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ARAŞTIRMA / RESEARCH

The value of FDG-PET/CT in the assessment of patients with non-Hodgkin's lymphoma of tonsil

Tonsil non-Hodgkin lenfomalı hastaların değerlendirilmesinde FDG-PET/BT'nin değeri

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Abstract

Purpose: The purpose of this study is to evaluate the value of FDG-PET/CT in staging and re-staging tonsillar lymphoma.

Materials and Methods: Twenty-nine patients with tonsillar lymphoma who had been evaluated with FDG-PET/CT in our center. The mean age was 44±20 years.The majority of patients presented with cervical lymphadenopathy. All patients included in this study were diagnosed on the basis of histopathology. Patients were indicated for primary tumor detection, metabolic characterization, staging, restaging and response to treatment.

Results: Twelve patients out of 29 were referred to our clinic for staging and 17 were for restaging. Five patients presented primary focus in tonsils and lymph node metastasis. Two patients presented no metastasis and primary focus in tonsils only. The remaining five patients who had tonsillectomy prior to PET/CT presented lymph node metastasis. FDG-PET/CT for restaging was performed on 17 patients with tonsillectomy and / or chemoradiotherapy. Seven patients had negative PET/CT results revealing cure, others had local recurrence and lymphatic metastasis. SUV max values of FDG-PET/CT were found to be 11 and higher where as SUVmax in patients with marginal zone lymphoma, Burkitt's lymphoma and mixed cellular lymphoma were 5.5, 9.5 and 7.6, respectively.

Conclusion: FDG-PET/CT imaging is a valuable tool for staging and as a follow-up modality for assessing the therapeutic response of patients suffering from primary extranodal lymphoma and in detecting malignancies.

Key words: Primary tonsillar lymphoma; FDG-PET/CT; extranodal non-Hodgkin's lymphomas; head and neck

Öz

Amaç: Bu çalışmanın amacı primer tonsil lenfomalarda FDG-PET/BT'nin evrelemedeki ve yeniden evrelemedeki değerini araştırmaktır.

Gereç ve Yöntem: Merkezimizde FDG-PET/BT uygulanmış 29 tonsil lenfomalı hasta değerlendirildi. Yaş ortalaması 44 ± 20 yıl idi. Bu çalışmaya dahil edilen tüm hastalarda histopatolojik olarak tanı konmuştu. Hastalar, primer tümör bulguları evreleme, metabolic karakterizasyon ve yeniden evreleme yapıldı.

Bulgular: Yirmidokuz hastanın 12'si kliniğimize evreleme, 17'si yeniden evreleme için yönlendirildi. Evreleme için müracaat eden 12 hastanın 5 tanesine tonsillektomi uygulanmış, geri kalan 7 tanesi ise henüz opere olmamıştı. PET/BT uygulaması öncesi tonsillektomi uygulanan hastaların beşinde de lenf nodu metastazı saptandı. Geri kalan 7 tane hastanın ise 5'inde tonsil ve beraberinde lenf nodu mestastazı saptanırken 2 tanesinde sadece tonsil tutulumu tespit edildi. Tedavi sonrası yeniden evreleme amacıyla FDG-PET/BT uygulanan 17 hastanın 7'sinde PET/BT negatif idi. Geri kalan 10 hastada lokal nüks ve lenfatik metastazlar saptandı. FDG-PET/BT'nin SUV maksimal değerlerinin ortalamaları sırasıyla marjinal zon lenfomalarda 5.5, Burkitt lenfomalarda 9.5 ve mikst sellüler tip lenfomalarda 7.6 olarak bulundu.

Sonuç: FDG-PET/BT görüntüleme, primer ekstranodal lenfoma ve malignitelerin teshisinde evreleme ve tedaviye yanıtın değerlendirilmesinde değerli bir araçtır.

