Extranodal NK/T-cell lymphoma manifesting as cutaneous lesions and intestinal perforation: A case report

Dear Editor,

We report a 70-year-old male patient with multifocal extranodal NK/T-cell lymphoma manifesting as cutaneous lesions and intestinal perforation. This patient presented with a 10-days history of bullae and nodules in the lumbar region, that was initially diagnosed to be varicella zoster infection. However, patient gave history of intermittent fever, and weight loss of about 10 kgs in the last 5 months.

The skin lesions progressed to ulcers with necrotic crusting over his back, abdomen and left thigh, along with closely set pustules under his right breast [Figures 1a and 1b]. Routine laboratory examinations results have been tabulated [Table 1]. Abdominal computed tomography revealed that the wall of the local transverse colon was thickened, rough and significantly enhanced, with some gas shadows around this area and in the abdominal cavity A skin biopsy from the lesion under the right breast and abdomen revealed many necrotic keratinocytes with epidermal ulceration There was predominantly angiocentric and angiodestructive lymphocytic infiltration in the entire dermis and fat lobules [Figures 3a–3c]. Immunohistochemistry showed that the tumour cells were positive for CD3, CD4, CD8 and CD56 and negative for CD20 [Figures 4a–4h]. Immunohistochemical staining of the left abdominal skin lesion showed that the neoplastic cells were positive for CD30, Epstein-Barr virus-encoded small RNAs and Ki-67 additionally.

The patient later developed cough, sore throat and intermittent fever up to 39.0°C, with progressively worsening of skin lesions. Laryngoscopy revealed a mass in the posterior pharyngeal wall; unfortunately, no biopsy specimen was obtained. On the 5th day of hospital stay, patient had a sudden intestinal perforation for which surgery was performed. The histopathological examination and immunohistochemical staining on the resected small intestinal tissue confirmed the diagnosis of extranodal NK/T cell lymphoma. Histopathological findings resembled the skin biopsy findings [Figures 5a and 5b]. Immunohistochemistry indicated that the atypical lymphocytes were positive for CD3, CD56, T-cell intracellular antigen 1, Epstein-Barr virus-encoded small RNAs, and perforin B, confirming a natural killer cell phenotype [Figures 5c–5f]. The Epstein-Barr virus-encoded small RNAs *in situ* hybridisation was positive for atypical lymphocytes. The proliferation marker, Ki-67, was positive in approximately 60.0% of

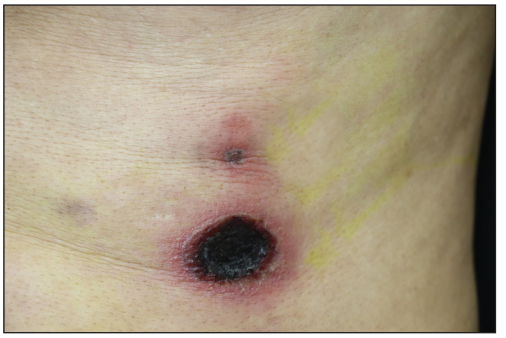

Figure 1a: An isolated nodular erythema was observed on the left lower abdomen with black scabs on the surface

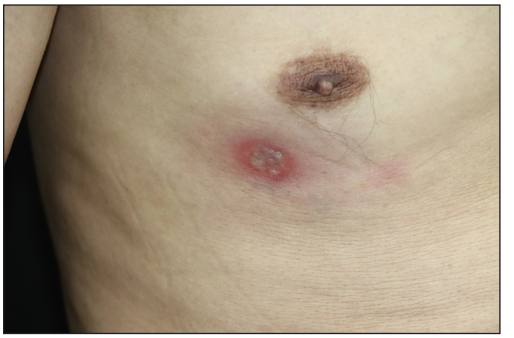

Figure 1b: During hospitalisation, there was nodular erythema under the right breast with densely distributed pustules on the surface

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Table 1: Laboratory examination results of the patient

Index	Actual value	Normal value
lymphocyte count	0.6 × 10^9/L	1.1–3.2 × 10^9/L
lymphocyte percentage	14.4%	20–50%
neutrophil percentage	75.8%	40–75%
albumin	33.4 g/L	40–55 g/L
aspartate aminotransferase	50.0 U/L	13–40 U/L
lactate dehydrogenase	370.1 U/L	120–250 U/L

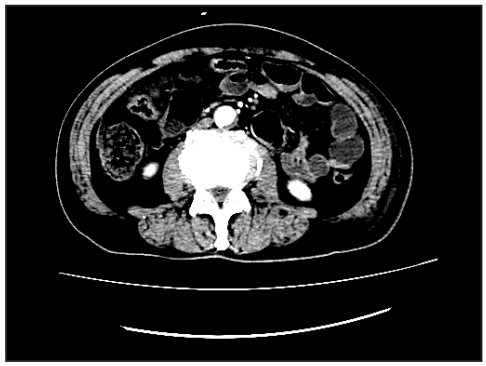

Figure 2: The local transverse colon was thickened, rough, and significantly enhanced. There were some gas shadows in the abdominal cavity

