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Incidental Pituitary Uptake on 18F-Fluorodeoxyglucose Positron Emission Tomography: Clinical Implications and Characteristics

18F-Florodeoksiglukoz Pozitron Emisyon Tomografisi'nde İnsidental Hipofiz Tutulumu: Klinik Özellikler ve Sonuçlar

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ABSTRACT

Aim: Positron emission tomography (PET)/CT using 18F-fluorodeoxyglucose (FDG) is a commonly used technique for staging and/or localization in various malignant diseases. Our study aimed to investigate the clinical laboratory and histopathological features of patients with incidental pituitary involvement.

Materials and methods: In this retrospective study, approximately 60,000 18-FDG PET/CT scans performed for various indications between May 2012 and December 2020 were reviewed to identify patients with pituitary involvement. The clinical and laboratory characteristics of these patients were investigated using the Hospital Information Management System.

Results: Twenty-five patients with incidental pituitary uptake were identified on 18F-FDG PET/CT scans. Eleven patients had macroadenomas. The mean SUVmax levels of the pituitary lesions and different malignancies were statistically similar (13.6 (5.40–38.80) and 11.7 (0.00–116.0), respectively. Six of the 25 patients had nonfunctional adenomas, one patient had a prolactinoma, and four patients had pituitary insufficiency based on hormonal evaluation. Two patients were found to have a pituitary adenoma on histopathological evaluation. One patient had a metastasis from lung carcinoma, as detected radiologically.

Conclusion: Incidental pituitary uptake is often overlooked, particularly in the patients with advanced metastatic disease. In individuals with a primary malignancy who are subjected to significant physiological stress from chemotherapy, surgery, and other interventions, timely diagnosing and management of pituitary insufficiency is crucial, as it can significantly impact morbidity and mortality. To develop diagnostic algorithms, predictive models, or systematic follow-up strategies, prospective studies are needed that include hormonal, radiological, and histopathological follow-up data on both the primary malignancy and pituitary metastases.

Keywords: 18F-fluorodeoxyglucose positron emission tomography, pituitary uptake, malignancy

ÖZET

Amaç: 18F-florodeoksiglukoz (FDG) kullanan pozitron emisyon tomografisi (PET)/BT, malign hastalıklarda evreleme ve/veya lokalizasyon için yaygın olarak kullanılan bir görüntüleme yöntemidir. Çalışmamızın amacı, insidental hipofiz tutulumu olan hastaların klinik laboratuvar ve histopatolojik özelliklerini araştırmaktır.

Materyaller ve yöntemler: Bu retrospektif çalışmada, Mayıs 2012 ile Aralık 2020 arasında çeşitli endikasyonlarla çekilen yaklaşık 60.000 18-FDG PET/BT hipofiz tutulumu olan hastaları belirlemek için incelendi. Bu hastaların klinik ve laboratuvar özellikleri hastane bilgi yönetim sistemi kullanılarak araştırıldı.

Sonuçlar: 18F-FDG PET/BT'de insidental hipofiz tutulumu olan yirmi beş hasta belirlendi. On bir hastada makroadenom vardı. Hipofiz lezyonlarının ve farklı malignitelerin ortalama SUVmax seviyeleri istatistiksel olarak benzerdi (sırasıyla 13,6 (5,40-38,80) ve 11,7 (0,00-116,0). 25 hastanın altısında hormonal değerlendirmeye göre nonfonksiyonel adenom, bir hastada prolaktinoma ve dört hastada hipofiz yetmezliği olduğu saptandı. İki hastada histopatolojik değerlendirmede hipofiz adenomu vardı. Bir hastada radyolojik olarak saptanan akciğer karsinomu metastazı saptandı.

Sonuç: İnsidental hipofiz tutulumu özellikle ileri metastatik hastalığı olan hastalarda göz ardı edilmektedir. Kemoterapi, cerrahi ve diğer müdahaleler nedeniyle ciddi fizyolojik strese maruz kalan malignitesi olan bireylerde, hipofiz yetmezliğinin zamanında teşhis edilmesi ve yönetimi, morbidite ve mortaliteyi önemli ölçüde etkileyebileceğinden çok önemlidir. Tanısal algoritmalar, öngörücü modeller ve sistematik takip stratejileri geliştirmek için hem primer malignite hem de hipofiz metastazları hakkında kapsamlı hormonal, radyolojik ve histopatolojik verilerin kullanıldığı prospektif çalışmalara ihtiyaç vardır.

