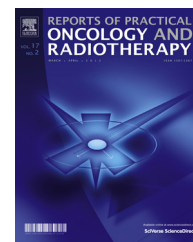




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Original research article

Carcinoma of unknown primary in the head and neck: The evaluation of the effectiveness of ^{18}F -FDG-PET/CT, own experience



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ABSTRACT

Aim: The aim of the present study was to estimate the clinical effectiveness of ^{18}F -FDG-PET/CT in the detection of the primary tumor in patients with histologically proven squamous cell carcinoma cervical lymph nodes metastasis from an unknown primary.

Background: ^{18}F -fluorodeoxyglucose positron emission tomography combined with CT (^{18}F -FDG-PET/CT) is believed to be very helpful in localization of primary tumor in CUP Syndrome patients.

Material and method: 41 patients referred to Poznan Medical University Department of Head and Neck Surgery from January 2010 to December 2013 with CUP Syndrome were included in the study. All patients presented fine-needle biopsy proven squamous cell carcinoma metastasis of the upper-, or mid neck lymph nodes. The final results were obtained from the histopathologic reports of tissue samples from anatomical regions suspected for primary tumor, additional imaging exams as well as clinical follow-up data.

Results: The ^{18}F -FDG-PET/CT successfully detected primary tumor in 7 out of 41 patients (17%). In two more cases the primary tumor was indicated in the lung. 24 of 41 patients (58.5%) analyzed in our study remained without evidence of a primary tumor. In 4 cases (9.75%) we did not reveal any pathology within the localizations indicated by PET/CT on panendoscopy. In 4 cases we obtained histological confirmation of neoplasm on panendoscopy despite the negative results of PET/CT examinations.

Conclusion: We may suppose a relatively high usefulness of ^{18}F -FDG-PET/CT in the diagnosis process of CUP Syndrome patients. High NPV may indicate patients with no symptoms of primary tumor, which allows to avoid extensive resection or extra imaging.

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1. Background

The diagnostic work-up of cervical lymph nodes metastasis from an unknown primary tumor (CUP Syndrome) includes physical examination with rigid or flexible endoscopy of upper aerodigestive tract, CT and/or MRI of the head and neck, additional imagings of chest and abdomen, fine-needle biopsy of the enlarged lymph nodes as well as panendoscopy with blind and directed tissue biopsies. Unfortunately, even such an extensive diagnostic process does not guarantee success – primary tumor detection. In consequence, detection rate of the primary tumor in patients with CUP Syndrome is less than 53.4%.⁹

In general, the prognosis for patients with CUP Syndrome is unfavorable. Their average survival is estimated for only a few months.¹ However, patients with lymph nodes metastasis, especially in the upper- or mid-jugular region are an exception. In 85% of these cases the primary tumor is localized in the head and neck region.² In consequence, the usual treatment of CUP Syndrome patients with highly suspected but not localized primary tumor in the head and neck includes neck dissection, bilateral tonsillectomy followed by adjuvant radiotherapy of all areas of the head and neck with high possibility of primary neoplasm.

It is obvious that correct primary tumor localization may carry through better locoregional treatment options for these patients and improve survival by reduction of side effects.

It is evaluated that conventional imaging modalities, like MRI or CT, detect approximately 10–35% of primary neoplasms in CUP Syndrome patients.¹ According to several studies, ¹⁸F-fluorodeoxyglucose positron emission tomography combined with CT (¹⁸F-FDG-PET/CT) is very helpful in localization of primary tumor. Its detection rate of the primary in patients with tumor metastasis in the head and neck, as well as in other body regions range between 24% and 53%.³

2. Aim

The aim of the present study was to estimate the clinical effectiveness of whole-body ¹⁸F-FDG-PET/CT in the detection of the primary tumor in patients with histologically proven squamous cell carcinoma cervical lymph nodes metastasis from an unknown primary.

3. Materials and methods

This retrospective investigation included 41 patients referred to Poznan Medical University Department of Head and Neck Surgery from January 2010 to December 2013 with CUP Syndrome. All patients presented fine-needle biopsy proven squamous cell carcinoma cervical metastasis of the upper-, or mid neck (regions I–III and V according to Medina⁴) (Table 1). Patients with metastasis in the neck nodes in region IV were also involved in our analysis whereas the frequent primary tumor outside the head and neck area.

In the first step of the diagnosis process each patient underwent a thorough clinical examination with an indirect mirror and rigid or flexible endoscopy of the upper aerodigestive

Table 1 – Cervical lymph nodes classification and probable primary tumor.⁴

Localization of lymph node metastasis	Probable primary tumor localization
Submental nodes	Anterior floor of mouth, lips
Submandibular nodes	Cheek, palate, tongue
Jugulodigastric nodes	Oropharynx, hypopharynx, nasopharynx, larynx, oral cavity
Upper jugular nodes	Hypopharynx, larynx, thyroid gland
Upper posterior cervical nodes	Nasopharynx
Mid jugular nodes	Thyroid gland, cervical esophagus
Lower jugular nodes	Thyroid gland, cervical esophagus
Supraclavicular nodes	Thyroid gland, lungs, gastrointestinal tract, urogenital tract, mammary gland
Posterior cervical triangle nodes	Nasopharynx

tract, neck ultrasound examination, X-ray of the thorax as well as contrast-enhanced CT of the head and neck region. Only patients with undetected pathological finding potentially related to cervical lymph node enlargement were further investigated. After receiving all the exam results and excluding distant metastasis in the thorax by imaging techniques, patients were qualified for (modified) radical neck dissection accompanied by panendoscopy consisting of bilateral tonsillectomy (if it had not been previously performed) and blind tissue specimens taken from macroscopically suspicious areas of mucosa of pharynx (nasal-, oro-, hypopharynx), larynx and esophagus. If there was still no evidence of primary tumor, PET/CT examination was considered.

41 consecutive patients (8 women, 33 men; aged 37–75 years; mean age 60.75) underwent PET/CT examination (scanner Philips Gemini TF) using ¹⁸F-FDG tracer in the amount of 9.3 mCi (SD 1.87 mCi) according to patient's body weight. PET/CT was recommended at least 6 weeks after surgical procedure and before adjuvant radiotherapy. Conditions for the implementation of the exam were normoglycemic after fasting for at least 6 h (70–130 mg/dl) and adequate rest. Each patient was obliged to drink at least 1 L of water. PET was performed 1 h after intravenous injection of FDG from head to proximal thigh. Attenuation-corrected and uncorrected slice images and maximum intensity projections were assessed and documented. Subsequently, contrast-enhanced CT of the whole body was acquired for anatomical accuracy and attenuation correction.

Each PET/CT examination was evaluated by one specialist in nuclear medicine. Lesions with increased tracer uptake were anatomically identified and their FDG uptake was quantified. Finally, each PET/CT exam was characterized as positive or negative for primary tumor. Furthermore, SUV max in every region of increased metabolic activity was measured and compared to the corresponding region on the contralateral side. In case of no visible primary tumor, SUV was measured in the tonsillar area and base of tongue as these are the areas where the tumor is most possible.

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