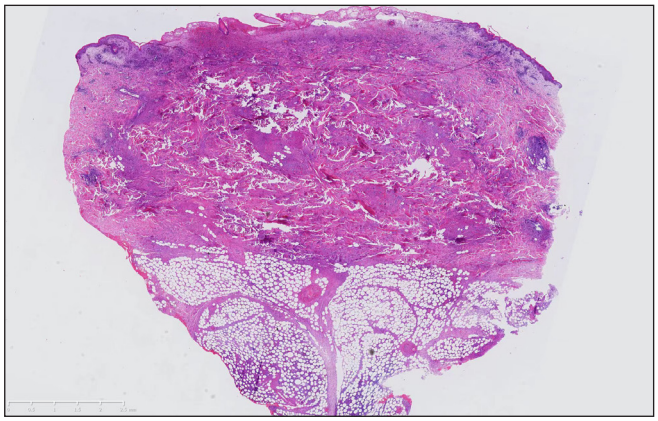

Figure 3a: Histopathology of the left lower abdominal lesion (H and E, ×10) Epidermal necrosis and ulcer formation, epidermal cell edema, a large number of lymphoid cells infiltrating around blood vessels in the superficial dermis, necrosis of collagen fibers in the dermis, and mixed infiltration of lymphoid cells and inflammatory cells into fat lobules.

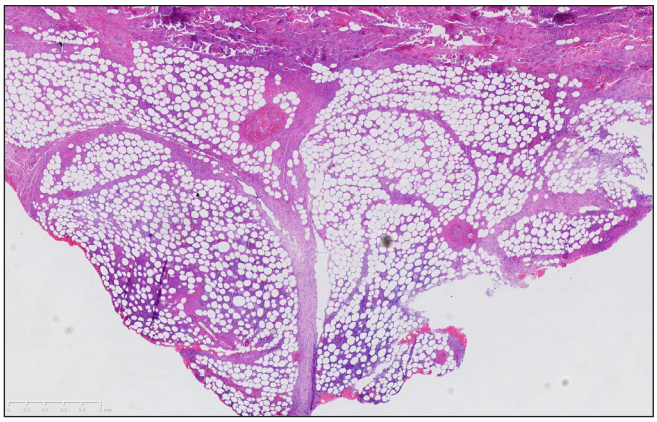

Figure 3b: Biopsy of the left lower abdominal lesion, showing atypical lymphoid cells infiltration of fat lobules mixed with inflammatory cells (H and E, ×20)

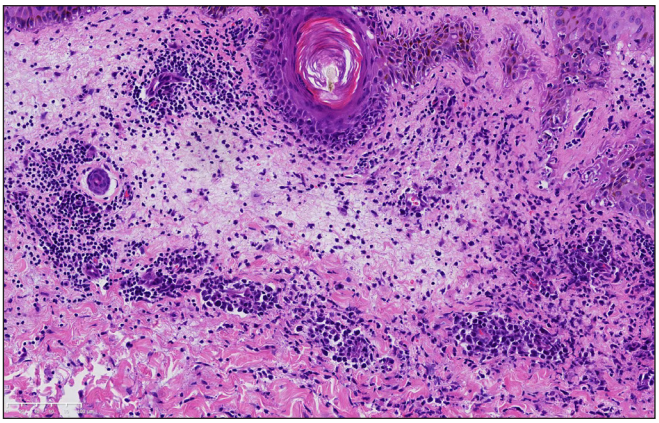

Figure 3c: Biopsy of the left lower abdominal lesion, showing atypical lymphoid cells distributed throughout the dermis infiltrated the vascular wall or around the blood vessels (H and E, ×200)

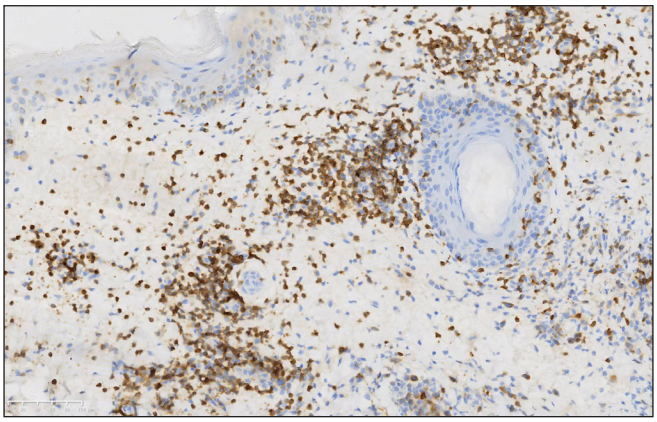

Figure 4a: Atypical lymphoid cells positive for clusters of differentiation 3 in the biopsy (clusters of differentiation 3, ×200)

the cells. These findings supported the diagnosis of secondary cutaneous extranodal NK/T-cell lymphoma.