Anahtar kelimeler: hipofiz tutulumu, malignite, 18F-florodeoksi glukoz pozitron emisyon tomografisi

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Introduction

Pituitary adenomas are benign lesions of the anterior pituitary gland that can be symptomatic or incidentally detected on magnetic resonance imaging (MRI). Most pituitary adenomas are benign, and MRI is the preferred radiological technique for detecting, differentiation, and monitoring these lesions in patients with suspected pituitary abnormalities[1,2]. Pituitary microadenomas, defined as lesions smaller than 10 mm, are often incidental findings and typically asymptomatic. In contrast, pituitary macroadenomas, defined as lesions larger than 10 mm, are more likely to present with mass effect symptoms and may cause hormonal deficiencies or excesses[2,3]. Benign adenomas typically appear as well-circumscribed, confined to sella turcica, with slow growth and limited invasion of surrounding structures[2]. In contrast, pituitary metastases or pituitary carcinomas, although rare, can mimic adenomas but often present as heterogeneous, rapidly growing masses with irregular borders and invasion of surrounding structures. Malignant lesions typically lead to the rapid onset of hormonal deficiencies and are more likely to cause diabetes insipidus[2,4].

Positron emission tomography (PET)/CT using 18F-fluorodeoxyglucose (FDG) is widely used for staging and localization in a variety of malignant diseases. Most benign and slow-growing pituitary lesions exhibit low metabolic activity and typically do not accumulate 18-FDG, rendering them undetectable on 18-FDG PET/CT imaging[5]. In literature, numerous studies have investigated the clinical significance of 18F-FDG uptake in the pituitary gland. Incidental accumulation in the pituitary mass is rare (0.007%-0.8%)[6-10]. In these studies, the final diagnoses following the evaluation of incidental pituitary 18F-FDG uptake included functioning pituitary adenomas, non-functioning adenomas, metastasis, hypophysitis, and pituitary cysts. Distinguishing pituitary metastases from benign lesions in cases of incidental 18-FDG uptake in the pituitary gland is critical for accurate staging, treatment decisions, and the management of associated pituitary hormone deficiencies, which may contribute to morbidity and mortality linked to the pituitary mass.

This retrospective study investigates the incidence of incidental 18-FDG pituitary uptake on whole-body PET/CT scans in patients with suspected or confirmed malignancies at a tertiary center. The clinical significance of unexpected hypermetabolic foci in the pituitary gland was also assessed using MRI and pituitary hormone assays.

Material and Method

In this retrospective study, approximately 60,000 18-FDG PET/CT scans performed for various indications by the nuclear medicine department were reviewed to identify cases with pituitary involvement. Pituitary involvement was defined as a standardized uptake value (SUV) greater than 2.5 in the pituitary gland. The clinical and laboratory characteristics of these patients were subsequently investigated using the Hospital Information Management System (HIMS).The following characteristics of 30 patients with pituitary involvement, identified between May 2012 and December 2020, were reviewed: primary malignancies, pituitary MRI characteristics (if available), pituitary functional evaluations, diagnoses of the pituitary lesion based on clinical and histopathological features (if applicable), and patterns of involvement of both the pituitary and primary lesions on 18-FDG PET/CT scans. Hormonal assays—including plasma ACTH, serum cortisol, prolactin, growth hormone (GH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and insulin-like growth factor 1 (IGF-1)—performed as part of the pituitary adenoma workup were analyzed. Five of the 30 patients were excluded for the following reasons: two patients had no accessible medical history, one patient did not undergo pituitary-related evaluation, and two patients were under 18 years old. In all included patients, a single 18-FDG PET/CT scan had been performed.

Statistical analysis

Descriptive statistics are summarized as counts and percentages for categorical variables and as means, standard deviations, and medians (interquartile range, minimum, and maximum) for continuous

