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Case Report

[18F]Fluorocholine PET/CT false positive: foreign body reaction mimicking low-grade glioma progression

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Abstract: A right frontoparietal neoplastic lesion was found in a young-aged patient with analgesic refractory headache. Surgical resection was performed, and the pathologist analysis turned out a cellular ependymoma with signs of anaplasia. In the follow-up, a MRI showed a suspicious lesion, so a [18F]Fluorocholine PET/CT was performed. An increased uptake was described in the right parietal region on the margin of residual cystic lesion. The patient got a complete resection which was confirmed later by MR. In the pathology analysis, a focally congestive cerebral parenchyma with a central histiocytic reaction to foreign body area was described. Foreign body reaction in brain tissue is a very rare immune response that has not been well studied. Haemostatic material has been reported as a possible trigger of this response in other organs and could be detected by [18F]FDG PET/CT. Following the experience of the current case report, [18F]Fluorocholine PET/CT could also show a false positive related to foreign body reaction.

Keywords: Foreign Body Reaction, deshydroxy-(18F) fluorocholine, Positron Emission Tomography, Low-grade glioma, Haemostatic material.

1. Introduction

Central nervous system (CNS) tumours are a challenging pathology, which require a very short time of action due to its high mortality. The global burden of CNS tumors has increased during the last 25 years. Also, the lack of specific symptoms and signs make imaging diagnosis a mainstay in CNS tumour management. The relation between the incidence and the mortality of CNS cancer guides towards the importance of early diagnosis to improve the survival of these patients [1]. Of all CNS tumours, gliomas are one of the most aggressive histological lines and the second most frequent brain tumour [2].

The first step for the brain tumour diagnosis comprises the use of Magnetic Resonance imaging (MRI) and Computerized Tomography (CT). MRI is the technique of choice due to its ability to obtain functional data on cellularity (MRI diffusion), vascularization (MRI perfusion) and metabolism (MRI spectroscopy) that are essential nowadays [3]. However, due to MRI recognized limitations on viable tumour and treatment-induced lesions differentiation, there is a need to develop new ways of diagnosis and characterize CNS tumours [4]. Specially in low-grade gliomas, the management is challenging, most of all in the post surgery phases, where the MRI could result inconclusive [5].

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A step beyond radiological imaging, nuclear medicine has an important role. Positron Emission Tomography (PET) is a molecular imaging technique that complements MRI in the study of gliomas, in situations such as treatment response evaluation [6]. [^{18}F]Fluorodeoxyglucose is the most used radiotracer in PET/CT imaging but jeopardizes the signal/background ratio due to high physiological uptake in normal brain parenchyma. Therefore, depending on the histopathologic nature of the lesion and the clinical question, other radiopharmaceuticals could be useful [7]. [^{18}F]Fluorocholine is a radiotracer that gets trapped to form a major membrane phospholipid by choline kinase, being a membrane proliferation marker [8]. About the [^{18}F]Fluorocholine biodistribution, it does not cross the blood-brain barrier, so it is helpful to study central nervous system lesions with rupture of this barrier, as primary brain tumour or metastasis [9, 10]. Also, [^{18}F]Fluorocholine has the potential to differentiate viable tumours from other entities, such as radionecrosis [11-13] and could fine-tune the diagnosis in complement with the MRI. This synergy between MRI and [^{18}F]Fluorocholine PET/CT could be particularly useful in the low-grade glioma posttherapy follow-up [14].

2. Case Presentation

We present a young-aged patient with a headache resistant to analgesic treatment, nausea and vomiting who had an episode of sensitivity loss and speaking difficulties. After an urgent cranial CT, a right frontoparietal lesion was diagnosed. The patient was taken to the neurosurgery department and a cranial MRI was performedwhich confirmed the presence of a neoplastic lesion. The surgery was guided by neuronavigation with 5-aminolevulinic acid and cortical and subcortical stimulation. Intraoperatively, a hard consistency heterogeneous tumour was found with a capsule in some parts of its extension. The 5-aminolevulinic acid showed a diffuse infiltration of white matter. The injury was closed with cellulose derivate hemostatic material (Surgicel®), and the dura mater was sutured with braided silk and adhesive fibrinogen/thrombin matrix. The histopathological analysis resulted in a cellular ependymoma with signs of anaplasia (WHO grade III). After the surgery, the patient underwent radiotherapy with some autolimited episodes of hemiparesis and dysarthria. Besides, he presented somesthetic crisis in his left arm, for which he refused pharmacological antiepileptic treatment. Post-surgical MRI showed signs of probable complete tumour resection.

Successive cranial MRI studies over the following 3 years showed superficial parenchymal enhancement in the surgical bed, initially attributed to post-surgery irritative changes, but which progressively acquired a more nodular and conspicuous morphology over a cystic lesion (figure 1). Further studies were recommended to complete the evaluation under the suspicion of recurrence. A [^{99m}Tc]Tc-MIBI SPECT/CT was reported as no significant uptake.