Anahtar kelimeler: Primer tolsil lenfoma; FDG-PET/BT; ekstranodal non-Hodgkin's lenfoma; bas ve boyun

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INTRODUCTION

Lymphoma is a general term for a histologically heterogeneous group of malignancies of the lymphoreticular system. Lymphoma is the second most common neoplasm of the head and neck after squamous cell carcinoma. Waldeyer's ring (including tonsil, nasopharynx, and base of tongue) is the most common extranodal site[1-5]. Primary extranodal non-Hodgkin's lymphomas (NHL) of the head and neck account for 10–20% of all NHL. The tonsil is the most common primary extranodal site of head and neck NHL, primary tonsillar lymphoma (TL) accounting for less than 1% of head and neck malignancies [2,3].

The majority of tonsillar lymphomas have an aggressive histology. The most common histological type of lymphoma involving the head and neck region is diffuse large B-cell lymphoma (DLBCL)[1,6,7].

Non-Hodgkin's lymphoma has a male predominance and tends to affect the older age group [4]. Primary tonsillar lymphoma has a peak incidence in the 6th and 7th decades of life in published series[2]. These lymphomas present as tonsillar swelling, cervical adenopathy, dysphagia, odynophagia, or with a sore throat.

18-fluorine fluorodeoxyglucose positron emissiontomography/computed tomography (FDG-PET/CT) imaging is increasinglyused in many centers for staging and assessment of the therapeutic response in patients diagnosed with lymphoma. Several studies have shown better performance of FDG-PET/CT for accurately staging lymphomas compared to computed tomography (CT) or magnetic resonance imaging (MRI) alone[1,6,8]. Furthermore, for assessment of the response to therapy, positron emission tomography/computed tomography (PET/CT) has high prognostic value[1,8-10].

The standardized uptake value (SUV), an index of glucose metabolism on FDG-PET image, is the ratio between the measured and expected uptake if FDG were distributed evenly throughout the body. The maximum SUV (SUVmax) has been used to evaluate the degree of malignancy, metabolic response to therapy, and early detection of disease recurrence[1,8-10].

Such valuable information may change the treatment plan and improve the prognosis. Integrated PET/CT offers the advantage of combining functional and anatomical information, and it has been shown to be more accurate[1,6]. Imaging studies of lymphomas involving tonsils have been less reported. The purpose of this study is to evaluate the value of FDG-PET/CT in staging and re-staging tonsil lymphomas.

MATERIALS AND METHODS

Patients

Twenty-nine patients with primary tonsillary non-Hodgkin's lymphoma (23 diffuse large B-cell lymphoma (DLBCL), one marginal zone B-cell lymphoma, one malignant T-cell lymphoma, two Burkitt lymphoma, two mixed cellular small and large cell lymphoma) who had been evaluated with FDG-PET/CT in the Okmeydani Training and Research Hospital.

Treatment consisted of a combination of chemotherapy and radiotherapy with/without surgery for the majority of patients. Patients were indicated for primary tumor detection staging, restaging, response to treatment and metabolic characterization.

Inclusion criteria: The study included the patients in whom, based on histopatological examination of the biopsied tumor, a primary lymphoma was diagnosed. Exclusion criteria: The patients with primary non-hodgkin lymphoma either then tonsil were excluded from the study. Seven out of 36 patients were excluded.

Patient preparations

Patients had fasted for at least 6 hours and their blood glucose levels were controlled before FDG injection. All of the patients had blood glucose levels lower than 200 mg/dl. No i.v. contrast material was used for the CT scans. Water-soluble iodinated contrast material diluted in 1,000 ml of water was given to each patient orally prior to the investigation. CT scans with oral contrast are performed to get a detailed image of the stomach and intestines. PET/CT Imaging:

Whole body PET/CT imaging was performed on a biograph (Siemens Biograph 6, Chicago, IL, USA) using a full-ring HI-REZ LSO PET and a six-slice CT scanner. Data were acquired 60 minutes

following the administration of FDG (296-555 MBq FDG according to body weight). The CT scan was performed first with the following parameters: 40-60 mAs, 140 kV and 5-mm section thickness. The CT data were matched and fused with the PET data. Attenuation-corrected PET images, CT images and PET/CT fused images were displayed using dedicated software (Esoft work station). FDG uptake was analyzed semiquantitatively by recording the SUVmax. Fused FDG-PET/CT images were analyzed in at least three planes – coronary, sagittal and axial – in the gray scale color table for PET.

