Metastatic cervical lymph nodes from incidental thyroid cancer mimicking lymphomatous involvement on 18F-FDG PET/CT images

Authors: Weilong Li, Liang Yin, Zhaowei Meng

Article type: Clinical image

Received: September 29, 2020.

Accepted: December 14, 2020.

Published online: December 30, 2020.

ISSN: 1897-9483
Title: Metastatic cervical lymph nodes from incidental thyroid cancer mimicking lymphomatous involvement on $^{18}$F-FDG PET/CT images

Article Type: Clinical Image

Short title: Metastatic lymph nodes mimicking lymphomatous involvement

Keywords: thyroid incidentaloma; primary splenic lymphoma; FDG PET/CT; metastatic lymph nodes; BRAF$^{V600E}$ gene

Order of Authors: Weilong Li, MD$^{1,2}$, Liang Yin, MD$^{1,3}$, Zhaowei Meng, MD, PhD$^{1}$

Weilong Li and Liang Yin as co-first authors contributed equally in the paper.

Affiliations of Authors:

1. Department of Nuclear Medicine, Tianjin Medical University General Hospital, Tianjin, P.R. China

2. Department of Nuclear Medicine, The Affiliated Yantai Yuhuangding Hospital of Qingdao University, Zhifu District, Yantai, Shangdong Province, P.R. China

3. Department of Nuclear Medicine, Pingjin Hospital, Characteristic Medical Center of Chinese People’s Armed Police Forces, 300162, Tianjin, P.R. China

Correspondence to:
Zhaowei Meng, MD, PhD, Department of Nuclear Medicine, Tianjin Medical University General Hospital, Anshan Road No. 154, Heping District, Tianjin, P.R. China, 300052; Telephone: 86-18622035159 Fax: 86-022-27813550
E-mail: zmeng@tmu.edu.cn. ORCID: 0000-0002-4478-878X
A 57-year-old man presented with splenic diffuse large B-cell lymphoma (DLBCL) confirmed by needle aspiration biopsy in a local hospital. $^{18}$F-FDG PET/CT scan was then performed for staging. He was noted to have splenomegaly with multiple hypermetabolic splenic masses involving splenic hilar lymph nodes ($SUV_{\text{max}}$, 18.3), (FIGURE 1A and 1B). Additionally, three focal thyroid lesions with $SUV_{\text{max}}$ of 20.3 and extensively enlarged cervical lymph nodes with even stronger $SUV_{\text{max}}$ of 45.1 were also identified (FIGURE 1A and 1C). FDG PET/CT findings of thyroid were highly suggestive for multifocal thyroid cancer. However, it was difficult to define whether the cervical lymphadenopathies were metastases from the thyroid cancer or involved by DLBCL. Ultrasound-guided fine needle aspiration biopsies (UG-FNABs) of the thyroid and bilateral cervical lymphadenopathies were then scheduled. Cytological examinations revealed papillary carcinoma cells and the stage of The Bethesda System for Reporting Thyroid Cytopathology was assigned as category VI (FIGURE 1D). Furthermore, thyroglobulin concentration in washout fluid was greater than 500 ng/ml and cells were positive for $\text{BRAF}^{V600E}$ mutation (FIGURE 1E). Based on the above results, the diagnosis of papillary thyroid cancer with bilateral cervical
lymph node metastases was clearly established. And thus the splenic lymphoma was identified as primary splenic lymphoma (PSL) staged at Ann Arbor stage II\textsubscript{SEA}. It was suggested to initiate chemotherapy for PSL and postpone management of the thyroid cancer. After 4 cycles of R-CHOP (rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisolone) regimen chemotherapy, interim PET/CT revealed complete remission of the PSL. Intriguingly, there was no significant change in cervical abnormalities (FIGURE 1F).

After the completion of all courses of chemotherapy, the patient underwent total thyroidectomy with radical central and bilateral lymph node dissection (VI, VII and bilateral II-V levels). The results of histopathological examination validated the findings of previous FNABs (pT3b, N1b, M0, Stage II/8\textsuperscript{th} AJCC). And the Ki67 immunostaining demonstrated a low proliferative index of only 2% for the primary tumor (FIGURE 1G) and metastatic lymph nodes. Four weeks after surgery, the patient was submitted to radioactive iodine-131 treatment (5.55 GBq) with stimulated-serum thyroglobulin (S-Tg) value of 5.6 ng/mL (TSH > 100U/mL and anti-thyroglobulin antibody negative). Post-therapy WBS showed radioiodine uptake only in the post-surgical remnant. Six months later, diagnostic WBS was negative under thyrotropin stimulation with S-Tg < 1ng/ml and no abnormality was found in neck ultrasonography. Until the time of submission, the patient was doing well.

A FDG-avid thyroid incidentaloma discovered during PET/CT examination performed due to unrelated thyroid disease is known as a “PAIN” phenomenon[1]. The incidence of this situation varied from 1.0% to 4.3%[2], and thyroid cancer could
represent approximately 35% of such cases, with PTC as the most frequent histological type[3]. Kaliszewski et al[2] reported that cytology results were the significant predictors of cancer occurrence in patients with “PAIN” phenomenon, and recommended surgery treatment in those patients with cytology assigned to category III or higher of the Bethesda system due to significant risk of thyroid malignancy. As far as we know, this is the first report of such extremely intense FDG uptake in metastatic lymph nodes from incidental PTC mimicking DLBCL involvement. This case exemplifies that accelerated glucose metabolism in thyroid cancer is not always dependent on poor differentiation and/or rapid proliferation, but may be due to genetic alterations, such as BRAFV600E mutation[4, 5]. It also highlights that cytological examination of FNAB is necessary for a “PAIN” phenomenon and preventing wrong staging of synchronous malignancy.

FIGURE 1
The maximum intensity projection (A), transaxial Computed Tomography and corresponding fused images (B) revealed splenomegaly with multiple hypermetabolic
hypodense masses involving splenic hilar lymph nodes ($SUV_{\text{max}}$, 18.3); In addition, three focal thyroid lesions in right lobe and isthmus with $SUV_{\text{max}}$ of 20.3 and extensively enlarged cervical lymph nodes with $SUV_{\text{max}}$ of 45.1 were also identified (C).

Cytological examination showed adenocarcinoma cells observed in the thyroid lesion with large and deeply stained nuclei, nuclear sulcus and inclusion bodies were observed easily (D, magnification×400); $\text{BRAF}^{V600E}$ mutation was positive in fine needle aspiration cells (E, ARMS fluorescence quantitative polymerase chain reaction).

The maximum intensity projection image of interim Positron Emission Tomography/Computed Tomography revealed complete remission of the primary splenic lymphoma, but there was no significant change in cervical abnormalities (F).

The Ki67 immunostaining demonstrated a low proliferative index of 2% for the primary papillary thyroid carcinoma (G, magnification×200).

Abbreviation: $SUV_{\text{max}}$, Maximum Standardized Uptake Value; $\text{BRAF}^{V600E}$ mutation, An activating mutation of the B isoform of the Raf kinase gene resulting in a valine to glutamic acid substitution at amino acid 600

**References**


**Compliance with ethical standards**

**Funding:** The present study was supported by Yantai Science and Technology Plan Project (No. 2018SFGY113) of LWL.

**Conflicts of interest:** No potential conflict of interest relevant to this article was reported.

**Ethical approval:** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institution and with the principles of the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

**Informed consent:** Informed consent was obtained from the patient for the anonymous use of patient clinical, imaging, and histologic data.