, advances in immunohistochemistry (IHC) and imaging modalities.

The question remains why they undetectable or at least are difficult to detect. There are various theories like regression of the primary lesion, inability to induce neoangiogenesis and many more. Its pathologist's nightmare and an oncologist's therapeutic dilemma. The need of the day is a multidisciplinary approach involving oncologist, pathologist nuclear medicine physician and radiologist in diagnosing this condition. The diagnostic algorithm includes mainly age, gender, histology, site of metastasis, distribution and natural history of disease, and expression of tissue specific markers by the malignant clones as revealed on immunostains, e.g. TTF-1 for thyroid gland and adenocarcinoma lung, PSA for prostate gland, estrogen/ progesterone receptors and gross cystic disease fluid protein-15 for breast cancer, etc. Despite extensive and expensive diagnostic work up, in almost 20-45% cases the site of their origin remains unknown.

The treatment of CUP syndrome has evolved over time from non specific protocols to disease specific protocols and surgery. So the correct and accurate delineation of the primary site is needed, in cases where surgical or specific treatment is planned. However, PET-CT can not be used as a screening test. Its main role is in defining the primary disease and disease extent, since they may derive substantial benefit, including prolonged survival, from directed treatment.

Various prospective studies and meta analysis reveal variable sensitivity and specificity of PET-CT ranging from 30-90%. In our experience the sensitivity and specificity is as high as 80% due to advances in recent PET scanners with increasing resolution of 4.5 mm and use of contrast protocols.

Keeping in mind that if it is a metastatic squamous cell carcinoma, the primary is found in the head and neck region in the majority of cases, barring a small number originating from nasal cavity, paranasal sinuses and salivary glands. Metastatic adenocarcinoma most often originates in a primary tumor below the clavicles, such as in the lung, the gastrointestinal (GI) tract, the genito-urinary (GU) tract, breast, and pancreas.

In our experience regarding CUP syndrome, a specific and case to case type approach should be followed for improving diagnostic accuracy. As a diagnostic CT along with PET will definitely be a superior choice over a low dose CT with PET.

Also special protocols should be adopted in different cases like triphasic protocol in patients with suspected hepatobiliary malignancy. PET-CT may be performed in patients with deranged renal parameters where PET with non contrast CT may be done. PET helps not only identifying the primary disease, but also provides information regarding disease extent, suitable target site for biopsy, areas with necrosis. Further in head and neck CUP syndromes it helps in planning radiation therapy in certain cases.

The idea of the editorial is to highlight and draw an attention on true indications of PET-CT in CUP syndrome. PET-CECT can play an integral role in the multidisciplinary diagnostic evaluation of patients with occult primary sites. In our experience we have observed that PET-CECT after doing exhaustive investigations might save both cost and time in diagnosis and initiation of treatment of the patient.