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PET/CT in the Imaging of CNS Tumors

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Central nervous system (CNS) tumors are quite rare but cause significant morbidity and mortality. Positron Emission Tomography (PET) is a widely utilized imaging modality within the field of nuclear medicine. CNS tumor diagnostics are an essential tool in the diagnosis and treatment of patients with glioma, offering valuable insights into tumor characteristics, treatment response and outcomes. A variety of different tracers are used in PET imaging of brain tumors including ^{18}F-labeled fluorodeoxyglucose ([^{18}F]FDG), markers showing amino acid metabolism, angiogenesis or inflammatory processes. In this article we describe possibility of use different tracers in different clinical scenario of CNS tumors.

Introduction

Central nervous system (CNS) consists of the brain and spinal cord, where. The brain is the central organ, it controls most of the body's activities by processing, integrating, and coordinating information received from the sensory nervous system. The spinal cord is a crucial component of the central nervous system, located in narrow bone canal, surrounded by the same three protective meninges.[1]

Brain tumors' symptoms vary between patients. They can range from clinically silent to severely disabling. The most common symptoms of brain tumors are headaches and seizures, very prevailing is also cognitive dysfunction.[2] Classical description of tumor associated headaches include intense pain worsening in the morning, with nausea and vomiting alongside. However, some patients may present new neurological symptoms or changes in the usual headache pattern.

Similarly, the spinal cord, surrounded by the vertebral column, may be interpreted by even

minor alterations, such as inflammation, herniated discs, or structural abnormalities. Patients may experience a range of effects, including pain, weakness, or neurological deficits, highlighting the importance of early diagnosis.[3] The primary symptom of spinal tumors is back pain, reported by 80% to 95% of patients. Other may experience motor weakness in the lower limbs, even paralysis. These symptoms are nonspecific, pain is often misinterpreted as musculoskeletal in nature, the neurological symptoms are sometimes misdiagnosed as conditions like a stroke. Because of this, correct diagnosis is not easy and can often be delayed.[4]

Section snippets

Prevalence and Mortality

CNS tumors are quite rare but cause significant morbidity and mortality. The probability of finding a brain tumor varies with age, generally increasing, with a maximum around 50-64 years of age.[1] In 2020 in Poland CNS tumors incidence were 7,3/100 000 in males, and 6,2/100 000 in females; while overall cancer incidence was 391,6/100 000 and 371,3/100 000, respectively. This means that they are responsible for approximately 1.7-1.9% diagnosed malignancies. Unfortunately, despite the low …

Classification

CNS tumors are heterogeneous cluster of neoplasms and thus there are many ways to divide them. The most common subdivisions are based on the initial nature of the lesion: differentiating primary brain tumors from metastatic lesions. For adults, the most common lesions are metastases.[10] The highest rates of identified brain metastases related to lung cancer, melanoma, or renal cancer.[11] In the case of primary brain tumors, age-related variation in diagnosis can also be found. In adults (over the …

Radiological Imaging Modalities

Modern medicine provides a broad range of diagnostic alternatives; however, not all are applicable to the diagnosis of CNS tumors. MRI is considered the gold standard for diagnosing tumors and compression of spinal cord due to its capability to distinguish between soft tissues.21, 22, 23 Special sequences in MRI have also found their way into nervous system imaging.[24] Diffusion-weighted imaging highlights changes caused by compression or tumor cell infiltration. Fluid-attenuated inversion …

PET/CT

Positron Emission Tomography (PET) is a widely utilized imaging modality within the field of nuclear medicine. The PET component effectively identifies areas of altered metabolic pathways increased metabolic activity or increased expression of certain receptors, which may suggest the

presence of tumor cells, while the CT component offers anatomical details.[30] A variety of different tracers are used in PET imaging mostly for oncological, cardiac, or neurological indications. ^{18}F-labeled …

[^{18}F]FDG

[^{18}F]FDG PET shows glucose metabolism and could be in oncology for diagnosis primary and metastatic tumors, as well in neurological disorders, such as, epilepsy, dementia, and Parkinson's disease.[33] In the assessment for metastatic disease in the spine, recognition of the normal or physiologic appearance of [^{18}F]FDG -PET is essential. …

Amino acid tracers

Amino acid PET, in particular, has garnered increased global acceptance as a supplementary method to anatomical MRI for multiple indications in glioma patients.[46] In contrast to the reliance on contrast enhancement in MRI, the uptake of radiolabeled amino acids is not confined to regions with disrupted blood-brain barriers, enabling the identification of no enhancing glioma subregions and establishing the presence of glioma recurrence subsequent to treatment The amino acid tracer O-(2-[^{18} …

PSMA

Prostate-specific membrane antigen (PSMA) is a membrane protein which was first isolated from prostate cancer cells.[64] With the ability to be labelled with both cyclotron and generator tracers, it is a widely available tracer that can be used in PET facility. It is currently the primary tracer for PET in the diagnosis of prostate cancer.[65] Recently, it has been extensively studied in a variety of cancers, including lesions of the breast,[66] liver[67] or central nervous system.[68] In the case of …

FAPI

Fibroblast activation protein is overexpressed in cancer-associated fibroblasts. Fibroblast activation protein inhibitor (FAPI) can be used as a PET tracer to investigate regions with heightened stromal activation in different malignancies.[92] Tracer accumulation is found in both primary tumors and metastatic lesions.[93] Derivatives of this tracer can be used for both imaging and therapy.[94] It is a fairly new tracer used in PET and is being intensively studied for various indications. For CNS …

Somatostatin Receptors

The binding properties associated with DOTA-conjugated peptides are crucial in the study of pheochromocytomas and paragangliomas (PPGLs), which are uncommon neuroendocrine tumors that synthesize catecholamines. PPGLs have increased expression of somatostatin receptors (SSTR), especially SSTR2 subtype. This characteristic allows theranostic approach that

integrates both diagnostic and therapeutic modalities. DOTA peptides, such as DOTATATE and DOTATOC, can be tagged with therapeutic beta …

Carbonic Anhydrase XII

Another possible imaging target in glioma patients is carbonic anhydrase XII (CA XII), a transmembrane enzyme expressed in glioma cells, irrespective of WHO grade, and does not show expression in healthy brain parenchyma.[111,112] This pattern of expression currently opens possibilities of theranostic approach in the future. First efforts to evaluate CA XII binding radiolabeled peptides performance in humans showed decent quality of imaging without significant toxicity.[113] In patients with …

Conclusion

CNS tumor diagnostics, particularly those based on PET molecular imaging, are an essential tool in the diagnosis and treatment of patients with glioma, offering valuable insights into tumor characteristics, treatment response and outcomes. Currently, amino acid markers play the greatest role in both diagnosis and therapy control. However, new markers such as PSMA and FAPI are increasingly being used. Discovery of new molecular targets allows the application of theranostic-based therapeutic …

CRediT authorship contribution statement

Katarzyna Barańska: Visualization, Writing – original draft, Writing – review & editing. **Katarzyna Niemas:** Visualization, Writing – original draft, Writing – review & editing. **Kacper Pełka:** Conceptualization, Supervision, Visualization, Writing – original draft, Writing – review & editing. **Jolanta Kunikowska:** Conceptualization, Supervision, Writing – original draft, Writing – review & editing. …

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. Without direct relevance to this work, JK reports participation on a Data Safety Monitoring Board and Advisory Board from Novartis and Terumo (personal fees); Consultant for Curie Science Center; lecture honoraria from Monrol and Novartis …

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