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Cervical lymph node hyperplasia on [^{18}F]-fluorodeoxyglucose positron emission tomography/computed tomography scan after treatment of children and adolescents with malignant lymphoma

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ABSTRACT

Purpose: To define imaging manifestations and clinical prognosis of cervical lymph node hyperplasia using [^{18}F]-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) scanning after treatment of children and adolescents with malignant lymphoma.
Methods: Children and adolescent patients with malignant lymphoma who had high FDG uptake in their cervical lymph nodes via PET/CT after treatment, which was not due to tumor recurrence or residue, were retrospectively analyzed.
Results: Twenty-seven patients with a median age of 12 years were included; 11 had Hodgkin's disease and 16 had non-Hodgkin's lymphoma. The time from PET/CT scan to completion of therapy was 1–36 months, 85.2% (23/27) of which took place within 12 months. Three patients had confirmed lymph node follicular hyperplasia by biopsy, while all 27 patients achieved disease-free survival during the follow-up period. The maximum standardized uptake values (SUV_{max}) of cervical lymph nodes were 2.2–16.2 and the maximum short axis ranged from 0.3 to 1.2 cm. Cervical lymph node hyperplasia was noted in neck levels I–V, and neck level II bilaterally had the highest incidence (100%). Bilateral cervical lymph node hyperplasia was symmetrical in terms of both the SUV_{max} and affected locations. Thymic hyperplasia and nasopharyngeal lymphoid hyperplasia were both observed in 24 patients (88.9%). There was no relationship in terms of the SUV_{max} between cervical lymph nodes and thymic tissue, cervical nodes or nasopharyngeal lymphoid tissue.
Conclusion: Cervical lymph node hyperplasia with high FDG uptake on PET/CT scans found after treating children and adolescents with malignant lymphoma can be benign processes. Awareness of this possibility may help avoid invasive procedures and over-treatment.

1. Introduction

Benign thymic and nasopharyngeal lymphoid hyperplasia following treatment has been reported in children and adolescents with malignancies [1–7]. According to our own diagnostic experience, we have previously identified benign lymphoid hyperplasia in lymph nodes of children and adolescents with malignant lymphoma following therapy. These hyperplastic lymph nodes present with high [^{18}F]-fluorodeoxyglucose (FDG) uptake on positron emission tomography/computed tomography (PET/CT) imaging and often cause a diagnostic dilemma for both radiologists and clinicians.

Cervical lymph nodes are common hyperplastic locations in children and adolescents with malignant lymphoma and their enlargement is easily found via physical examination during follow-up [1]. Therefore, it is necessary to accurately diagnose cervical lymph node hyperplasia in order to avoid invasive procedures and over-treatment.

The present study was designed to define the manifestations and clinical prognosis of cervical lymph node hyperplasia on FDG

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PET/CT scans after treating malignant lymphoma in children and adolescents.

2. Materials and methods

2.1. Patient selection

The medical records of malignant lymphoma patients who had undergone FDG PET/CT between October 2007 and October 2012 were retrospectively reviewed. The eligibility requirements for inclusion were as follows: age ≤18 years, no symptoms of recurrence or residue on PET/CT imaging during the follow-up after cessation of antitumor therapy, cervical lymph nodes with high FDG uptake on PET/CT imaging, no antitumor therapy after PET/CT, a minimum follow-up period of 12 months following PET/CT scan, and no tumor recurrence or residue during the clinical follow-up or by lymph node biopsy. The exclusion criteria were as follows: other malignant tumor history, acquired immunodeficiency syndrome (AIDS), and antitumor therapy after PET/CT.

The criteria for clinical evaluation of no tumor recurrence or residue were as follows: histopathologically negative results on lymph biopsy, lymph nodes with high FDG uptake diminished or disappeared on follow-up physical examinations and imaging without antitumor therapy, lymph nodes remained the same size for a minimum follow-up period of 12 months without antitumor therapy, and no clinical symptoms of tumor recurrence for a minimum follow-up period of 12 months without antitumor therapy.

This study was performed with the approval of the institutional review board of the Cancer Center at Sun Yat-sen University. For all patients, parental informed consent was obtained prior to the PET/CT scan.