Statistical analysis

Descriptive statistics was used to describe baseline demographic and clinical profile of all patients' data. SUV has been used to follow up response to therapy. Because SUV is dependent on a patient's body weight and the radiotracer injected, corrections for residual activity in the syringe and tubing and for the dose of FDG at time of injection are required to prevent incorrect results

The sites suggested by FDG-PET/CT were confirmed by histopathologic analysis of tissue obtained by biopsy or surgery, considered as the gold standard.

RESULTS

There were 12 male patients (42%) and 17 female patients (58%). The mean age was 44±18 years (age range 8–86 years) (Table 1). The majority of patients presented with cervical lymphadenopathy. Patients applied to the doctor with a complaint of cervical adenopathy (n:17), sore throat (n:16), tonsillar swelling (n:14), dysphagia (n:12) and some other systemic symptoms (n:5). The duration of symptoms ranged from 1 week to 2 months. All patients included in this study were diagnosed on the basis of histopathology. The histologic verification was done by tonsillectomy in 5 patients and biopsy in 24 patients (14 left, 12 right and 3 bilateral tonsils) (Table 2).

Histologically, 23 patients (79%) had high-grade diffuse large B-cell lymphoma,2 (7%) had burkitt lymphoma, 1 (3.5%) malignT-cell lymphoma, 1 (3.5 %) had marginal zone B-cell lymphoma and 2 (7%) had mixed cellular small and large cell lymphoma (Figure 1).

FDG-PET/CT was applied to 29 patients; 12 for staging and 17 for restaging. Seven out of 12 patients admitted for staging, were preoperative and 5 patients were postoperative. Two out of 7 patients with FDG uptake was seen in tonsils only (SUVmax:22± 8),tonsil and unilateral jugular chain LAP in 2, bilateral supradiafragmatic and infradiafragmatic LAP in 2 and bilateral supradiafragmatic and infradiafragmatic LAP with bone and spleen metastasis in 1 patient.

In 5 post-tonsillectomy patients metastasis were found, as followed; 3 Unilateral jugular chain LAP (in one additional splenic involvement), 1 bilateral jugular chain LAP, 1 bilateral jugular chain LAP with bone metastasis.

Of the 17 patients assessed for re-staging, 6 received tonsillectomy and 11 received CT + RT. In four out of six patients with tonsillectomy, FDG-PET/CT was negative, revealing cure. In one patient unilateral jugular chain LAP, and in another one bilateral juguler LAP with nodule in lungs were found. In three out of 11 patients who received CT and RT, FDG-PET/CT was negative, revealing cure. Local recurrence and bilateral juguler LAP was seen in 2 patients, local recurrence and unilateral juguler LAP in 6.

Table 1. Clinical characteristics of patients included in the study (n=29)

	N (%=)
Sex	
Male	12 (41)
Female	17 (59)
Age (Median (range))	44±18 years (8–81 years)
Lymphoma type	
Diffuse large B-cell lymphoma	23 (79)
Marginal zone B-cell lymphoma	1 (3.5)
Malignant T-cell lymphoma	1 (3.5)
Burkit lymphoma	2 (7)
Mixt cellular lymphoma	2 (7)

