Medicine®

CLINICAL CASE REPORT

OPEN

A Case Report: The Diagnosis and Therapeutic Evaluation for a Rare Disease of Langerhans Cell Histiocytosis Involving Thyroid

Ye-Feng Cai, MD, Qing-Xuan Wang, MD, Chun-Jue Ni, MD, Si-Yang Dong, MD, Lin Lv, MD, Quan Li, MD, En-Dong Chen, MD, and Xiao-Hua Zhang, MD

Abstract: Langerhans cell histiocytosis (LCH) involving the thyroid gland is extremely rare. Currently, the diagnosis and therapeutic evaluation for LCH involving thyroid is a challenge.

We reported a rare case of LCH involving thyroid, presenting as painless thyroid goiters, and successfully performed positron emission tomography/computed tomography (PET/CT) to make an accurate diagnosis and therapeutic evaluation for LCH.

Although the histology or cytology is the golden standard for the diagnosis of LCH involving thyroid, the PET/CT should be keep in mind when LCH involving thyroid with inconclusive cytologic results. During the treatment of LCH, PET/CT can be performed to assess the therapeutic effect and select the most effective and reliable treatment for LCH.

(*Medicine* 94(44):e1891)

Abbreviations: FDG = fluorodeoxyglucose, FNAB = fine-needle aspiration biopsy, LCHL = angherans cell histiocytosis, PET/CT = positron emission tomography/computed tomography, SUV = standard uptake value.

INTRODUCTION

Langerhans cell histiocytosis (LCH) is a rare monoclonal disease, of which incidence rate is 4 to 5 per 1 million individuals, and mortality rate is about 3% in adults.[1,2] Its clinical presentation is highly variable because it can affect multiple organs, such as lung, bone, skin, lymph nodes, hypothalamopituitary axis, and other multiple sites.[3,4] However, due to the fact that involvement of the thyroid either as an isolated mass or as part of multisystemic disease is extremely rare, the diagnosis and therapeutic evaluation for such disease is still controversial. According to preliminary statistics, there were only less than 80 reported cases of LCH involving the thyroid gland. To the best of our knowledge, few studies had reported that the positron emission tomography/computed tomography (PET/CT) was used for diagnosis and therapeutic evaluation for LCH involving thyroid in detail.

The purpose of this article was to report a case and describe the use of PET/CT to make a diagnosis and therapeutic evaluation for LCH involving thyroid.

CASE REPORT

A 27-year-old man came to our hospital with painless thyroid nodules that had been present for more than 3 months. He had no symptoms, such as dysphagia, dyspnea, hoarseness, appetite changes, weight changes or palpitations, and no history of thyroid cancer. In the past, there was no treatment for his thyroid nodules. Thyroid ultrasound showed diffused hypoechogenicity and a $28 \times 13 \times 22$ mm hypoechoic nodule on the right side of the thyroid and a $16 \times 7 \times 11$ mm hypoechoic nodule on the left. Thyroid function tests were as follows: thyroid-stimulating hormone (TSH): 1.67 mIU/L (0.35–4.94 mIU/L); free triiodothyronine (FT3): 5.49 pmol/L (3.67–10.43 pmol/L); and free thyroxine (FT4): 11.3 pmol/L (7.5–21.1 pmol/L). Additionally, calcitonin, parathyroid hormone, thyroglobulin, antithyroglobulin, and antimicrosomal antibodies were also within normal range. Fine-needle aspiration biopsy (FNAB) showed atypical hyperplasia in thyroid nodule and considered the possibility of Langerhans cells infiltration (Fig. 1A). With the consideration of the thyroid nodules with limitation of cytologic results and LCH usually involving multiple systems, additional PET/CT was performed, and the result showed fluorodeoxyglucose (FDG) intense accumulation in the thyroid (SUV value = 7.2) and in the vertebral body of S1–2 (SUV value = 10.7) (Fig. 2A, B). Further questioning about his medical history revealed incidental slight pain in sacrococcygeal region. Therefore, according to his symptom and the result of PET/CT, we got a biopsy in the vertebral body of S1–2 and confirmed the LCH by the positive immunohistochemical staining of CD1α and S100 (Figure 1B–D). The final diagnosis was multisystemic LCH. Subsequently, the patient received a series of treatments containing chemotherapy (2 cycle VPE + MTX [Vindesine 4 mg + Etoposide 100 mg + Methotrexate 1.0 g] + 1 cycle IAE [Ifosfamide 3 g + Mesna 3.2 g + Etoposide 100 mg + Cytosine-arabinoside 200 mg] + 1 cycle MiniBEAM [Carmustine 125 mg + Etoposide 50 mg + Cytosine-arabinoside 150 mg + Melphalan 50 mg] + 1 cycle

