Primary adrenal extranasal NK/T cell lymphoma with subcutaneous involvement demonstrated on FDG PET/CT
A clinical case report
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Abstract
Rationale: Primary adrenal non-Hodgkin lymphomas are predominant diffuse large B cell lymphoma with frequently bilateral adrenal involvement, but the occurrence of nasal type extranodal NK/T cell lymphoma is relatively rare.

Patient concerns: A 40-year-old woman complaining of left back pain for 2-month was admitted to our department.

Diagnosis: Based on the feature of enhanced computed tomography (CT) images which showed huge bilateral well-defined adrenal masses with heterogeneous enhancement, she was tentatively diagnosed as having primary adrenal malignancy. Postoperative pathology revealed the diagnosis of primary adrenal Epstein-Barr virus-associated nasal type extranodal NK/T-cell lymphoma.

Interventions: Then, she underwent 18F-fluoro-2-deoxy-D-glucose (18F-FDG) positron emission tomography (PET)/CT examination for staging, which showed homogeneously increased FDG uptake in the right adrenal gland and left thigh subcutaneous lesion, as well as heterogeneous increased FDG uptake in the left adrenal gland region with no abnormal uptake in the nasal cavity. Subsequently, the patient has performed 7 cycles of gemcitabine, L-asparaginase, ifosfamide, dexamethasone, etoposide (GLIDE) regimen and autologous stem cell transplantation.

Outcomes: Fortunately, the subsequent 2 follow-up PET/CT scans within 1 year revealed complete resolution with no abnormal FDG uptake in the initially involved sites after 7 cycles of GLIDE chemotherapy and autologous stem cell transplantation.

Lessons: The enhanced CT and FDG PET/CT features of primary adrenal extranasal NK/T cell lymphoma are huge bilateral well-defined adrenal masses with heterogeneous enhancement, high FDG uptake, especially with subcutaneous involvement. And the awareness of this entity may help clinicians to differentiate it from other primary adrenal tumors and make reasonable therapeutic strategies. Besides, FDG PET/CT scan is very useful for the treatment follow-up of the primary adrenal extranasal NK/T cell lymphoma.

Abbreviations: 18F-FDG = 18F-fluoro-2-deoxy-D-glucose, CT = computed tomography, EBV = Epstein-Barr virus, NHL = non-Hodgkin lymphomas, PET/CT = positron emission tomography/computed tomography, PRA = plasma renin activity, SUVmax = maximal standardized uptake value.

Keywords: 18F-FDG PET/CT, primary adrenal extranasal NK/T cell lymphoma

1. Introduction
Extranodal NK/T cell lymphoma, usually with an NK cell phenotype and positivity for Epstein-Barr virus (EBV), is an extranodal non-Hodgkin lymphoma (NHL).[1] And the most common involved extranodal site is a nasal cavity, and others include the Waldeyer ring, upper airway, skin, gastrointestinal tract, testis, lung, thyroid, or adrenal glands.[2–9] Primary adrenal NHLs are predominant diffuse large B cell lymphoma (>70%) with frequently bilateral adrenal involvement,[10–13] but the occurrence of nasal type extranodal NK/T cell lymphoma is relatively rare. Herein, we report a case with primary bilateral adrenal NK/T cell lymphoma with subcutaneous involvement.

2. Case report
A 40-year-old woman with a 2-month history of left back pain was admitted to our clinic. Physical examination revealed no abnormalities. Laboratory tests showed a slightly increased adrenaline and plasma renin activity (recumbent position) levels at 123ng/L (reference range, 60–104ng/L) and 2.6ng/mL.h (reference range, 0.05–0.79ng/mL.h), respectively. Abdominal enhanced computed tomography (CT) (Fig. 1A and C; axial; B and D: sagittal) presented well-defined bilateral adrenal masses with the diameter of 75cm (Fig. 1A and B, black arrows) and 31cm (Fig. 1C and D, white arrows), showing heterogeneous...
enhancement. She was tentatively diagnosed as having primary adrenal malignancy based on the CT findings. Subsequently, the patient underwent left adrenalectomy and ipsilateral nephrectomy. Postoperative pathology showed proliferating lymphocytes with necrosis, infiltration of plasma cells and tissue cells. The immunohistochemical staining revealed that proliferative lymphocytes were positive for CD3ε, CD30, CD56, granzyme B, EBER1/2-ISH, as well as a high proliferation index (Ki-67) of about 70%, but negative for PCK, CD20, CD5, CD4, CD8, CD21, or CD79a. Background plasma cells were positive for CD79a, CD138, Igκ (P), Igλ (P). No rearrangement peaks of the TCRγ gene were detected by gene rearrangement detection. Combined with the above morphological findings, immunohistochemical staining and gene rearrangement results, the diagnosis of EBV-associated nasal type extranodal NK/T-cell lymphoma was confirmed.

