Brain scintigraphy with ^{99m}Tc-tetrofosmin for the differential diagnosis of a posterior fossa tumor

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Abstract

A 60-year-old woman harbouring a tumour in the cerebellum. Anatomic brain imaging by computed tomography and magnetic resonance imaging were not conclusive of the lesion's nature. Imaging by ^{99m}Tc-tetrofosmin single-photon emission tomography (SPET) showed increased radiotracer accumulation in the lesion, indicating a vascular supply, membrane permeability and cellular metabolic activity, which is suggested to facilitate tracer uptake by lesions located in the posterior fossa. The patient underwent surgery and haemangioblastoma was confirmed by histology. Differential diagnosis is discussed. ^{99m}Tc-tetrofosmin scintiscan contributed to diagnostic information.

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Introduction

Functional metabolic imaging by single-photon emission tomography (SPET) of intracranial space-occupying lesions can provide information about the metabolic status of brain tumors, their biological behavior and their vascularity and possibly predict the type and grade of malignancy. These studies can supplement the neuromorphological workup provided by computed tomography (CT) and magnetic resonance imaging (MRI) [1]. Several radiotracers have been used for brain SPET imaging, such as technetium-99m-sestamibi (^{99m}Tc-MIBI) and ^{99m}Tc-tetrofosmin (^{99m}Tc-TF), yet their biological behaviour and capabilities are still under investigation [2].

We report a case of a posterior fossa brain tumor, in which CT and MRI were inconclusive of the lesion's nature. ^{99m}Tc-TF SPET was then performed and found diagnostically useful.

Case report

A 60-year-old woman was admitted to our hospital complaining of a severe headache lasting for over a week. A CT scan was performed and revealed a lesion in the left cerebellar hemisphere. Brain MRI that ensued demonstrated a heterogeneously enhanced lesion surrounded by edema and causing displacement of the fourth ventricle (Fig. 1). Although morphologic imaging was not conclusive of the lesion's nature, the diagnosis of glioma was suspected and a ^{99m}Tc-TF brain, SPET was performed for further evaluation.

The scintigraphic study was performed 30 min after the intravenous injection of 925 MBq of ^{99m}Tc-TF. The radiopharmaceutical was prepared using a domestically available powder kit (Myoview™, General Electric Healthcare Ltd, Buckinghamshire, UK) that was reconstituted with ^{99m}Tc pertechnetate ($^{99m}TcO_4^-$) sterile solution in our Nuclear Medicine Department. Imaging was implemented in a dual-head γ-camera (Millennium™ VG3, General Electric Medical Systems – Europe, Buc cedex, France) equipped with a pair of high-resolution, parallel-hole collimators. The matrix was set at 128×128 pixels; the photopeak was centred at 140 keV, with a symmetrical 20% window. The tomographic imaging parameters consisted of a 360°-rotation angle, a 3°-step-and-shoot technique and an acquisition time of 30 sec per frame. Raw imaging data were reconstructed using the Butterworth-filtered back-projection algorithm, generating tomographic views of the brain in the 3 planes (transverse, coronal, and sagittal). Radiotracer accumulation in the brain was assessed visually.

The lesion displayed profound ^{99m}Tc-TF uptake in scintitomographic imaging (Fig. 2). The tumor was excised surgically. Microscopically, the tumor showed a dense network of vascular channels with accumulation of lipid droplets within stromal cells. The immunohisto-

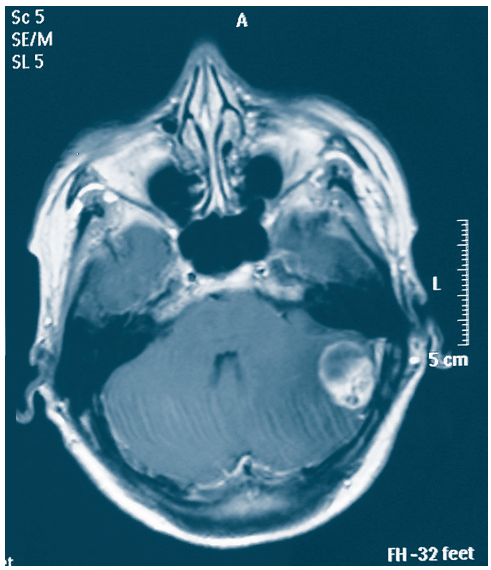

Figure 1. T1-weighted MRI obtained after gadolinium infusion, shows an enhancing mass in the left cerebellum.