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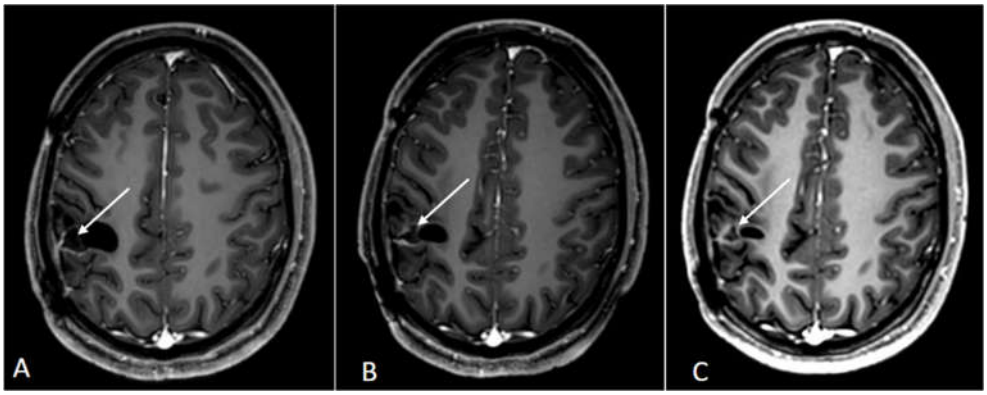

Figure 1. Brain MRI studies. T1-3D post gadolinium in the axial plane from A) Postsurgical control (2 years after first surgery), B) Postsurgical control (2 years and a half after first surgery) and C) Postsurgical control (3 years after first surgery). A lesion can be seen in the surgical bed (white arrow) that progressively adopts a more nodular morphology with better delimited peripheralcontrast uptake.

The patient was presented at the multidisciplinary committee, and it was decided to perform a [^{18}F]Fluorocholine PET/CT to asses the metabolic behaviour of the radiological image. The brain [^{18}F]Fluorocholine PET/CT showed an increased uptake of punctate morphology at the level of the right parietal cortex, on the external margin of the residual cystic lesion (figure 2). After this finding a functional MRI (f-MRI) was performed to assess the possibility of a rescue surgery. The described lesion did not present any anatomical relation with the brain motor cortex, so the patient was proposed for a resection. The patient accepted and he was programmed for the surgery.

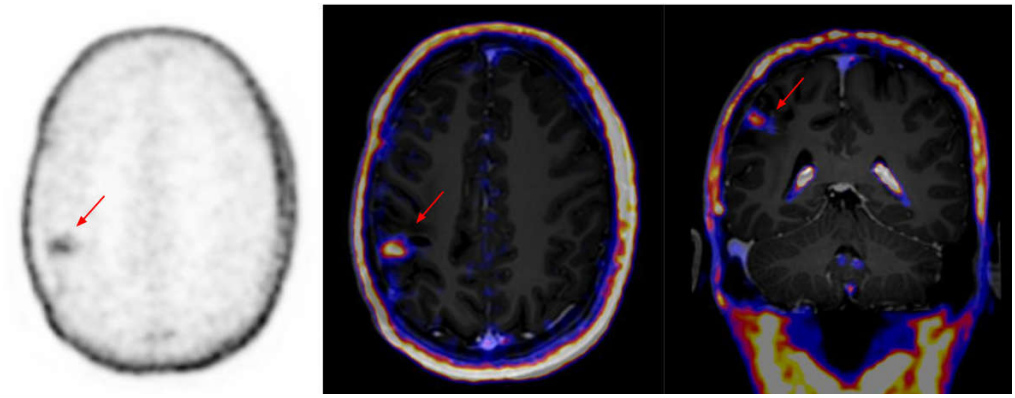

Figure 2. Plain [^{18}F]Fluorocholine PET/CT and fusion with contrast-enhanced T1-MRI . A hypermetabolic lesion (red arrow) was reported adjacent to surgical locule, in the parietal lobe.

This second surgery was performed with a neuronavigator to localize the lesion and under neurophysiological control. The motor region was identified, located anterior to the injury (as indicated by -imaging f-MRI) and a macroscopically complete resection was performed. In the postoperative period, the patient did not present any neurological symptoms and was discharged without any incidence.

One month after the surgery, the patient had a postsurgical MRI that confirmed the complete resection of the contrast enhanced nodule but with an enhancement around the loculum and the meninx, which was blamed on the postsurgical changes. Microscopically, it was described as a pseudoencapsulated lesion, surrounded by brain parenchyma constituted by astrocytes of which some were reactive, without atypia nor mitosis. In the central area, a foamy-cytoplasm cell proliferation was shown, being CD68 positive. Also, few lymphocytes against foreign body from the previous surgery were found (figure 3).

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The histopathological analysis concluded that the piece had focally congestive cerebral parenchyma and a central area with histiocytic reaction to foreign body with absence of malignant neoplastic cells.