Table 2. Patient details and histopathology

Patient	Sex	Age	Histopathology	Prosdure	L/R		CT	RT
1	F	59	diffuse large B-cell lymphoma	Biopsy	L	restaging	yes	yes
2	M	8	burkit lymphoma	tonsillectomy	R	Staging	no	no
3	F	43	diffuse large B-cell lymphoma	Biopsy	L	Staging	no	no
4	F	26	diffuse large B-cell lymphoma	Biopsy	R	Staging	no	no
5	F	53	diffuse large B-cell lymphoma	Biopsy	R	restaging	yes	yes
6	F	81	diffuse large B-cell lymphoma	Biopsy	L	restaging	yes	yes
7	M	21	diffuse large B-cell lymphoma	tonsillectomy	L	restaging	yes	yes
8	F	46	diffuse large B-cell lymphoma	tonsillectomy	R	Staging	no	no
9	M	45	diffuse large B-cell lymphoma	Biopsy	R	restaging	yes	no
10	M	57	mixt cellular lymphoma	tonsillectomy	B	restaging	yes	yes
11	F	41	diffuse large B-cell lymphoma	Biopsy	R	Staging	no	no
12	F	29	diffuse large B-cell lymphoma	Biopsy	L	restaging	yes	yes
13	M	69	diffuse large B-cell lymphoma	Biopsy	L	Staging	no	no
14	F	48	diffuse large B-cell lymphoma	Biopsy	L	restaging	yes	yes
15	M	58	diffuse large B-cell lymphoma	Biopsy	L	Staging	no	no
16	F	33	diffuse large B-cell lymphoma	Biopsy	R	restaging	yes	yes
17	M	60	marginal zone B-cell ymphoma	tonsillectomy	L	restaging	no	yes
18	F	53	diffuse large B-cell lymphoma	Biopsy	L	restaging	yes	yes
19	F	71	malignant T-cell lymphoma	tonsillectomy	R	Staging	no	no
20	F	61	diffuse large B-cell lymphoma	Biopsy	L	restaging	yes	yes
21	M	23	diffuse large B-cell lymphoma	Biopsy	R	Staging	no	no
22	M	45	diffuse large B-cell lymphoma	tonsillectomy	R	restaging	yes	yes
23	F	30	diffuse large B-cell lymphoma	tonsillectomy	B	restaging	yes	yes
24	M	11	burkit lymphoma	tonsillectomy	B	restaging	var	no
25	F	36	diffuse large B-cell lymphoma	Biopsy	R	restaging	yes	yes
26	M	46	diffuse large B-cell lymphoma	tonsillectomy	R	Staging	no	no
27	F	22	diffuse large B-cell lymphoma	Biopsy	L	restaging	yes	yes
28	M	21	diffuse large B-cell lymphoma	Biopsy	L	Staging	no	no
29	F	86	mixt cellular lymphoma	tonsillectomy	L	Staging	no	no

Male : M, Female : F, Left: L , Right:R, Bilaterally: B, Chemotherapy: CT, Radiotherapy: RT

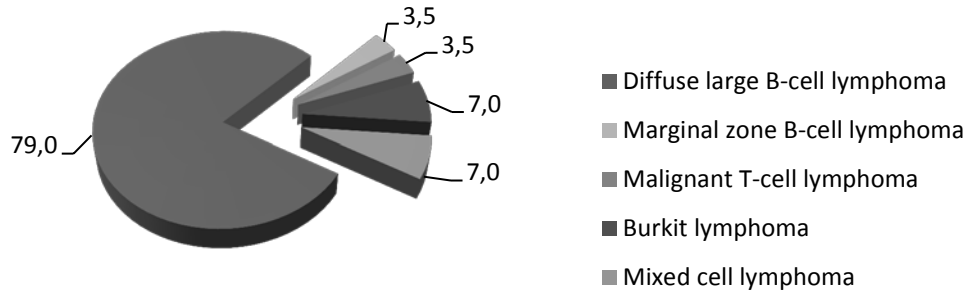

Figure 1. Histologic subtypes of primary tonsil non-Hodgkin's lymphoma

The SUVmax value of primary tumor and metastatic lymph nodes ranged from 5.5 to 46.SUVmaxvalue of cervical metastatic lymph node basically matched that of the primary tumor.