Editor: Majid Assadi.
Received: July 10, 2015; revised: September 25, 2015; accepted: September 29, 2015.
From the Department of Oncology (Y-FC, Q-XW, S-YD, LL, QL, E-DC, X-HZ); and Department of Anesthesiology, the First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China (C-JN).
Correspondence: Xiao-Hua Zhang, Department of Oncology, the First Affiliated Hospital of Wenzhou Medical University, Wenzhou Medical University, No. 2 Fuxue Lane, Wenzhou 325000, China (e-mail: zxhoncology@126.com).
Co-correspondence: Quan Li, Department of Oncology, the First Affiliated Hospital of Wenzhou Medical University, Wenzhou Medical University, No. 2 Fuxue Lane, Wenzhou 325000, China (e-mail: lqsky1106@126.com).
Y-FC and Q-X W contributed equally to the writing of this article.
Y-FC and X-HZ designed the study. Q-XW and C-JN collected data. LL and S-YD prepared figures. E-DC, QL, Y-FC, and X-HZ reviewed the results, interpreted data, and wrote the manuscript. All authors saw and approved the final version of the paper.
This work was supported by a grant from the National High Technology Research and Development Program of 863 project of China (NO. 2012AA02A210).
The authors have no conflicts of interest to disclose.

ISSN: 0025-7974
DOI: 10.1097/MD.0000000000001891

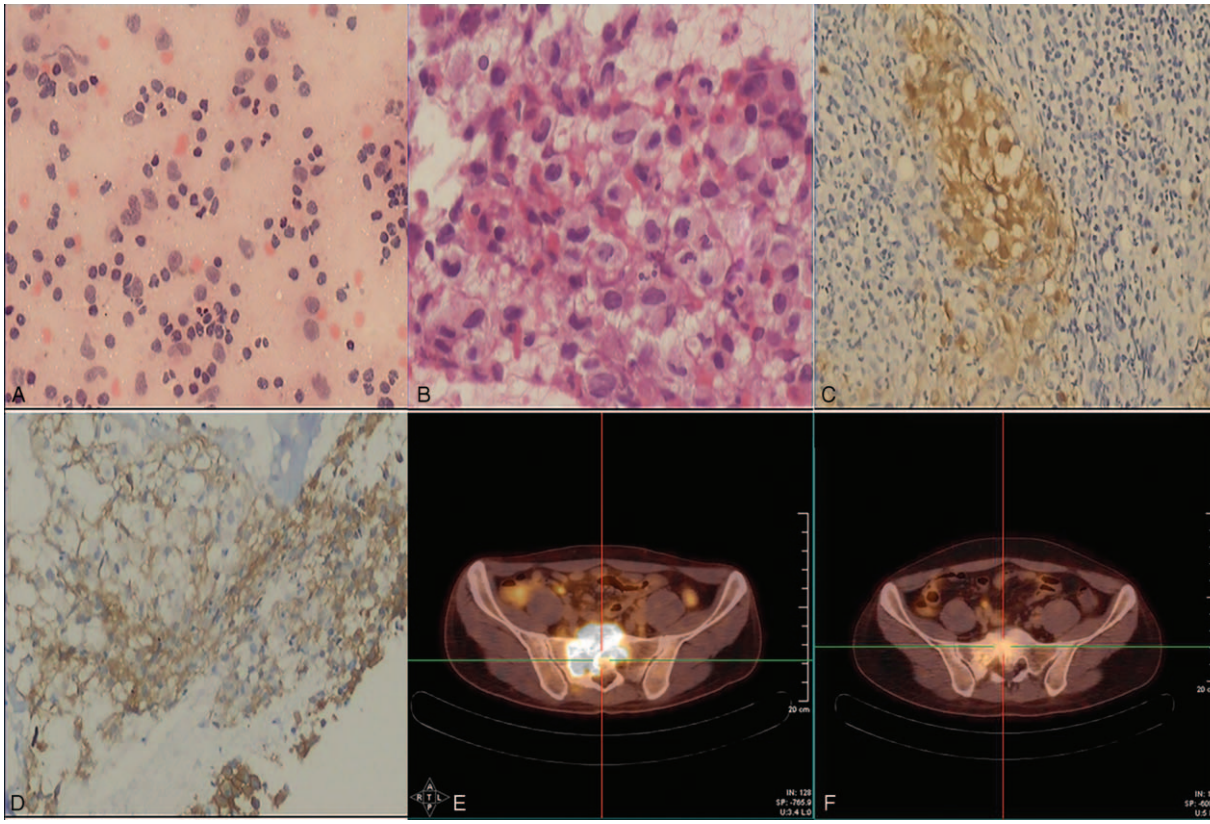

FIGURE 1. A, Fine-needle aspiration cytology of thyroid showed the possibility of Langerhans cells infiltration (200×). B, The pathologic findings of vertebral body of S1-2 showed Langerhans cell proliferation (200×). C, The positive immunohistochemical staining of S100 (200×). D, The positive immunohistochemical staining of CD1α (200×). E, Before treatment, the result of PET/CT (2012.03) showed intense accumulation in the vertebral body of S1-2 (SUV value = 10.7). F, After treatment, the result of PET/CT (2012.11) showed slight accumulation in the vertebral body of S1-2 (SUV value = 4.3). PET/CT = positron emission tomography/computed tomography.

BEAM [armustine 600 mg + Etoposide 150 mg + Cytosine-arabinoside 300 mg + Melphalan 200 mg]) and autologus bone marrow stem cell transplantation. After about 8 months' treatment, PET/CT was performed to evaluate the therapeutic effect, and showed that the SUV in vertebral body of S1−2 (SUV value = 4.3) reduced significantly compared with the previous PET/CT(2015.03) (Figure 1E, F). The results suggested the treatments of LCH were effective. At follow-up, he made a good clinical recovery. At present, there is no tumor recurrence in this patient.

