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Original Research

Diagnostic value of ^{18}F-fluordesoxyglucose positron emission tomography for patients with brain metastasis from unknown primary site

Fabian Wolpert [a,*], Michael Weller [a], Anna Sophie Berghoff [b], Elisabeth Rushing [c], Lisa Michaela Füreder [b], Gregory Petyt [d], Henning Leske [c], Nicolaus Andratschke [e], Luca Regli [f], Marian Christoph Neidert [f], Roger Stupp [g], Rolf Stahel [g], Reinhard Dummer [h], Thomas Frauenfelder [i], Patrick Roth [a], Nicolas Reyns [j], Philipp Antonio Kaufmann [k], Matthias Preusser [b], Emilie Le Rhun [a,l,m,n]

[a] *Department of Neurology and Brain Tumor Center, University Hospital and University of Zurich, Frauenklinikstrasse 26, CH-8091, Zurich, Switzerland*
[b] *Department of Medicine I, Clinical Division of Oncology, Comprehensive Cancer Center-CNS Tumours Unit (CCC-CNS), Medical University of Vienna, 18-20 Waehringer Guertel, AT-1090, Vienna, Austria*
[c] *Department of Neuropathology, University Hospital Zurich, Schmelzbergstrasse 12, CH-8091, Zurich, Switzerland*
[d] *Department of Nuclear Medicine, Lille University, CHU Lille, 59000, Lille, France*
[e] *Department of Radiation Oncology, University Hospital Zurich, Rämistrasse 100, CH-8091, Zurich, Switzerland*
[f] *Department of Neurosurgery, University Hospital Zurich, Frauenklinikstrasse 10, CH-8091, Zurich, Switzerland*
[g] *Department of Oncology, University Hospital Zurich, Rämistrasse 100, CH-8091, Zurich, Switzerland*
[h] *Department of Dermatology, University Hospital Zurich, Gloriastrasse 31, CH-8091, Zurich, Switzerland*
[i] *Institute of Diagnostic and Interventional Radiology, University Hospital Zurich, Rämistrasse 100, CH-8091, Zurich, Switzerland*
[j] *Department of Neurosurgery, Lille University, Inserm, CHU Lille, U1189 - ONCO THAI - Image Assisted Laser Therapy for Oncology, 59000, Lille, France*
[k] *Department of Nuclear Medicine, University Hospital Zurich, Rämistrasse 100, CH-8091, Zurich, Switzerland*
[l] *Neuro-oncology, Department of Neurosurgery, University Hospital Lille, Salengro Hospital, Rue Emile Laine, FR-59037, Lille, France*
[m] *Neurology, Department of Medical Oncology, Oscar Lambret Center, FR-59020, Lille, France*
[n] *Inserm U-1192, Villeneuve d'Ascq, France*

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* *Corresponding author*: Fax: +41 44 255 45 07.
E-mail address: fabian.wolpert@usz.ch (F. Wolpert).

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KEYWORDS
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GPA

Abstract ***Background:*** In 30% of patients with brain metastasis (BM), neurological symptoms are the first clinical manifestation of systemic malignancy, referred to as BM from cancer of unknown primary site (BM-CUPS). Here, we define the diagnostic value of ^{18}F-fluordesoxyglucose positron emission tomography (FDG-PET/CT) in the workup of BM-CUPS.
Methods: We screened 565 patients operated for BM at the University Hospital Zurich and identified 64 patients with BM-CUPS with data on both FDG-PET/CT and contrast-enhanced chest/abdomen computed tomography (CT) available at BM diagnosis. A cohort of 125 patients with BM-CUPS from Lille and Vienna was used for validation.
Results: FDG-PET/CT was not superior to chest/abdomen CT in localising the primary lesion in the discovery cohort, presumably because most primary tumours were lung cancers. However, FDG-PET/CT identified additional lesions suspicious of extracranial metastases in 27 of 64 patients (42%). The inclusion of FDG-PET/CT findings shifted the graded prognostic assessment (GPA) score from 3 with CT alone to 2.5 for PET/CT ($p = 3.8 \times 10^{-5}$, Wilcoxon's test), resulting in a predicted survival of 5.3 versus 3.8 months ($p = 6.1 \times 10^{-5}$; Wilcoxon's test). All observations were confirmed in the validation cohort.
Conclusions: Lung cancers are the most common primary tumour in BM-CUPS; accordingly, CT alone shows similar overall sensitivity for detecting the primary tumour as FDG-PET/CT. Yet, FDG-PET/CT improves the accuracy of staging by detecting more metastases, reflected by decreased GPA scores and decreased predicted survival. Therefore, randomised trials on patients with BM should standardise methods of staging, notably when stratifying for GPA.

1. Introduction

In a third of patients with the diagnosis of brain metastasis (BM), neurological symptoms are the first clinical manifestation of systemic malignancy: BM from cancer of unknown primary site (BM-CUPS) [1,2]. In 10% of patients with BM-CUPS, a primary tumour is never identified [1,3].

Young age, high Karnofsky performance score (KPS), low number of BM, absence of extracranial metastases and controlled primary tumour are predictors of favourable outcomes in patients with BM in general. The first four criteria are used to determine the graded prognostic assessment (GPA) score [3,4].

Targeted therapies and immunotherapy may improve overall survival in subgroups of patients with BM selected for molecular characteristics of the primary tumours [5–8]. Therefore, identifying the primary lesion and further extracranial metastases are a major clinical need in patients with BM-CUPS to define prognosis and treatment [4,9]. Chest/abdomen CT has commonly been considered the most valuable diagnostic test in patients with BM-CUPS, detecting the primary tumour in more than 80% of patients, largely because lung cancer is the most prevalent primary tumour among patients with BM-CUPS [1,2]. ^{18}F-Fluordesoxyglucose position emission tomography (FDG-PET/CT) has been established as a routine method in the diagnostic workup and follow-up of patients with cancer [10,11]. Here, we evaluated the role of FDG-PET/CT compared with chest/abdomen CT in localising the primary lesion and for staging in patients with BM-CUPS.

2. Patients and methods

2.1. Patients

We screened the archives of the University Hospital Zurich for patients who were operated for BM between January 2004 and December 2014: Of 565 patients identified, 126 were diagnosed with metastasis from a solid extracranial tumour as the first manifestation of disease, further referred to as patients with BM-CUPS. Data on both FDG-PET/CT and contrast-enhanced chest/abdomen CT were available at BM diagnosis for 64 patients (Fig. 1). A validation cohort of 125 patients with BM-CUPS was derived from a cohort of 220 patients followed up at the Medical University of Vienna, Austria ($n = 100$) and the University Hospital Lille, France ($n = 120$) (Fig. A.1). The study was approved by the Cantonal Ethics Committee Zurich.

2.2. Assessments

Only patients who had both FDG-PET/CT and contrast-enhanced chest/abdomen CT were considered. The primary tumour was considered identified if a lesion suspicious of tumour and matching histology of BM were reported. For determination of staging capabilities, reports of radiologists (CT) and nuclear medicine specialists (FDG-PET/CT) were compared. Lesions suspicious of extracranial metastasis were considered as true positive based on the judgement of the treating oncologist under consideration of all histological and imaging