SUVmax values of FDG-PET/CT were found to be 11 and higher where as SUVmax in patients with marginal zone lymphoma, Burkitt's lymphoma and mixed cellular lymphoma were 5.5,9.5 and 7.6, respectively Discussion:

In current study, we retrospectively evaluated the clinical outcomes according to the maximum standardized FDG-PET/CT uptake (SUVmax) values of the primary lesion and local or distant metastasis. We found that higher SUVmax in both staging and restaging revealed higher probability of metastasis. As much as we know, there is no study with large series on primary tonsil lymphoma evaluated with FDG-PET/CT.

Tonsillar lymphoma accounts for about 80% of the non-Hodgkin's lymphomas of Waldeyer's ring. The majority of tonsillar lymphomas have an aggressive histology. The most common type of lymphoma involving the head and neck region is diffuse large B-cell lymphoma[1-6]. Our results showed 80% DLBCL.

Non-Hodgkin's lymphoma has a male predominance and tends to affect the older age group[4].Primary tonsillar lymphoma has a peak incidence in the 6th and 7th decades of life in published series[2]. Our results contradicted to the literature with female predominance and tend to affect the younger age group with a peak incidence in the 2th and 4th decades of life .In our study, the median age was 44 years, with 6 (20%) of the patients above 60 years (4F:2M). Our data was consistent with the study of Byun et al., in which the median age of patients at was 50 years. Byun had described equal gender distribution whereas we had a female predominance[10].

Diagnosis and staging is critical in the treatment of patients with head and neck cancer. To establish treatment planning and prognosis of patients; accurate initial assessment of the primary site, nodal involvement, and metastasis evaluation is crucial.

Reports of FDG-PET/CT related to primary extranodal lymphomas in other locations (such as breast, thyroid, pancreas, etc) are uncommon but have been reported[3,5,7]. Reports about primary tonsillar lymphoma are even rarer.

Physiologic or reactive FDG uptake is accumulation of FDG within macrophages and lymphocytes, seen in the lymphatic structures of the head and neck (Waldeyer ring, lymph nodes, and lymphatic channels). Physiological FDG accumulation is also seen in extraocular muscle, masticatory muscle, vocal cord, and the major salivary glands: parotid, submandibular, and sublingual gland. Infection, or inflammation that may or may not be due to recent surgery, chemotherapy, or radiation therapy, can also result in FDG accumulation and should be taken into account in the interpretation of FDG-avid lesions in the head and neck[11].Diagnosis of tonsillitis is generally determined with symmetric

high FDG accumulations, whereas tonsillar lymphoma usually presents as a unilaterally enlarged palatine tonsil[12,13].

High SUV uptake may predict for a more aggressive B-Non Hodgkin Lymphoma[14]. Clinically, SUVmax>2.5 was often set as the criteria of malignant lesions. Previous studies had shown that the higher the SUVmax value, the higher the degree of malignancy and, that the SUVmax value of aggressive lymphoma was higher than that of the indolent lymphoma[15,16]. Schöderet al found out that when SUVmax>11, the aggressiveness of lymphoma was greater. In this study, the SUVmax values of 25 primary tumors were higher than 11, and the SUVmax value of cervical metastatic lymph node basically matched that of the primary tumor[16].Our results are consistent with the literature.

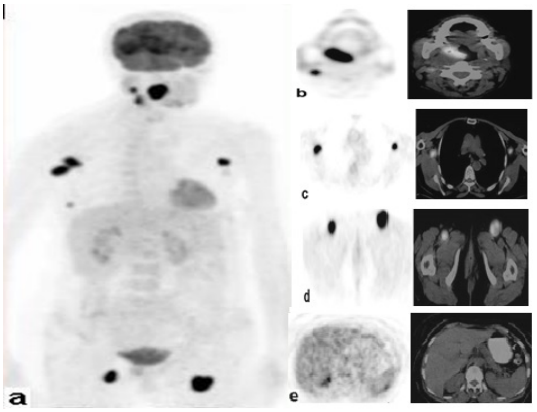

Figure 2. Findings of a 71-year-old patient at initial staging performed by FDG-PET/CT. Maximum-intensity projection (MIP) of FDG-PET data (figure2a), trans-axial FDG-PET, and fused PET/CT (trans-axial) images revealed increased FDG uptake is seen in right tonsil area (SUVmax: 22), right submandibular, upper right juguler group (figure 2b), bilateral axillary fossa (SUVmax: 15)(figure 2c), bilateral femoroinguinal lymphatic station (figure 2d) and posterolateral subcapsular spleen area (figure 2e).