The written informed consent for the case report was obtained from this patient, and the consent procedure was approved by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University.

DISCUSSION

Langerhans cell histiocytosis can be confirmed as one organ or a systemic disease, with lung, bone, and central nervous system being the most favored sites of involvement.[5,6] The incidence of LCH involving the thyroid gland either as an isolated lesion or as a part of multisystemic disease is extremely rare. Due to the first symptom of LCH involving thyroid, which often shows painless thyroid nodules and the lack of other apparent presentations, the LCH involving thyroid is very easy to be ignored. Thyroid fine-needle aspiration is useful in establishing the diagnosis. However, it can be confused with other far more common thyroid diseases and the misdiagnosis rate is not low.[7] Considering the LCH is a multisystemic disease and has a high misdiagnosis rate, the diagnosis of LCH involving the thyroid or multisystem can be a medical puzzle. Although the diagnostic thyroidectomy was considered as an exact diagnostic method for LCH involving thyroid, it had a lot of complications after thyroidectomy and had no benefit for multisystem LCH. Several publications reported that PET/CT is a competent examination for thyroid nodules with inconclusive cytologic results.[8,9] Giovanella et al[10] had suggested that PET/CT can be performed for LCH. In this case, PET/CT was performed to help make an accurate diagnosis of LCH involving thyroid. Moreover, it plays an important role to find other potential LCH lesions, which has a great guiding effect on the diagnosis of LCH. Additionally, the FDG uptake is predictive to therapeutic response during the course of cancer treatment and a lot of studies recommended that the PET/CT is of great value in the therapeutic evaluation of cancer treatment.[11–13] In our case, the result of PET/CT suggested that the multisystemic LCH had a radiologic remission and a good clinical recovery during the subsequent follow-up period.