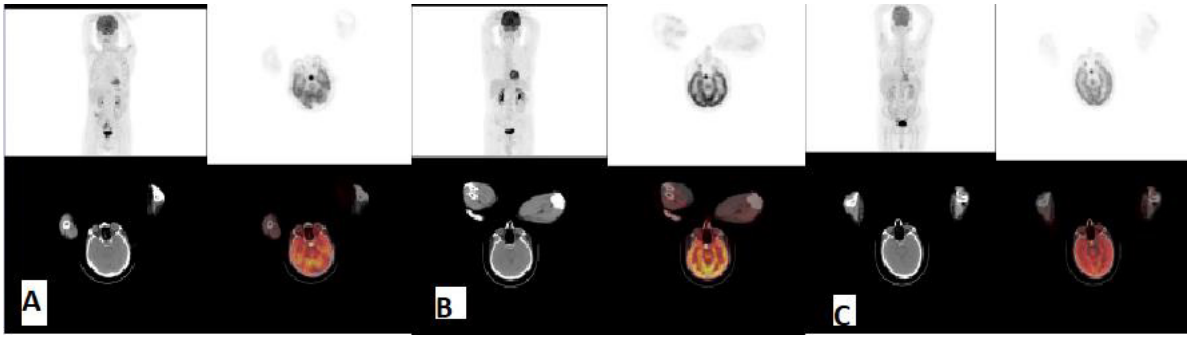


Figure 1 A: A male patient evaluated for mantle cell lymphoma was found to have a 20x17x17 mm pituitary adenoma/metastasis with pituitary insufficiency due to the lesion. We cannot discriminate between a pituitary adenoma and metastasis from a primary malignancy due to the lack of histopathological evaluation or follow-up 18-FDG PET/CT. B: A male patient, initially evaluated for a primary unknown malignancy–with no malignancy ultimately detected– was found to have a 13x13x11 mm pituitary adenoma on MRI. The patient underwent transsphenoidal surgery due to pituitary apoplexy. The final diagnosis revealed low staining for luteinizing hormone on histopathological evaluation. C: A male patient evaluated for esophageal adenocarcinoma was not evaluated with a pituitary MRI or pituitary hormonal assessment, despite showing pituitary uptake on 18-FDG PET/CT. This was due to progressive disease, and the patient died shortly after diagnosis.

variables. The Shapiro–Wilk test was used to assess the normality of continuous variables. Differences in categorical variables between groups were compared using the Chi-square or Fisher's exact test, as applicable. A p-value of <0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS statistics 20 software.

Ethics approval: This study was conducted according to the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of the University (ethical committee decision number: İ03-234-25).

Results

Patient Characteristics

Of the 25 patients included in the study, twenty one patients were female, and seven had died during the study period. The indications for the 18-FDG PET/CT scans were as follows: seven patients had lung cancer; one had infective endocarditis; two had gastrointestinal malignancies (esophageal carcinoma and rectal carcinoma); six had hematological malignancies; one had skin cancer; one had nasopharyngeal carcinoma; and one had renal carcinoma. Two patients had malignancies of unknown primary origin. In one case, no underlying malignancy was identified following extensive diagnostic evaluation. In the other, multiple metastatic lesions were detected; but the primary tumor focus could not be determined before the patient's death. Additionally, pulmonary nodule was detected in two patients. Some patient examples are presented in Figure 1.

Radiological evaluation

Eleven patients underwent pituitary MRI evaluation, and all of them had macroadenomas. The median SUVmax levels of the pituitary lesion and primary malignancy were 13.6 (range=5.40–38.80) IQR= 12.27 and 11.7 (range=0.00–116.0), IQR=22.78, respectively. The mean SUVmax levels of the pituitary lesion and lung, gastrointestinal, and hematological malignancies were statistically similar on PET/CT scan (Table 1).

Hormonal and Histopathological Evaluation

Seventeen of the 25 patients were not evaluated for hormonal status. Six of the 25 patients had nonfunctional adenomas in the hormonal evaluation. One patient, evaluated for a pulmonary nodule, was diagnosed with prolactinoma based on the hormonal evaluation.

Three of the 25 patients had pituitary insufficiency based on the hormonal evaluation. One of these three patients underwent transnasal transsphenoidal endoscopic surgery (TNTS) due to pituitary apoplexy. The patient, evaluated for an unknown malig-

Table 1 The SUVmax levels of pituitary lesions and Primary Malignancies

Malignancy (n)	Pituitary SUVmax	Malignancy SUVmax	P value[1]
Lung (7) median (min-max) IQR	10.30 (6.70-22.20) 5.00	18.20 (7.90-116.00) 19.50	0.091*
Gastrointestinal (4)	17.42 ±8.67	8.47±3.48(5.30-13.20)	0.928**
Hematolojik (6)	15.62±4.53(10.00-22.20)	15.54±16.38(0.00-37.10)	0.950**
P level[2], ***	0.230	0.162	

Unless otherwise specified, the data are presented as mean ± SD, (min-max). [1]Comparison of SUVmax of pituitary and primer malignancy, [2]comparison of pituitary SUVmax levels across different malignancies. *Wilcoxon test, **Student's t-test, ***Kruskal-Wallis test.

nancy and no malignancy was detected, was found to have a pituitary adenoma with low staining for luteinizing hormone on histopathological evaluation. Another one of these patients, who had lung carcinoma, was radiologically evaluated for metastasis, and the third had mantle cell lymphoma.

The other patient, who underwent TNTS surgery, had a pituitary adenoma without immunohistochemical evaluation and did not have pituitary insufficiency.

