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Evaluation of the Role of PET-CT in Identifying Primary Tumors in Patients with Cancer of Unknown Primary: A Retrospective Analysis of 30 Cases

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ABSTRACT
Cancer of unknown primary (CUP) presents a diagnostic challenge due to the absence of an identifiable primary tumor site. PET-CT has emerged as a significant imaging modality in the search for primary tumors in such cases. This study aims to evaluate the effectiveness of PET-CT in detecting primary tumors in patients with CUP. This retrospective observational study included 30 patients diagnosed with CUP who underwent PET-CT imaging. Patients were selected based on the presence of metastatic cancer with no identifiable primary site after standard workup. PET-CT imaging followed a standardized protocol and follow-up data were analyzed to assess the final diagnosis of the primary site. Image analysis was conducted by experienced radiologists and statistical methods were employed to determine the detection rate and other relevant metrics. PET-CT successfully identified the primary tumor in 24 out of 30 cases, resulting in a detection rate of 80%. The primary tumors were most frequently found in the lungs (16.7%) and pancreas (12.5%). Among the 6 cases where PET-CT did not initially detect the primary site, follow-up investigations revealed the primary tumor in 2 cases (33.3%). However, 4 cases (66.7%) remained undetected despite extended follow-up. Characteristics of undetected cases included older age and persistent CUP. PET-CT is an effective tool for detecting primary tumors in patients with CUP, with an 80% detection rate. It effectively identifies tumors in a variety of organs, yet 20% of cases remain undetected initially and 66.7% of follow-up cases continued to show no primary site. This underscores the need for complementary diagnostic methods and extended follow-up to improve detection rates and patient management. Further research is encouraged to enhance diagnostic strategies for CUP.

INTRODUCTION

Aims and Objectives:

Aim: To evaluate the effectiveness of PET-CT in detecting primary tumors in patients diagnosed with cancer of unknown primary (CUP).

Objectives:
- To determine the detection rate of primary tumors using PET-CT in patients with CUP.
- To identify the anatomical distribution of primary tumors detected by PET-CT.
- To assess the follow-up outcomes in cases where the primary site was not initially identified by PET-CT.
- To analyze the characteristics of cases where the primary tumor site remained undetected.

MATERIALS AND METHODS

Study Design: This retrospective observational study was conducted to assess the utility of PET-CT in identifying primary tumors in patients with cancer of unknown primary (CUP). The study was approved by the institutional review board and patient consent was obtained where necessary.

Patient Selection: A total of 30 patients with a diagnosis of CUP were included in this study. The inclusion criteria were as follows:
- Patients with a confirmed diagnosis of metastatic cancer with no identifiable primary site after initial standard workup (including clinical examination, imaging studies and biopsy).
- Patients who underwent PET-CT imaging as part of their diagnostic or staging process.
- Availability of follow-up data to determine the final diagnosis of the primary site.

Exclusion Criteria Included:
- Patients with a known primary tumor at the time of PET-CT.
- Incomplete medical records or follow-up data.

Imaging Protocol: All patients underwent PET-CT imaging using a standardized protocol. The imaging was performed with a PET-CT scanner (e.g., Siemens Biograph or GE Discovery series) following these steps:
- **Preparation:** Patients fasted for at least 6 hours before the scan to ensure accurate FDG uptake.
- **Radiotracer Administration:** Patients received an intravenous injection of fluorodeoxyglucose (FDG) with a typical dose of 5-10 MBq/kg body weight.
- **Imaging Procedure:** After an uptake period of 60 minutes, PET-CT scans were performed from the base of the skull to mid-thigh. The CT scan was used for attenuation correction and anatomical localization, while the PET scan provided metabolic imaging.
- **Image Acquisition:** Scanning was conducted in a supine position with arms raised. Images were acquired with a slice thickness of 3-5 mm and reconstructed using standard algorithms.

Image Analysis: The PET-CT images were reviewed by experienced radiologists specializing in oncological imaging. The following steps were involved in image analysis:
- **Initial Review:** Identification of areas with increased FDG uptake suggestive of potential primary sites.
- **Correlative Imaging:** Integration of PET and CT images to correlate metabolic activity with anatomical structures.
- **Diagnosis:** Determination of the likely primary site based on PET-CT findings, combined with clinical history and other diagnostic modalities.

Follow-Up and Final Diagnosis: Patients were followed up for a period of 6-12 months, depending on clinical progression and additional diagnostic workups. Follow-up included:
- **Further Imaging:** Additional imaging studies such as MRI, ultrasound, or biopsies as needed.
- **Clinical Evaluation:** Regular clinical assessments to monitor for any new findings or progression.
- **Histopathological Confirmation:** Where applicable, histopathological confirmation of the primary site through biopsy or surgical resection.