In clinical settings, the diagnosis of LCH involving the thyroid or other rare isolated lesions is a challenge, since it is difficult to get ideal biopsy specimens in thyroid nodules for the identification of LCH. According to our clinical practice, some easily ignored lesions, such as bone area, suitable for biopsy and

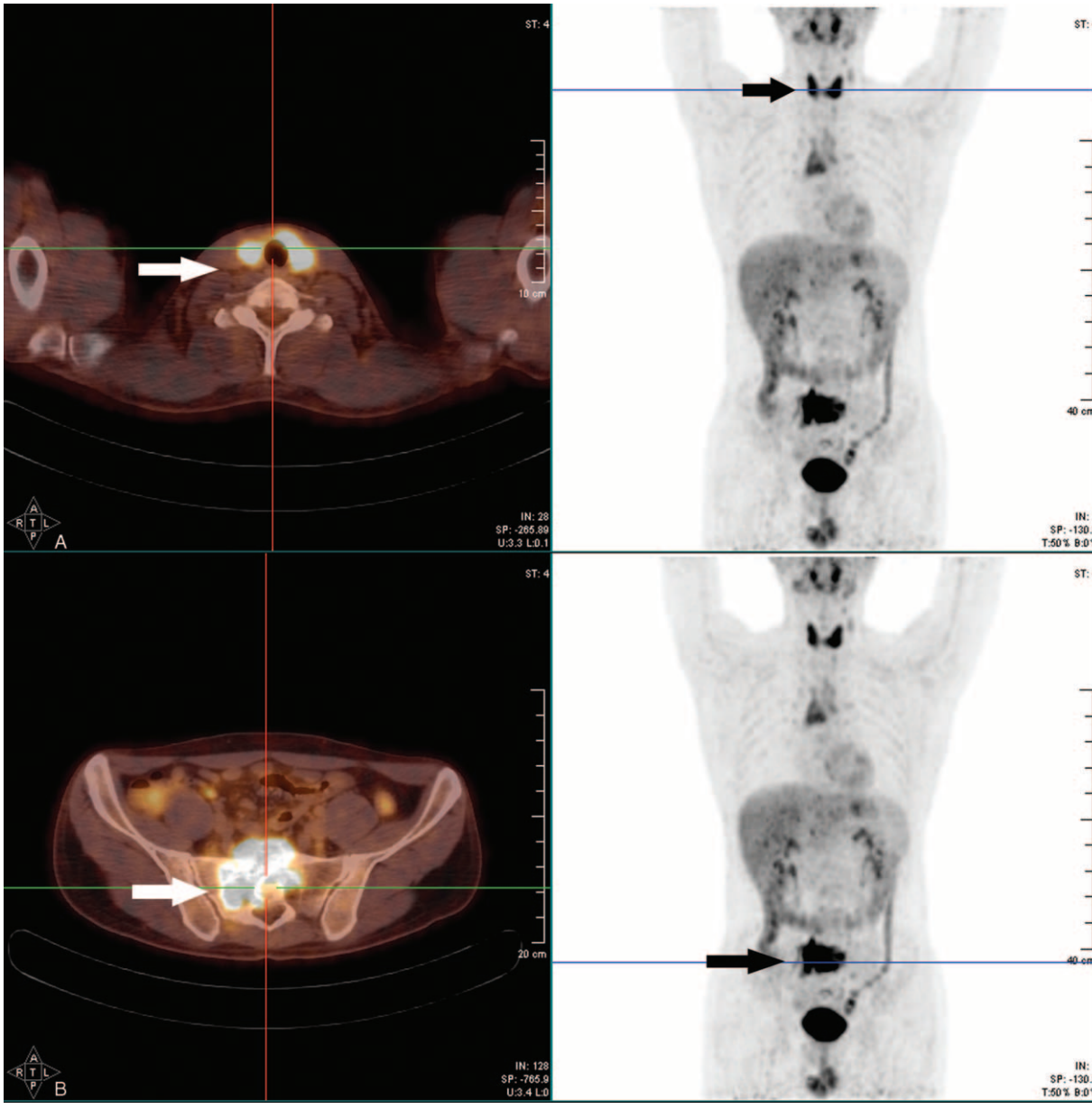

FIGURE 2. PET/CT (2012.03) showed FDG intense accumulation in the (A, arrow) thyroid (SUV value = 7.2) and (B, arrow) the vertebral body of S1-2 (SUV value = 10.7). FDG = fluorodeoxyglucose, PET/CT = positron emission tomography/computed tomography.

immunohistochemical detection, can be found by the imaging technology of PET/CT. During the treatment of LCH, PET/CT can be performed to assess the therapeutic effect, the therapeutic response, and the surveillance.