Discussion

In our study, incidental pituitary uptake detected on 18F-FDG PET/CT among malignancy patients were evaluated. The mean SUVmax levels of the pituitary lesions and different malignancies were statistically similar. Hormonal evaluation was omitted in 17 of the 25 patients, despite the presence of a pituitary macroadenoma. Six of the 25 patients had nonfunctional adenomas, one patient had a prolactinoma, and three patients had pituitary insufficiency based on hormonal evaluation. Histopathological evaluation revealed a pituitary adenoma in two patients. One patient had a lung carcinoma metastasis through radiological imaging.

18-FDG PET/CT is a valuable imaging method for staging malignancies, based on the higher uptake of radiopharmaceutical-labeled glucose in malignant cells, and providing whole-body scanning capabilities. Incidental 18-FDG uptake in the pituitary is rare due to its small size and low metabolic rate[6]. Our study reveals that approximately 0.05% of the patients demonstrated pituitary uptake, consistent with the existing literature[6]. Incidental 18-FDG uptake may also be attributed to the lower resolution in the pituitary region when compared to 18-FDG PET/CT and MRI, which reduces the likelihood of detecting microadenomas[11]. In the literature and in our study, specific 18-FDG uptake in pituitary adenomas has not been determined. In our study, all patients were diagnosed with macroadenomas, preventing a comparison with microadenomas. However, the literature suggests that adenoma size is the most significant determinant of 18-FDG uptake[6].

In our study, the cause of the uptake remains uncertain, as it was not confirmed by pathological examination using immunohistochemistry or by follow-up data after treatment in most patients. There have been case reports and studies in the literature describing pituitary uptake on 18F-FDG PET/CT scans. In a case report, a PET/CT scan performed for a mucosa-associated lymphoma on right eyelid revealed incidental pituitary uptake. Following MRI detection of a pituitary macroadenoma, histopathological examination established the diagnosis of a nonfunctioning adenoma[12]. In another notable case report, a patient with recurrent malignant melanoma who had undergone multiple surgical excisions and chemotherapy was found to have sellar and suprasellar lesions on pituitary MRI. These were initially presumed to be metastatic; however, histopathological examination following surgical resection revealed them to be pituitary adenomas[13]. Therefore, histopathological evaluation is essential in certain cases to ensure accurate diagnosis. In a further documented case report, a patient diagnosed with

non-Hodgkin lymphoma, PET/CT scan for staging showed intense uptake in the pituitary, which completely disappeared after four cycles of CHOP chemotherapy [14]. Case reports also have documented incidental 18- FDG uptake in functional pituitary adenomas, including prolactinoma, gonadotropinoma, somatotropinoma, and corticotropinoma[11]. 18-FDG PET/CT might have important diagnostic value in Cushing's disease[15]. In the literature, pituitary 18-FDG PET/CT uptake was detected in 0.073% of patients, and no radiological evidence of metastasis from primary malignancy. Histopathological examination of three patients revealed two cases of acromegaly and one case of a nonfunctional adenoma[6]. In another study, pituitary uptake occurred in 0.23% of the patients, with pituitary adenoma being the most frequently identified etiology (58%), followed by tubercular hypophysitis (8.5%) [10].

Incidental pituitary uptake is often overlooked in both the literature and our study, particularly in patients with advanced metastatic disease. In cases with primary malignancy, especially those involving macroadenomas, pituitary insufficiency (such as central hypothyroidism or central hypocortisolism) should be considered. Given the significant physical stress from chemotherapy, surgery, and other procedures in these patients, it is crucial not to overlook pituitary insufficiency, as it can have substantial impact on morbidity and mortality. Due to overlapping radiographic features, particularly in patients with a history of cancer, distinguishing pituitary metastases from adenomas based solely on imaging can be challenging. While radiological and clinical evaluations can differentiate metastatic lesions from benign ones in certain situations, this may not be possible in the case of slow-growing malignancies. Since pituitary 18-FDG uptake does not indicate metastasis, histopathological evaluation remains essential for a definitive diagnosis.

As with similar studies in the literature, our study is limited by a small cohort size and a retrospective design. Furthermore, hormonal, histopathological, and follow-up radiological evaluations were not performed in the majority of patients.

There is a need for future studies in which hormonal, radiological, and histopathological evaluations are performed on all patients with incidental pituitary uptake identified on 18F-FDG PET/CT, including those with microadenomas, to distinguish between malignant and non-malignant uptakes and contribute to the development of diagnostic algorithms, predictive models, or systematic follow-up strategies. In conclusion, the 18-FDG uptake can sometimes be misinterpreted as metastases in patients with diagnosed malignancy, it is essential to consider the clinical context, other diagnostic findings, and hormonal evaluation when interpreting 18-FDG PET/CT images showing notable pituitary uptake. Additionally, non-malignant conditions should not be disregarded. In this patient group, which is under significant physical stress, evaluating and treating pituitary insufficiency is essential.

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