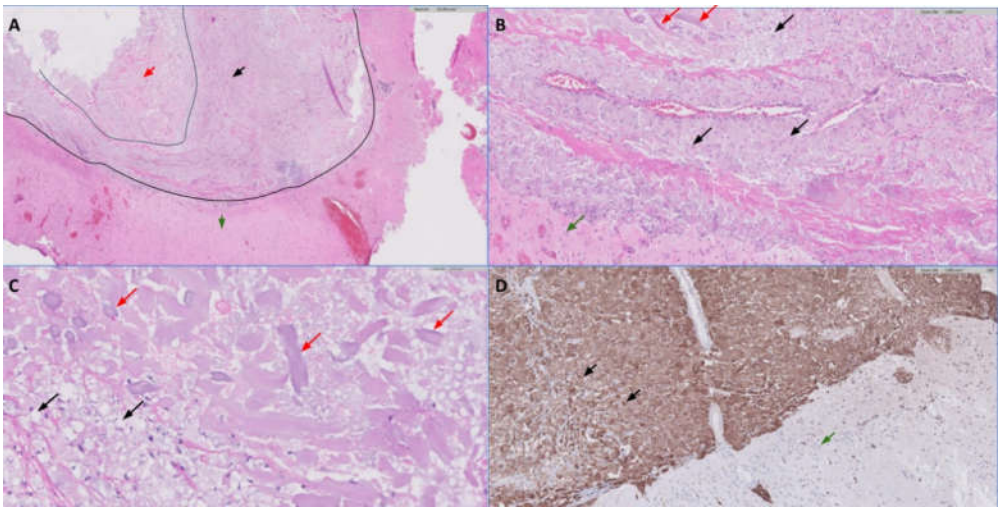

Figure 3. Anatomopathological image of the second surgery piece. Arrows point to different cellular structures: textiloma (red arrow), foamy histiocytes staining with CD68 (black arrow) and reactive brain parenchyma (green arrow). A) Hematoxylin-Eosin x20; B) Hematoxylin-Eosin x40; C) Hematoxylin-Eosin x40; D) Immunohistochemistry

3. Discussion

Foreign body reactions after surgery have been described in different tissues in the human body and against different kinds of materials [15]. This entity is one of the factors that pushes to improve the research in biocompatibility of surgical products [16]. However, foreign body reactions have not been well studied in the CNS and they are very rarely reported, mostly as individual case reports or case series studies. Among these reports, we find the use of material for endovascular therapy [17, 18] or hemostasis intra-operative chemical agents [19]. The authors of the present case report hypothesize that this reaction could be triggered by two potentially harmful surgical materials. The first considered possibility is that neurosurgical patties released microscopical fibres that brought out the foreign body reaction, however, literature do not describe this possibility [20]. This fibre was not found in the histological analysis and some authors defend the strength and durability of the cellulose that compacts the cotton fibers [21]. Our second hypothesis was that cellulose derivate hemostatic material was used by the neurosurgeons in the first surgical intervention. This hemostatic material has been frequently applied in our center neurosurgery interventions since 2016. Foreign body reaction against these derivates have been reported in the literature by several clinical cases [22]. In [^{18}F]FDG PET/CT studies a similar reaction has been described in other organs as lungs [23]. Also, our patient histological pattern could fit adequately in this context [24].

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Intracranial foreign body reaction is a rare immune response and usually appears within weeks to months after a surgery with clinical. Imaging features of the entity could be similar to tumour progression [25]. It has been reported that it could share radiologic characteristics with neoplasms in CT and MRI studies as the presence of a granuloma with peripheral contrast enhanced in CT [26]. MRI also could show well-circumscribed masses with central hypointensity and peripheral contrast-enhancement that in several cases could be confused with a tumoural lesion [27]. This false positive diagnosis could make the patient undergo surgery without real need [28].

In our knowledge and after a bibliographic research, it seems that there is not enough literature that describes the behavior of [^{18}F]Fluorcholine in the study of foreign body reaction, nor PET/CT role in the management of these patients. Despite the lack of specific literature, the clinical case reported by Jang et al. [19] remarked that the MRI spectroscopic study showed an elevated choline in comparison with the rest of the measurables aminoacids. Some authors pointed out that normalized SUVmean from [^{18}F]Fluorcholine and normalized integral values of choline in spectroscopy could show a positive correlation [29]. There is a need for more studies that gather a significant sample to clarify the role of [^{18}F]Fluorcholine in the differential diagnosis of foreign body reaction. Faced with the lack of evidence, it seems that histopathologic analysis is the gold standard to differentiate between neoplastic tissue and foreign body reaction [30].

4. Conclusions

The introduction of new procedures and materials in surgical practice could induce diagnostic mistakes in imaging techniques, and this fact must be considered to avoid unnecessary invasive approaches. There is a need to report false positive explorations to reduce these avoidable interventions. Foreign body reaction in central nervous tissue could be shown as an uptake focus in [^{18}F]Fluorcholine PET/CT, mimicking a neoplastic lesion.

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