Subsequently, she underwent $^{18}$F-fluoro-2-deoxy-D-glucose ($^{18}$F-FDG) positron emission tomography (PET)/CT examination for staging. PET/CT images showed homogeneously increased FDG uptake in the right adrenal gland (maximal standardized uptake value (SUVmax) of 15.7, Fig. 2A, H, I, and J: thick arrows) and left thigh subcutaneous lesion (SUVmax of 12.5, Fig. 2A, K, L, and M: arrows), as well as heterogeneous increased FDG uptake in the left adrenal gland region (SUVmax of 8.3, Fig. 2A, E, F, and G: thin arrows). The whole body PET/CT revealed no abnormal uptake of FDG in the nasal cavity (Fig. 2A, B, C, and D), indicating that the bilateral adrenal masses might be primary lesions with subcutaneous involvement. Then, the patient performed 7 cycles of gemcitabine, L-asparaginase, ifosfamide, dexamethasone, etoposide (GLIDE) regimen and autologous stem cell transplantation. Fortunately, the subsequent 2 follow-up FDG PET/CT scans within 1 year revealed complete resolution with no abnormal FDG uptake in the initially involved sites after chemotherapy and autologous stem cell transplantation (Fig. 2N and O).

The Ethics Committee of West China Hospital of Sichuan University, Chengdu, China, waived the need to obtain informed consent.

### 3. Discussion

Extranodal NK/T-cell lymphoma is a subtype of mature T- and NK-cell lymphomas that most often involve the nasal region (nasal NK/T-cell lymphoma), with a broad range of morphologic appearances, frequent necrosis, and angioinvasion. Extranasal NK/T-cell lymphoma is most common in Asia (eg, China, Korea, and Japan) and in native populations of Central and South America (eg, Peru and Mexico), accounting for 5% to 10% of all NHL. The median age at presentation is approximately 52 years with a male predominance. Primary adrenal
FDG PET is very useful. Apart from the demonstration of tracers. $^{18}$F-Fluorodopa PET/CT and $^{11}$C-Hydroxyephedrine have been used for imaging of adrenal medullary lesions, such as pheochromocytoma, and $^{11}$C-Metomidate PET/CT has been used for adrenocortical imaging like adrenocortical carcinoma. While for imaging of adrenal lymphoma, $^{18}$F-FDG PET/CT is a useful diagnostic and follow up imaging modality in patients with an adenral disease, which can not only help to do staging but also evaluate therapeutic response. Primary adrenal extranasal NK/T cell lymphoma, although a rare entity, should always be considered in patients with huge bilateral adrenal masses.

**4. Conclusions**

In conclusion, we presented a rare case of primary adrenal extranasal NK/T cell lymphoma with subcutaneous involvement demonstrated on $^{18}$F-FDG PET/CT. Besides, $^{18}$F-FDG PET/CT is a useful diagnostic and follow up imaging modality in patients with an adenral disease, which can not only help to do staging but also evaluate therapeutic response. Primary adrenal extranasal NK/T cell lymphoma, although a rare entity, should always be considered in patients with huge bilateral adrenal masses.

**Author contributions**

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**References**

[1] Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood 2016;127:2375–90.

[2] Li YX, Fang H, Liu QF, et al. Primary testicular natural killer/T-cell lymphoma: a CARE-case report and review of literature. Medicine (Baltimore) 2015;94:e1151.

[3] AlShemmari SH, Ameen RM, Sajnani KP. Extranodal lymphoma: a CARE-case report and review of literature. Medicine (Baltimore) 2018;97:e1552.

[4] Chu CS, Au WY, Shek TW, et al. Primary CD56 positive lymphomas of the gastrointestinal tract. Cancer 2001;91:525–33.

[5] Ye ZY, Cao QH, Liu F, et al. Primary esophageal extranasal NK/T cell lymphoma with biphasic morphology: a case report and literature review. Medicine (Baltimore) 2015;94:e1151.

[6] Zhang WL, Ma S, Jug R, et al. Primary testicular natural killer/T-cell lymphoma: a CARE-case report and review of literature. Medicine (Baltimore) 2018;97:e0181.

[7] Zhang J, Li YX, Fang H, et al. Clinical features and treatment outcome of nasal-type NK/T-cell lymphoma of Waldeyer ring. Blood 2008;112:3057–64.