Although PET is better for the assessment of metastasis in lymph nodes that appear morphologically normal according to size criteria, CT is more accurate for assessing the level and size of nodes, the number of nodes in conglomerate nodal masses, and the presence of extracapsular spread factors that are important for determining the prognosis of patients; macroscopic extranodal spread carries a 10 times greater risk of recurrence and reduces survival by 50% compared with nodes that have either no or only microscopic extracapsular spread. Also, intense 18F-FDG uptake by the primary tumor may obscure uptake by adjacent enlarged lymph nodes, thereby resulting in false-negative results. Therefore, a combination of PET/CT is likely to result in more accurate nodal staging than PET or CT alone[9,17,18].

Our series shows an excellent overall outcome in every age group, especially for the DLBCL. Because high 18FFDG uptake of malignant tissue is associated with a high proliferation rate, one can assume that metabolic imaging is an indicator of tumor aggressiveness, individual tumor chemosensitivity, or tumor resistance to the planned treatment[19].In normal individuals, 18F-FDG uptake in the spleen is less than that in the liver and does not change significantly with age. The splenic uptake greater than hepatic uptake is considered abnormal, diffusely increased splenic uptake, greater than hepatic uptake, is a relatively reliable indication of lymphomatous involvement of the spleen in lymphoma, showing an extranodal extra lymphatic involvement. On FDG-PET/CT, lymphomatous involvement of the spleen may manifest as either focal or diffuse uptake. Rini et al.[20] reported that using splenic uptake greater than hepatic uptake as the criterion for a positive study, FDG-PET/CT had a very high sensitivity (92–100%) for detecting splenic disease. NHL had the trend of multi-center origin or distant spread, and the most commonly involved organs were the abdominal organs[21,22]. Thus; FDG PET/CT has another obvious advantage of performing whole body imaging in the staging and restaging of NHL which helps the distant organ metastasis detection.

In current study application of FDG-PET/CT resulted a change of staging in 20% with nodal disease (6 patients) and in 17% with extranodal disease (5 patients; 1 lung, 2 bone, 2 spleen metastasis).

In conclusion, FDG-PET/CT imaging has proven to be of value for staging, restaging and as a follow-up modality for assessing the therapeutic response of patients suffering from primary extra- nodal tonsil lymphoma and in detecting distant metastatic disease.