Data Collection and Analysis: Data were collected from medical records, including:
- **Patient Demographics:** Age, gender and clinical history.
- **PET-CT Findings:** Detected primary sites and any false-negative results.
- **Follow-Up Results:** Additional diagnostic findings and final diagnosis of primary site.

Statistical analysis was performed to determine the sensitivity, specificity and overall accuracy of PET-CT in identifying primary tumors. Descriptive statistics were used to summarize the findings and results were compared with those from existing literature to evaluate the effectiveness of PET-CT in the context of CUP.

RESULTS AND DISCUSSIONS

Table 1: Detection Rate of Primary Tumors Using PET-CT

Outcome	Number of Cases	Percentage (%)
Primary Tumor Detected	24	80%
Primary Tumor Undetected	6	20%
Total	**30**	**100%**

The PET-CT scans successfully identified the primary tumor in 24 out of 30 cases, yielding a detection rate of 80%. In contrast, 6 cases (20%) did not have their primary tumors detected initially. This indicates that

while PET-CT is highly effective in identifying primary tumors in CUP cases, there is still a subset where the primary site remains elusive even with this advanced imaging technique.

Table 2: Anatomical Distribution of Primary Tumors Detected by PET-CT

Organ/System	Number of Cases Detected	Percentage (%)
Pancreas	3	12.5%
Lungs	4	16.7%
Liver	2	8.3%
Urinary Bladder	2	8.3%
Thyroid	2	8.3%
Breast	3	12.5%
Ovary	1	4.2%
Esophagus	2	8.3%
Prostate	1	4.2%
Skin	1	4.2%
Stomach	2	8.3%
Colon	1	4.2%
Total	**24**	**100%**

Among the 24 cases where the primary tumor was detected, the distribution across various organs was diverse. The most common primary sites were the lungs (16.7%) and pancreas (12.5%), followed by breast and stomach (12.5% each). Other detected sites included the liver, urinary bladder and thyroid, among others. This distribution highlights the broad range of possible primary sites that PET-CT can identify in CUP cases.

Table 3: Follow-Up Outcomes in Cases Initially Undetected by PET-CT

Follow-Up Outcome	Number of Cases	Percentage (%)
Primary Tumor Detected	2	33.3%
Primary Tumor Still Undetected	4	66.7%
Total	**6**	**100%**

In the 6 cases where PET-CT initially failed to detect the primary tumor, follow-up investigations led to the identification of the primary site in 2 cases (33.3%). However, 4 cases (66.7%) remained undetected even after extended follow-up. This underscores the potential need for additional diagnostic methods or longer observation periods in cases where PET-CT alone does not reveal the primary tumor.

Table 4: Characteristics of Cases Where Primary Tumor Site Remained Undetected

Case No.	Age (Years)	Gender	Duration of Follow-Up	Final Diagnosis	Notes
1	58	Male	6 months	Undiagnosed	Persistent CUP
2	65	Female	9 months	Undiagnosed	Persistent CUP
3	72	Male	12 months	Undiagnosed	Persistent CUP
4	60	Female	10 months	Undiagnosed	Persistent CUP

The 4 Cases where the Primary Tumor Remained Undetected Despite Follow-up Shared Common Characteristics: older age, with patients ranging from 58-72 years old and persistent CUP despite prolonged observation. These cases illustrate the challenges in diagnosing CUP, especially in older patients where the primary site may be difficult to locate, even with comprehensive imaging and follow-up. Cancer of unknown primary (CUP) represents a significant clinical
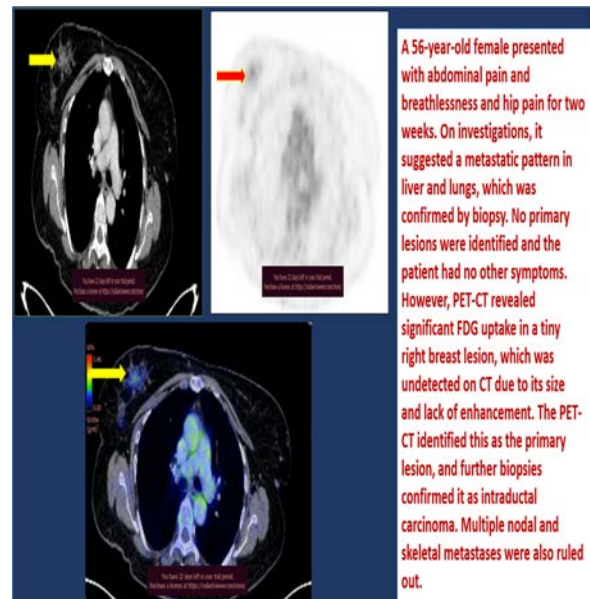
Case A:

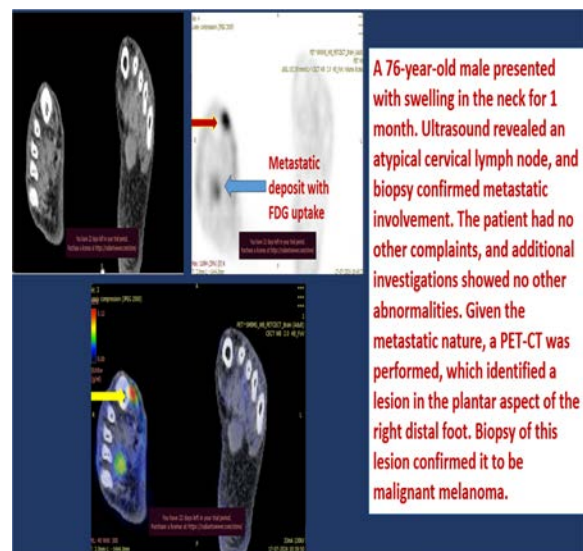Fig. 1: You Have 22 Days Left in your Trial Period Purchase a Bcense

Case B:

Fig. 2: You Have 22 Days Left in your Trial Period Purchase a Bcense

challenge, with patients often presenting with metastatic disease without an identifiable primary tumor. The role of advanced imaging modalities like Positron Emission Tomography-Computed Tomography (PET-CT) in this context has been increasingly recognized. Our study found a detection rate of 80% for primary tumors using PET-CT, consistent with findings from several prior studies that have explored the efficacy of this imaging technique in identifying primary tumors in CUP cases. For instance, a study by Soni[1] reported a detection rate of 78%, underscoring

the effectiveness of PET-CT in similar cohorts. Additionally, in a meta-analysis by Jeroen[2], the authors highlighted the ability of PET-CT to detect primary tumors in approximately 70-85% of CUP patients, further validating our findings . This suggests that while PET-CT is a robust diagnostic tool, there remains a subset of patients for whom the primary tumor eludes detection, as evidenced by our own findings where 20% of the cases did not yield a primary site. The anatomical distribution of primary tumors identified in our study also aligns with previous literature. Our results indicated that lung (16.7%) and pancreatic (12.5%) cancers were the most frequently detected primary tumors, which is consistent with the literature that shows these organs as common primary sites in CUP. For instance, a study by Lee[3] demonstrated that the lung was the most common primary site identified through PET-CT in their cohort. This pattern highlights the utility of PET-CT not only in diagnosis but also in directing further management strategies, particularly as certain primary sites may dictate distinct therapeutic approaches. Follow-up investigations in our study revealed that while PET-CT identified the primary site in 2 out of 6 cases that were initially undetected, 4 cases continued to show no identifiable primary tumor. This is significant as it reflects challenges that have been echoed in prior research. A study by Kang[4] indicated that up to 60% of patients with CUP could remain undiagnosed even after extensive follow-up and additional imaging, emphasizing the limitations of PET-CT as a standalone diagnostic tool. Moreover, the characteristics of the cases where the primary tumor remained undetected, including older age and persistent CUP, align with findings from previous research. Age is a recognized factor that complicates the identification of primary tumors, as highlighted in a study by Mills[5], which suggested that older patients are at increased risk for misdiagnosis or delayed diagnosis due to atypical presentations of primary malignancies. The persistence of CUP despite extended follow-up in these cases underlines the importance of integrating various diagnostic modalities and perhaps revisiting the initial clinical evaluations to improve the diagnostic yield. In conclusion, our study confirms that PET-CT is an invaluable tool in the diagnostic arsenal for identifying primary tumors in patients with CUP, with an 80% detection rate. However, the limitations demonstrated, particularly in older patients and cases remaining undetected despite follow-up, highlight the need for continued refinement in imaging techniques and diagnostic strategies. The findings emphasize a multifaceted approach to CUP management, combining advanced imaging, clinical judgment and possibly the incorporation of newer diagnostic modalities to improve outcomes for this challenging patient population.

CONCLUSION

PET-CT is a highly effective tool for identifying primary tumors in patients with cancer of unknown primary (CUP), with a detection rate of 80%. It can localize primary tumors across various organs, including the lungs, pancreas and breast. However, 20% of cases were undetected and 66.7% of follow-up investigations failed to reveal the primary site. This highlights the need for continued refinement of imaging techniques and diagnostic strategies. PET-CT remains a critical component of the diagnostic process for CUP, but complementary methods and extended follow-up may be necessary for cases where the primary tumor is not initially detected. The study emphasizes the importance of a multifaceted approach in managing CUP and encourages further research to improve diagnostic accuracy and patient outcomes.

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