However, there are several potential limitations in this study. Firstly, the LCH involving thyroid is extremely rare and the use of PET/CT for this is unusual. Therefore, there are not enough studies to make a literature review of the use of PET/CT in LCH involving thyroid. Secondly, we only make a case report and sum up some experience of diagnosis and therapeutic evaluation for LCH involving thyroid. More cases should be enrolled to summarize more reliable diagnostic and therapeutic experience.

In conclusion, LCH involving thyroid is a rare disease. The diagnosis and therapeutic evaluation for LCH involving thyroid is a medical puzzle. When the thyroid nodule FNAB results showed the possibility of Langerhans cells infiltration, the LCH involving thyroid should be considered. The PET/CT should be kept in mind for LCH involving thyroid, which provides evidence to select the most effective and reliable treatment, and contributes to the individualized treatment for LCH.

REFERENCES

1. Nicholson HS, Egeler RM, Nesbit ME. The epidemiology of Langerhans cell histiocytosis. *Hematol/Oncol Clin N Am.* 1998;12:379–384.
2. Donadieu J, Rolon MA, Thomas C, et al. Endocrine involvement in pediatric-onset Langerhans' cell histiocytosis: a population-based study. *J Pediat.* 2004;144:344–350.

3. Howarth DM, Gilchrist GS, Mullan BP, et al. Langerhans cell histiocytosis: diagnosis, natural history, management, and outcome. *Cancer.* 1999;85:2278–2290.
4. Kleinjung T, Woenckhaus M, Bachthaler M, et al. Langerhans' cell histiocytosis with bilateral temporal bone involvement. *Am J Otolaryngol.* 2003;24:265–270.
5. Malpas JS. Langerhans cell histiocytosis in adults. *Hematol/Oncol Clin N Am.* 1998;12:259–268.
6. Lieberman PH, Jones CR, Steinman RM, et al. Langerhans cell (eosinophilic) granulomatosis. A clinicopathologic study encompassing 50 years. *Am J Surg Pathol.* 1996;20:519–552.
7. Marupudi KC, Karanth SS, Thomas J. Langerhans cell histiocytosis presenting as hypothyroid goitre: a unique presentation. *BMJ Case Rep.* 20142014.
8. de Geus-Oei LF, Pieters GF, Bonenkamp JJ, et al. 18F-FDG PET reduces unnecessary hemithyroidectomies for thyroid nodules with inconclusive cytologic results. *J Nuclear Med.* 2006;47:770–775.
9. Czepczynski R, Stangierski A, Oleksa R, et al. Incidental (1)(8)F-FDG uptake in the thyroid in patients diagnosed with PET/CT for other malignancies. *Nuclear Med Rev Central Eastern Europe.* 2011;14:68–72.
10. Giovanella L, Ceriani L, Crippa S, et al. Imaging in endocrinology: Langherans cell histiocytosis of the thyroid gland detected by 18FDG-PET/CT. *J Clin Endocrinol Metab.* 2007;92:2866–2867.
11. Surasi DS, Bhambhvani P, Baldwin JA, et al. (1)(8)F-FDG PET and PET/CT patient preparation: a review of the literature. *J Nuclear Med Technol.* 2014;42:5–13.
12. Puranik AD, Purandare NC, Shah S, et al. Role of FDG PET/CT in assessing response to targeted therapy in metastatic lung cancers: morphological versus metabolic criteria. *Indian J Nuclear Med.* 2015;30:21–25.
13. Tantiwongkosi B, Yu F, Kanard A, et al. Role of (18)F-FDG PET/CT in pre and post treatment evaluation in head and neck carcinoma. *World J Radiol.* 2014;6:177–191.