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LETTER TO THE EDITOR

Successful treatment of nasal-type extra-nodal natural killer/T cell lymphoma with simultaneous involvement of the thyroid, liver, and pancreas

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Dear Editor,

Extra-nodal NK/T cell lymphomas (ENKLs) reflect their putative cellular origins from both NK cells and T cells [1]. For stage III/IV lymphomas, chemotherapy is the mainstay of treatment. However, conventional anthracycline-based regimens are ineffective. Recommended chemotherapy protocols are based on the use of L-asparaginase combined with other effective drugs [2]. Herein, we report a case of nasal-type ENKL with thyroid, liver, and pancreas involvement, which has never previously been reported. The treatment was L-asparaginase with an anthracycline-based regimen that led to a favorable response.

A 54-year-old man presented with abdominal fullness for 2 months accompanied with poor appetite, intermittent steatorrhea, and weight loss of 9 kg. The initial laboratory data disclosed hyperbilirubinemia with abnormal liver biochemistry profiles (Table 1). No evidence of viral hepatitis was found, and the autoimmune profiles were all within normal ranges. Computed tomography (CT) revealed a diffuse puffy appearance of the pancreatic parenchyma (Fig. 1a). Fludeoxyglucose positron emission tomography (FDG-PET) revealed increased uptake in the pancreas, liver, thyroid glands, and right nasal cavity (Fig. 1b). Subsequent endoscopic ultrasonography examination and endoscopic ultrasonography–guided fine-needle aspiration biopsy for the pancreatitis work-ups, however, did not produce a conclusive result. The patient was subsequently treated with prednisolone empirically for autoimmune pancreatitis. The response was poor, as demonstrated by the deterioration of the laboratory profiles within 10 days (Table 1). Liver biopsy was therefore performed. The pathology tests revealed atypical lymphocyte infiltration with strong expression of both CD3 and Epstein–Barr virus (EBV)-encoded RNA with negative CD56 expression. A final diagnosis of nasal-type extra-nodal NK/T cell lymphoma (ENKL) was thus made. Induction chemotherapy with two cycles of L-asparginase, cyclophosphamide, doxorubicin, vincristine, and prednisolone (L-CHOP) treatment resulted in favorable clinical response with the regression of all clinical symptoms, abnormal laboratory profiles, and EBV viral loads. Two cycles of L-asparaginase, etoposide, dexamethasone, cytarabine, and cisplatin treatment (L-ESHAP) were then administered for consolidation. After the chemotherapy treatments, the total bilirubin level returned to normal and no EBV viral load was detected (Table 1). Repeated CT confirmed regression of the prior pancreas findings (Fig. 1c), and FDG-PET revealed that the abnormalities observed in the pancreas, liver, thyroid glands, and nasal cavity were resolved (Fig. 1d). The patient subsequently received upfront autologous peripheral blood stem cell transplantation (auto-PBSCT) 5 months after the diagnosis was made. The patient remains in complete remission 14 months after the auto-PBSCT.

Extra-nasal-type ENKL accounts for the remaining 20% of patients and involves the intestines, skin, testes, lungs, eyes, adrenal glands, brain, breasts, tongue, thyroid, and pancreas [3–8]. Our case exhibited simultaneous involvement of the thyroid, pancreas, and liver, which has never been reported before. The options for frontline therapy were limited because

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Table 1 Laboratory data at key intervals during the treatment course

Item	At presentation	10 days after methylprednisolone 2 kg/mg	1 week after L-CHOP cycle 1	2 weeks after L-CHOP cycle 1	4 weeks after L-CHOP cycle 1	2 weeks after L-CHOP cycle 2	4 weeks after L-CHOP cycle 2	2 weeks after L-ESHAP cycle 1	4 weeks after L-ESHAP cycle 1	2 weeks after L-ESHAP cycle 2	Before transplantation
T-BIL (mg/dL)	2.46	32.15	28.17	20.74	6.98	4.04	2.31	2.03	0.97	0.94	0.45
D-BIL (mg/dL)	1.81	19.60					1.07				
AST (U/L)		58	28			26	24	28	29		25
ALT (U/L)	380	632	96	80	117	80	36	68	51	34	27
ALP (U/L)	458	412	308		339	297	242	268	204	200	76
GGT (U/L)	325	1000	657	313	213	221	150	140	166	136	41
Lipase (U/L)	599	201	12					< 6			
EBV viral load (IU/mL)		163684			< 40	Undetectable					
Free T4 (ng/dL)		0.72	0.89								

Abbreviations: *T-bil* total bilirubin, *D-bil* direct bilirubin, *AST* aspartate transaminase, *ALT* alanine transaminase, *ALP* alkaline phosphatase, *GGT* gamma-glutamyl transpeptidase, *EBV* Epstein–Barr virus, *T4* thyroxine

Normal values: T-BIL, 0.3–1.0 mg/dL; D-BIL, 0.03–0.18 mg/dL; AST, 8–31 U/L; ALT, 0–41 U/L; ALP, 34–104 U/L; GGT, 9–64 U/L; Lipase, 29–103 U/L; EBV viral load, undetectable; Free T4, 0.70–1.48 ng/dL