REFERENCES

1. Schrepfer T, Haerle SK, Strobel K, Schaefer N, Hälg RA, Huber GF. The value of (18) F-fluorodeoxyglucose positron emission tomography/computed tomography for staging of primary extranodal head and neck lymphomas.Laryngoscope. 2010;120:937-44.
2. Mohammadianpanah M, Omidvai S, Mosalei A, Ahmadloo N. Treatment results of tonsillar lymphoma: a 10-year experience. Ann Hematol. 2005;84:223-226.
3. Wang XY, Wu N, Zhu Z, Zhao YF. Computed tomography features of enlarged tonsils as a first symptom of non-Hodgkin's lymphoma. Chin J Cancer. 2010;29:556-60.
4. King AD, Lei KI, Ahuja AT. MRI of primary non-Hodgkin's lymphoma of the palatine tonsil.Br J Radiol. 2001;74:226-229.
5. Ezzat A, Ibrahim E, El Weshi A, Khafaga YM, AlJurf M, Martin JM et al. Localized non-Hodgkin's lymphoma of Waldeyer's ring: clinical features, management, and prognosis of 130 adult patients. Head Neck. 2001;23:547-58.
6. Paes FM, Kalkanis DG, Sideras PA,Serafini AN. FDG PET/CT of extranodal involvement in non-Hodgkin lymphoma and Hodgkin disease. Radiographics. 2010;30:269-91.
7. Ngeow JY, Quek RH, Ng DC, Hee SW, Tao M, Lim LC et al. High SUV uptake on FDGPET/ CT predicts for an aggressive B-cell lymphoma in a prospective study of primary FDG-PET/CT staging in lymphoma. Ann Oncol. 2009;20:1543–7.
8. Kapoor V, Fukui MB, McCook BM. Role of 18FFDG PET/CT in the treatment of head and neck cancers: principles, technique, normal distribution, and initial staging. AJR Am J Roentgenol. 2005;184:579-587.
9. Schaefer NG, Hany TF, Taverna C, Seifert B, Stumpe KD, von Schulthess GK et al. Non-Hodgkin lymphoma and Hodgkin disease: coregistered FDG PET and CT at staging and restaging - do we need contrast-enhanced CT? Radiology. 2004;232:823-9.
10. Byun B, Na I, Cheon G, Kang HJ, Kim KM, Lee SS et al. Clinical significance of 18FFDG uptake by primary sites in patients with diffuse large B cell lymphoma in the head and neck: a pilot study. Ann Nucl Med. 2008;22:645-51.
11. Blodgett TM, Fukui MB, Snyderman CH, Branstetter BF 4th, McCook BM, Townsend DW et al. Combined PET-CT in the head and neck. Physiologic, altered physiologic, and artifactual FDG uptake. Radiographics.2005;25:897-912.
12. Zhang MJ, Jiang JJ, Jiang MS, He W. F-18 FDG PET/CT in primary tonsillar lymphoma. Clin Nucl Med. 2010;35:710-2.
13. Hosokai R, Imai C, Takachi T, Yoshida S, Iwabuchi H, Imamura M et al. Reactive tonsillar enlargement with strong 18F-FDG uptake after chemotherapy for tonsillar diffuse large B-cell lymphoma. J Pediatr Hematol Oncol. 2011;33:e87-8.
14. Zhang MJ, Jiang JJ, Jiang MS, He W. F-18 FDG PET/CT in primary tonsillar lymphoma. Clin Nucl Med. 2010;35:710-2.
15. Juweid ME, Cheson BD. Role of positron emission tomography in lymphoma. J Clin Oncol. 2005;23:4577-80.
16. Schoder H, Noy A, Gonen M, Weng L, Green D, Erdi YE et al. Intensity of 18fluorodeoxyglucose uptake in positron emission tomography distinguishes between indolent and aggressive non-Hodgkin'slymphoma. J Clin Oncol. 2005;23:4643-51.
17. Adams S, Baum RP, Stuckensen T, Bitter K, Hör G. Prospective comparison of 18F-FDG PET with conventional imaging modalities (CT, MRI, US) in lymph node staging of head and neck cancer. Eur J Nucl Med. 1998;25:1255–260.
18. Yang D, Min J, Jeong Y, Ahn JS, Kim YK, Cho SH et al. The combined evaluation of interim contrast-enhanced computerized tomography (CT) and FDG-PET/CT predicts the clinical outcomes and may impact on the therapeutic plans in patients with aggressive non-Hodgkin's lymphoma. Ann Hematol. 2009;88:425-32.
19. Toma P, Granata C, Rossi A, Garaventa A. Multimodality imaging of Hodgkin disease and non-Hodgkin lymphomas in children. Radiographics. 2007;27:1335-54.
20. Rini JN, Leonidas JC, Tomas MB, Palestro CJ. 18F-FDG PET versus CT for evaluating the spleen during initial staging of lymphoma. J Nucl Med. 2003;44:1072-4.
21. Saito A, Takashima S, Takayama F, Kawakami S, Momose M, Matsushita T. Spontaneous extensive necrosis in non-Hodgkin lymphoma: prevalence and clinical significance. J Comput Assist Tomogr, 2001;25:482-6.
22. Comert M, Ersoy Gunes A, Saydam G. Diffüz büyük b-hücreli lenfoma. Turkiye Klinikleri J Hem Onc-Special Topics. 2012;5:35-42.