2.2. FDG PET/CT imaging

Scanning was performed using a dedicated PET/CT system (Discovery ST-16; GE Medical Systems, Milwaukee, WI, USA). Patients fasted for 6 h before intravenous injection with ^{18}F-FDG (4.4–7.4 MBq/kg). The patient then lay down and rested in a dark room for 45–60 min prior to PET/CT imaging. The patients were scanned in a supine position from the skull to the middle part of the femur. CT scan was performed prior to PET, and the resulting data were used to generate a PET attenuation correction map. PET images were reconstructed with a slice thickness of 3.75 mm using the ordered subsets expectation maximization (OSEM) iterative image reconstruction method. PET, CT, and fused PET/CT images were generated for review on a Xeleris computer workstation (GE Medical Systems).

2.3. Image interpretation

All PET/CT scans were reviewed retrospectively by two experienced nuclear medicine physicians. The location and size of cervical lymph nodes with high FDG uptake were recorded. Concomitant disease, such as thymic and nasopharyngeal lymphoid hyperplasia, and lymph nodes with high FDG uptake in other locations were also recorded. The maximum standardized uptake values (SUV_{max}) was defined as the highest activity concentration within the target tissue with respect to the injected does per kilogram of body weight, as determined by using the standard software of the manufacturer.

2.4. Statistical analysis

The SUV_{max} of bilateral cervical lymph nodes were recorded, and the symmetry ratios of the bilateral cervical lymph nodes were analyzed using *t*-tests. The SUV_{max} of cervical lymph nodes and the SUV_{max} of nasopharyngeal lymphoid tissue were recorded and underwent a Pearson correlation analysis. Similarly, the SUV_{max} of the cervical lymph nodes and the SUV_{max} of thymic tissue were recorded and underwent a Pearson correlation analysis.

3. Results

3.1. Patients and clinical features

A total of 27 patients who satisfied the selection criteria were recruited for this study; 19 were male and 8 were female. The median age was 12 years (range 3–18 years). Eleven patients had Hodgkin's disease (HD) and 16 had non-Hodgkin's lymphoma (NHL). Of the 11 patients with HD, 4 had nodular sclerosis HD, 3 had mixed cellularity HD, and 4 had lymphocyte predominant HD. According to the Ann Arbor staging system, one HD was stage I, five were stage II, two were stage III, and three were stage IV. Of the 16 patients with NHL, 3 had Burkitt's lymphoma, 3 had diffuse large B cell lymphoma, 3 had lymphoblastic lymphoma, 5 had anaplastic large cell lymphoma, 1 had natural killer (NK)/T cell lymphoma, and 1 had peripheral T cell lymphoma. According to the Ann Arbor staging system, 1 NHL was stage I, 2 were stage II, 5 were III, and 8 were stage IV.

All patients finished their anti-tumor therapy, the protocols for which were chosen according to stage and pathology subtype. No patient had symptoms of recurrence or residue before PET/CT imaging, and all relevant blood tests, including complete blood counts and lactate dehydrogenase levels, were normal.

Only four patients did not have high FDG uptake cervical lymph nodes before treatment or during treatment. Eight patients had lymphoma infiltration in the cervical lymph nodes before treatment, but did not have high FDG uptake in cervical lymph nodes during treatment. Fifteen patients had small cervical lymph nodes with slightly increased FDG uptake or without FDG uptake at the end of treatment, but cervical lymph nodes became enlarged and had higher FDG uptake during follow-up.

The range of time from the end of therapy to the PET/CT scans was 1–36 months (median, 6 months); 23 patients had scans conducted less than 12 months after the last treatment, whereas two patients had scans <24 months after treatment, and 2 patients <36 months after treatment.

3.2. PET/CT manifestation of cervical lymph node hyperplasia

All patients had high FDG uptake in their cervical lymph nodes; the SUV_{max} ranged from 2.2 to 16.2 (median, 5.4). The maximum short axis of the cervical lymph nodes ranged from 0.3 to 1.2 cm (median, 0.8 cm). The locations of cervical lymph nodes with high FDG uptake are listed in Table 1.

All 27 patients had high FDG uptake in bilateral neck level II lymph nodes (100%). High FDG uptake in bilateral cervical lymph nodes had a symmetrical distribution in 18 patients (66.7%).

Table 1
The location and frequency of cervical lymph nodes with high [^{18}F]-fluorodeoxyglucose uptake.

Neck level	Left (no. of patients)	Right (no. of patients)
Retropharyngeal	0	1
Ib	3	2
II	27	27
III	6	5
IV	4	3
V	5	4