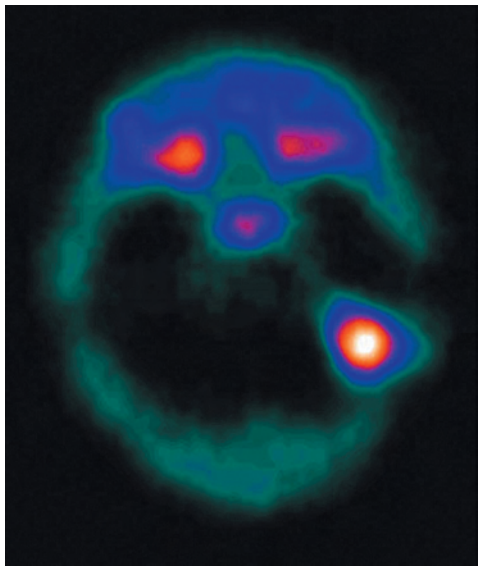

Figure 2. ^{99m}Tc-tetrofosmin SPET showing marked radiotracer accumulation in the tumour in the same region of MRI findings.

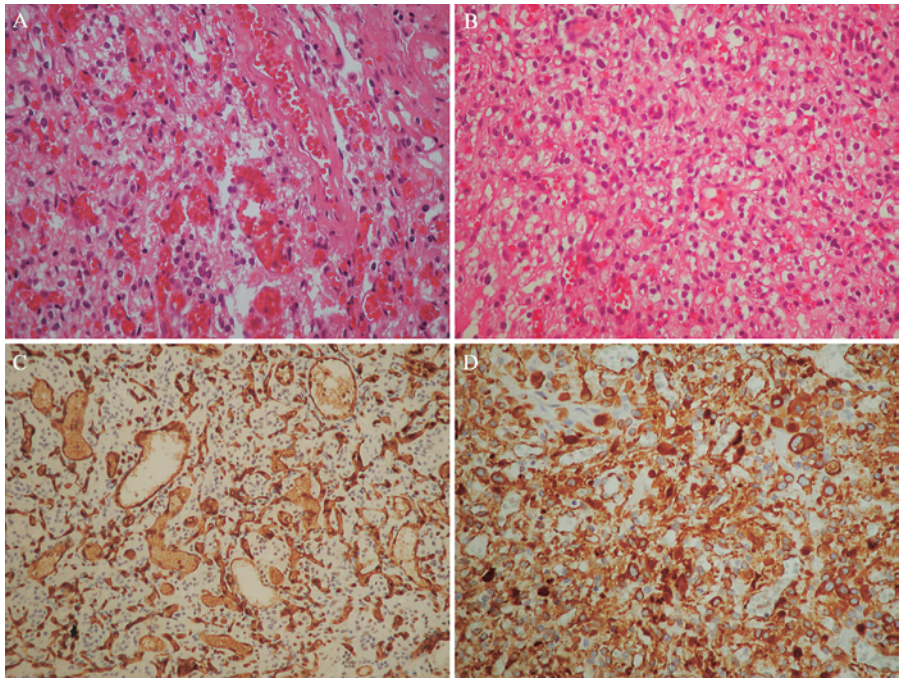

Figure 3. A. Haemangioblastoma with numerous thin-walled vessels and stroma cells most of them are vacuolated (H-Ex400). **B.** Accumulation of lipid droplets within stromal cells (H-Ex400). **C.** CD31 immunohistochemical expression in capillary endothelial cells, but not in stromal cells. **D.** Strong vimentin immunoihistochemical expression in stromal cells.

chemical analysis revealed CD31 expression in capillary endothelial cells and vimentin expression in stromal cells (Fig 3). The cellular proliferation rate (Ki-67) – as assessed by the MIB-1 immunostaining labeling index – was less than 1%, while flow cytometry of the excised lesion revealed that the cell fraction in the S-phase was 1.92%. The histopathological findings were consisted with a haemangioblastoma.