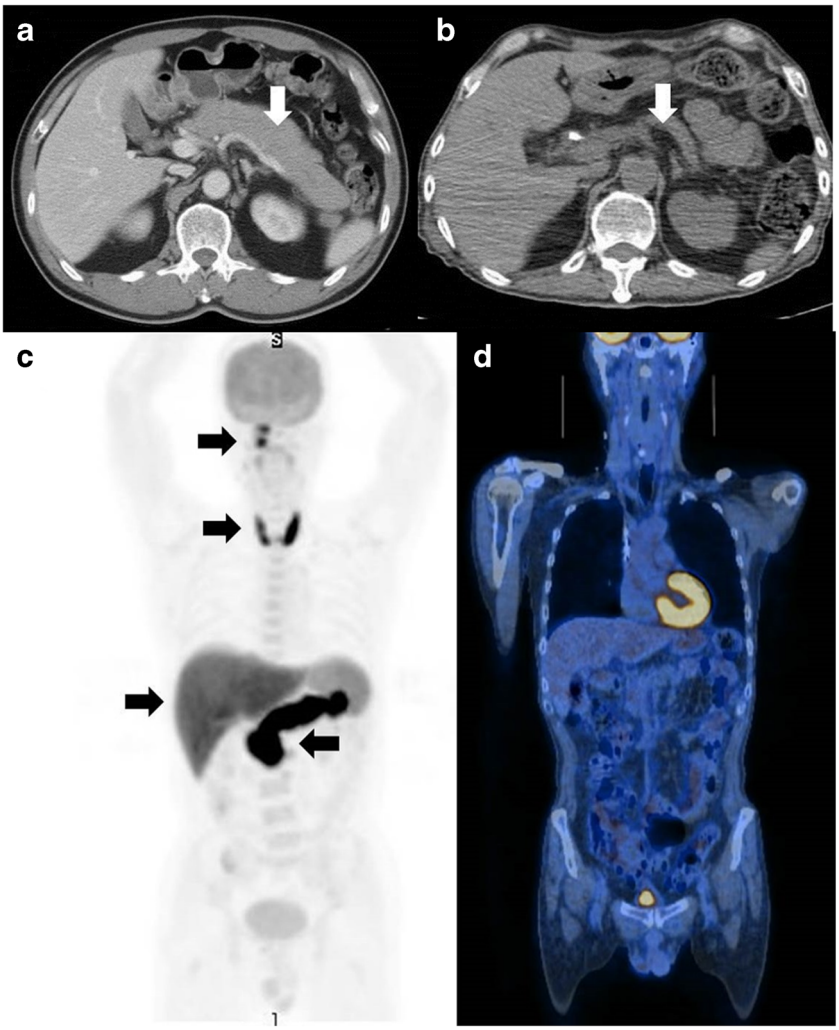

Fig. 1 (**a**) CT and (**b**) FDG-PET images before chemotherapy with two cycles of L-asparginase, cyclophosphamide, doxorubicin, vincristine, and prednisolone treatment and two cycles of L-ESHAP; (**c**, **d**) after treatment. (**a**) Diffuse puffy appearance of the pancreatic parenchyma (white arrow). (**b**) Increased FDG uptake at the pancreas, liver, thyroid glands, and right nasal cavity (black arrows). (**c**) Normal appearance of the pancreas after chemotherapy (white arrow). (**d**) Increased FDG uptake is completely resolved at the pancreas, liver, thyroid glands, and right nasal cavity

of the patient's poor liver profile. An anthracycline-based induction worked well in this case. However, because of the aggressive nature at the initial presentation, intensified regimens for consolidating the response were considered necessary. An L-ESHAP regimen was thus administered, followed by auto-PBSCT as the ultimate consolidation therapy. This treatment plan demonstrated satisfactory results in this case, suggesting that a stepwise strategy of chemotherapy with gradual intensification might help patients who similarly have suboptimal initial clinical status.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, Advani R, Ghielmini M, Salles GA, Zelenetz AD, Jaffe ES (2016) The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood 127(20):2375–2390. https://doi.org/10.1182/blood-2016-01-643569
2. Tse E, Kwong Y-L (2016) Diagnosis and management of extranodal NK/T cell lymphoma nasal type. Expert Rev Hematol 9(9):861–871. https://doi.org/10.1080/17474086.2016.1206465
3. Au W, Weisenburger DD, Intragumtornchai T, Nakamura S, Kim WS, Sng I, Vose J, Armitage JO, Liang R, for the International Peripheral T-Cell Lymphoma Project (2009) 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 113(17):3931–3937. https://doi.org/10.1182/blood-2008-10-185256
4. Liu W, Hua R, Zhang J-F, Huo Y-M, Liu D-J, Sun Y-W (2013) First report of primary pancreatic natural killer/T-cell nasal type lymphoma. Eur Rev Med Pharmacol Sci 17(3):318–322
5. Zhang J, Wang M, Yang X, Liu C, He X (2017) Primary pulmonary extranodal NK/T-cell lymphoma of nasal type misdiagnosed as pneumonia: a case report and literature review. Medicine (Baltimore) 96(49):e8914. https://doi.org/10.1097/MD.0000000000008914

6. Suzumiya J, Takeshita M, Kimura N, Morioka E, Sakai T, Hisano S, Okumura M, Kikuchi M (1993) Sinonasal malignant lymphoma of natural killer cell phenotype associated with diffuse pancreatic involvement. Leuk Lymphoma 10(3):231–236. https://doi.org/10.3109/10428199309145888
7. Zhou C, Bu X, Li X, Liu L, Xie X, Zhuo S, Yin H (2015) Pancreas metastasization of nasal NK/T-cell lymphoma: a case report. Cell Biochem Biophys 73(1):17–20. https://doi.org/10.1007/s12013-015-0563-2
8. Li Y, Damjanov I (2016) Extranodal NK/T cell lymphoma causing cardiorespiratory failure. Case Rep Hematol 2016:2394809. https://doi.org/10.1155/2016/2394809