Nuclear Medicine

Lacrimal gland uptake on F-18 florbetapir amyloid positron emission tomography scan

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ABSTRACT

In 2012, the Food and Drug Administration (FDA) approved the use of F-18 florbetapir to estimate β-amyloid neuritic plaque density when indicated. A normal scan will show increased radiotracer uptake in the white matter. Mild uptake in salivary glands, skin, muscles, and bones is considered normal. Being a new and infrequently performed study, familiarity with normal biodistribution and variants is important. We hereby present 2 cases with F-18 florbetapir uptake in lacrimal glands. Patients had no symptoms or known systemic conditions to explain this uptake. We speculate that lacrimal gland uptake of F-18 florbetapir could represent a normal variant.

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Introduction

β-Amyloid neuritic plaques are extracellular deposits of the insoluble neurotoxic β-amyloid protein. These plaques are seen in cortical gray matter of patients with Alzheimer disease (AD) [1]. Positron emission tomography (PET) amyloid imaging allows assessment of density and distribution of amyloid neuritic plaques in cortical gray matter [2,3].

F-18 florbetapir is 1 of 3 F-18-labeled amyloid PET radiopharmaceuticals approved by the U.S. Food and Drug Administration and the European Medicines Agency [4–6]. Distribution of F-18 florbetapir in the absence of amyloid deposition results in a clear gray matter-white matter contrast. Positive scans, on the other hand, show cortical uptake of radiotracer resulting in reduction or loss of the distinct contrast between gray and white matter [5]. A normal amyloid PET scan has a high negative predictive value, reported to be 96% with florbetaben [7], and almost excludes the diagnosis of AD in a patient with cognitive impairment [5]. A positive scan, however, is not specific and can be seen with other types of neurologic conditions as well as in older people with normal cognition [5].

The recommended dose of 18F-florbetapir is 370 MBq (10 mCi) in a maximum volume of 10 mL administered as an intravenous bolus, followed by a saline flush [3].

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Recommended uptake time is 30-50 minutes [8] and images should be acquired for 10 minutes [5,6].

As imaging findings of amyloid PET scan have prognostic value and may alter the treatment, recognition of normal variations is very important. Here, we report 2 cases of lacrimal gland uptake of 18F-florbetapir.

Case reports

Case 1
A 70-year-old woman with progressive memory and language impairment was referred for amyloid PET/CT scan. Medical history was unremarkable except for gastroesophageal reflux disease and osteopenia. F-18 florbetapir PET/CT scan showed diffuse and symmetric cortical uptake of radiotracer in the gray matter of frontal, temporal, parietal, and occipital lobes, indicating deposition of amyloid neuritic plaques. There was also moderate to intense radiotracer uptake within the lacrimal glands bilaterally (Fig. 1). The patient had no relevant clinical signs or symptoms.

Fig. 1 – Bilateral lacrimal gland uptake: (A) Axial attenuation corrected image of the brain and (B) fused PET/CT axial image acquired 36 minutes after intravenous injection of 10.7 mCi of F-18 florbetapir demonstrate intense radiotracer uptake in the lacrimal glands bilaterally (arrows). PET/CT, positron emission tomography/computed tomography.

Case 2
A 67-year-old man had progressive cognitive and behavioral changes. He had a past medical history of prostate cancer. F-18 florbetapir PET/CT scan showed diffuse uptake of radiopharmaceutical in the gray matter and subsequent loss of gray-white distinction, compatible with moderate to frequent β-amyloid neuritic plaque deposition. Moreover, there was mild to moderate radiotracer uptake unilaterally in the left lacrimal gland (Fig. 2). Again, the patient had no positive ophthalmologic signs or symptoms.

Fig. 2 – Unilateral lacrimal gland uptake: (A) Axial attenuation corrected image of the brain and (B) fused PET/CT axial image acquired 31 minutes after intravenous injection of 10.7 mCi of F-18 florbetapir demonstrates diffuse cortical uptake compatible with moderate to frequent β-amyloid neuritic plaques and mild uptake in the left lacrimal gland (arrow). PET/CT, positron emission tomography/computed tomography.
Discussion

Amyloid PET/CT has revolutionized the workup and management of patients with cognitive impairment. Imaging findings have been reported to change diagnosis or management plans in up to 68% of patients [9,10]. Amyloid imaging also has prognostic value as it helps predict the risk of subsequent cognitive decline in patients with mild cognitive impairment and cognitively normal older adults [11]. For interpretation of amyloid PET scans, knowledge of physiological distribution and normal variations is important.

In a normal scan, the highest level of F-18 florbetapir uptake is in the white matter [3]. Radiotracer uptake in the scalp, salivary glands, muscles, and bones has been described and is considered normal biodistribution [6]. β-Amyloid neuritic plaques do accumulate in the lacrimal glands in humans, and this could explain the binding of amyloid PET agents to lacrimal glands in patients with AD [12]. The exact molecular mechanism of binding of amyloid PET agents to amyloid plaques is not fully understood, but molecular dynamic simulations suggest that the agent is placed in surface grooves along the amyloid fibril axis [13]. This model provides an alternate hypothesis of nonspecific accumulation of PET amyloid agents within the salivary glands.

C-11 Pittsburgh compound B (C-11 PiB) has been reported to bind to lacrimal glands in a mouse model of Alzheimer’s [14]. There are no human reports of lacrimal gland uptake with any of the Food and Drug Administration-approved amyloid PET agents: florbetapir, flutemetamol, or florbetaben. Other radiopharmaceuticals that have been reported or are known to show lacrimal gland uptake are gallium (Ga)-67 citrate [15], Tc-99m-exametazime (HMPAO) [16], Ga-68 PSMA agents PSMA-11 (HBED-CC) [17] and DCFPyL [18], as well as sodium iodide, and pertechnetate due to presence of sodium iodide symporters in the lacrimal gland [19]. Although bilateral lacrimal gland uptake of radiotracers can be common and nonspecific, unilateral lacrimal gland uptake of radiotracers such as Ga-67 is favored to represent a focal process such as inflammation or tumor as reported in a case of lymphoma involvement of the lacrimal gland [20]. According to our literature search, F-18 florbetapir uptake has not been described previously in the lacrimal glands, neither bilaterally nor unilaterally. F-18 florbetapir uptake in the lacrimal glands could represent a normal variant. Other possible etiologies could include inflammation, neoplasms, systemic diseases such as sarcoidosis and amyloidosis, or early deposition of amyloid protein secondary to Alzheimer’s disease.

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