Discussion

Haemangioblastoma is the most common vascular tumor of the central nervous system (CNS) [3, 4]. It accounts for approximately 2% of all intracranial space occupying lesions and most frequently is located in the cerebellum, the spinal cord, and the brainstem [5, 6]. Haemangioblastomas are either sporadic, or associated with about 20%-30% of von Hippel-Lindau (VHL) disease cases. Patients with VHL disease usually have multiple tumors. The symptoms of these lesions are either related to local mass effects, or to obstruction of the cerebrospinal fluid flow [7]. Surgical resection is the treatment of choice. A major concern regarding these lesions is the risk of hemorrhage that may occur spontaneously, intraoperatively, or postoperatively and seems to correlate with tumor size [8]. Furthermore, surgical mortality rate may be high [9, 10]. It is therefore important for the neurosurgeon to be aware that the lesion to be excised is a haemangioblastoma. The constellation of CT and MRI findings are not always conclusive, since the morphologic features of other entities like gliomas, metastases and cavernomas can be nearly identical and should be included in the differential diagnosis. Angio-

graphy is invasive and may induce complications [11, 12]. The SPET scan seems to be helpful for the differential diagnosis of these tumors.

Various radiotracers have been used, for brain SPET, including thallium-201 (^{201}Tl) ^{99m}Tc-bound compounds – such as ^{99m} Tc-MIBI and ^{99m}Tc-methionine, iodine 123-a-methyl tyrosine [13-15] and ^{99m}Tc-TF. ^{99m}Tc-TF is a lipophilic cationic diphosphine with tumor-seeking properties, routinely used for myocardial perfusion imaging [16]. Its uptake mechanism bears similarities to ^{99m}Tc-MIBI, as it depends mainly on regional blood flow and cell membrane integrity: it enters cells mainly via passive transport driven by the negative potential of the intact cell membrane and mostly localizes within the cytosol while only a fraction passes into the mitochondria [17, 18].

Little has been reported up to now on the value of ^{99m}Tc-TF to image brain tumors *in vivo*; nevertheless, certain uptake and metabolism studies on human glioma cell lines, substantiate a plausible clinical superiority over ^{99m}Tc-MIBI for brain tumor evaluation [19, 20]. Clinical brain SPET studies have shown that ^{99m}Tc-TF can differentiate tumor recurrence from radiation necrosis, predict glioma grade and meningioma aggressiveness, and differentiate neoplastic from non-neoplastic intracerebral hemorrhage [21-30] To our knowledge, no other imaging study has to date addressed the usefulness of ^{99m}Tc-TF brain SPET for the diagnosis of haemangioblastoma. Kondo et al (2001) reported that ^{201}Tl can distinguish haemangioblastomas from gliomas in the posterior fossa [31]. However, due to the 140 keV-γ-ray energy of ^{99m}Tc, its higher photon flux and spatial resolution, imaging by ^{99m}Tc-labeled compounds, has advantages over ^{201}Tl and a significantly lower radiation burden to the patient [2, 13]. Brain SPET has shortcomings in evaluating tumors located in the posterior fossa, because they seem to have a low radiotracer uptake. Barai et al (2004) suggested that brain scintigraphy is not a sensitive diagnostic modality for differentiating radiation necrosis from tumor recurrence, even for high grade gliomas, in the posterior fossa [32]. Our experience indicates that gliomas and metastatic lesions, from renal and pulmonary cancers, located in the posterior brain fossa, display a relative lower ^{99m}Tc-TF uptake, as compared to gliomas or metastases located supratentorially [unpublished data]. *In conclusion,* since ^{99m}Tc-TF uptake depends on regional blood flow that haemangioblastomas are highly vascular tumors, this may contribute to the increased radiotracer uptake of these tumors. Considering the above, we believe that the differential diagnosis of any lesion in the cerebellum demonstrating significant ^{99m}Tc-TF uptake, should include haemangioblastoma. In this case, CT findings were not conclusive.

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