[8] Shrestha MM, Dixit A, Patel M, et al. Primary esophageal extranasal NK/T cell lymphoma: a case report. Medicine (Baltimore) 2015;94:e1151.
[7] Zhang J, Wang M, Yang X, et al. Primary pulmonary extranodal NK/T-cell lymphoma of nasal type misdiagnosed as pneumonia: a case report and literature review. Medicine (Baltimore) 2017;96:e8914.

[8] Li JH, He HH, Cheng Y, et al. Primary thyroid extranasal NK/T-cell lymphoma associated with good outcome: a case report and literature review: a case-compliant article. Medicine (Baltimore) 2016;95:e3460.

[9] Hu L, Xu W, Wang M, et al. A case report of primary unilateral adrenal NK/T-cell lymphoma: good clinical outcome with trimodality treatment. BMC Cancer 2017;17:15–9.

[10] Al-Fiar FZ, Pantalony D, Shepherd F. Primary bilateral adrenal lymphoma. Leuk Lymphoma 1997;27:543–9.

[11] Grigg AP, Connors JM. Primary adrenal lymphoma. Clin Lymphoma 2003;4:154–60.

[12] Ozimek A, Diebold J, Linke R, et al. Bilateral primary adrenal non-Hodgkin’s lymphoma — a case report and review of the literature. Eur J Med Res 2008;13:221–8.

[13] Kim YR, Kim JS, Min YH, et al. Prognostic factors in primary diffuse large B-cell lymphoma of adrenal gland treated with rituximab-CHOP chemotherapy from the consortium for improving survival of lymphoma (CISL). J Hematol Oncol 2012;5:15–9.

[14] Yamaguchi M, Suzuki R, Oguchi M. Advances in the treatment of extranodal NK/T-cell lymphoma, nasal type. Blood 2018;131:2528–40.

[15] Li CC, Tien HF, Tang JL, et al. Treatment outcome and pattern of failure in 77 patients with sinonasal natural killer/T-cell or T-cell lymphoma. Cancer 2004;100:366–75.

[16] Au WY, Weisenburger DD, Intragumtornchai T, et al. Clinical differences between nasal and extranasal natural killer/T-cell lymphoma: a study of 136 cases from the International Peripheral T-Cell Lymphoma Project. Blood 2009;113:3931–7.

[17] Laurini JA, Perry AM, Bolesen E, et al. Classification of non-Hodgkin lymphoma in Central and South America: a review of 1028 cases. Blood 2012;120:4795–801.

[18] Chim CS, Ma SY, Au WY, et al. Primary nasal natural killer cell lymphoma: long-term treatment outcome and relationship with the international prognostic index. Blood 2004;103:216–21.

[19] Shet T, Suryawanshi P, Epari S, et al. Extranodal natural killer/T cell lymphomas with extranasal disease in non-endemic regions are disseminated or have nasal primary: a study of 84 cases from India. Leuk Lymphoma 2014;55:2748–53.

[20] Mantzios G, Tarigotis P, Velou P, et al. Primary adrenal lymphoma presenting as Addison’s disease: case report and review of the literature. Ann Hematol 2004;83:460–3.

[21] Levy NT, Young WF Jr, Habermann TM, et al. Adrenal insufficiency as a manifestation of disseminated non-Hodgkin’s lymphoma. Mayo Clin Proc 1997;72:818–22.

[22] Arora S, Vargo S, Luperin AR. Computed tomography appearance of spontaneous adrenal hemorrhage in a pheochromocytoma. Clin Imaging 2009;33:144–7.

[23] Dunning KK, Wudhikarn K, Safo AO, et al. Adrenal extranodal NK/T-cell lymphoma diagnosed by fine-needle aspiration and cerebrospinal fluid cytology and immunophenotyping: a case report. Diagn Cytopathol 2009;37:856–55.

[24] Thompson MA, Habra MA, Routhbort MJ, et al. Primary adrenal natural killer/T-cell nasal type lymphoma: first case report in adults. Am J Hematol 2007;82:299–303.

[25] Sharma P, Singh H, Dhull VS, et al. Adrenal masses of varied etiology: anatomical and molecular imaging features on PET-CT. Clin Nucl Med 2014;39:251–60.

[26] Berk V, Yildiz R, Akdemir UO, et al. Disseminated extranodal NK/T-cell lymphoma, nasal type, with multiple subcutaneous nodules: utility of 18F-FDG PET in staging. Clin Nucl Med 2008;33:365–6.

[27] Ko KY, Liu CJ, Ko CL, et al. Intratumoral heterogeneity of pretreatment 18F-FDG PET images predict disease progression in patients with nasal type extranodal Natural Killer/T-cell lymphoma. Clin Nucl Med 2016;41:922–6.