After consultation with oncologists and haematologists, we proposed further investigations to define the lymphoma stage, but the patient refused. The patient experienced rapid disease progression, followed by death 3 months after the diagnosis.

Extranodal NK/T-cell lymphoma is a rare non-Hodgkin's lymphoma associated with Epstein–Barr viral infection, with

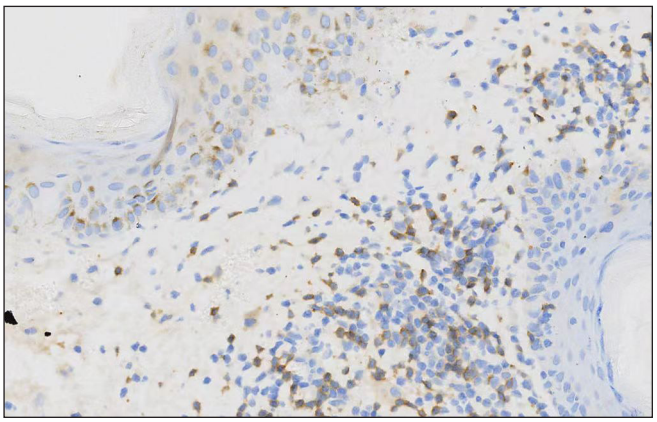

Figure 4b: Atypical lymphoid cells partially positive for clusters of differentiation 8 in the biopsy (clusters of differentiation 8, ×200)

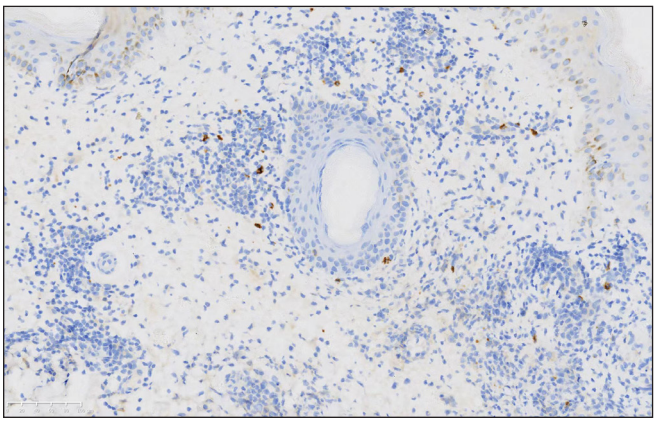

Figure 4c: Atypical lymphoid cells negative for clusters of differentiation 20 in the biopsy (clusters of differentiation 20, ×200)

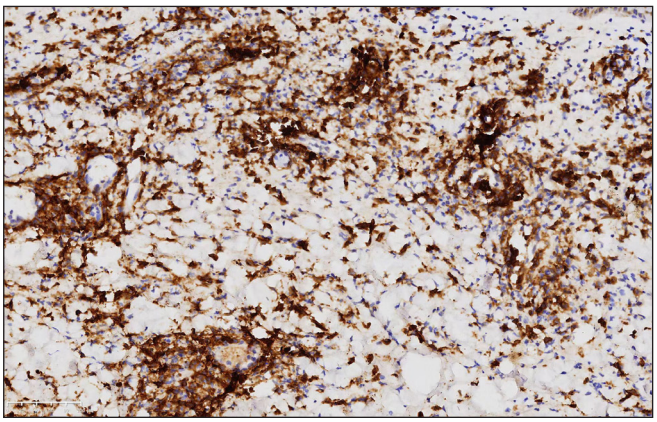

Figure 4d: Atypical lymphoid cells positive for clusters of differentiation 56 in the biopsy (clusters of differentiation 56, ×200)

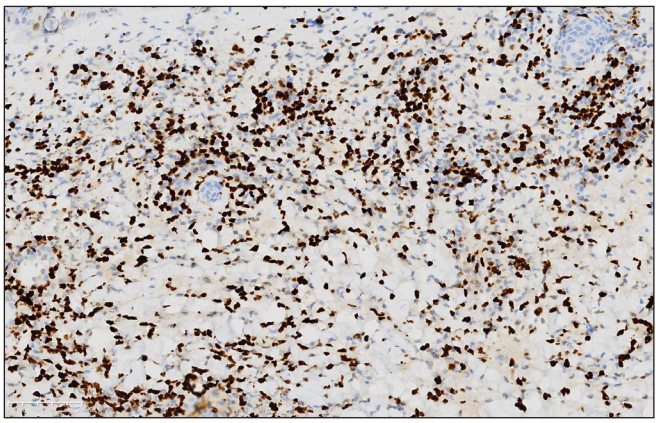

Figure 4e: Atypical lymphoid cells partial positive for Ki-67 in the biopsy (Ki-67, ×200)

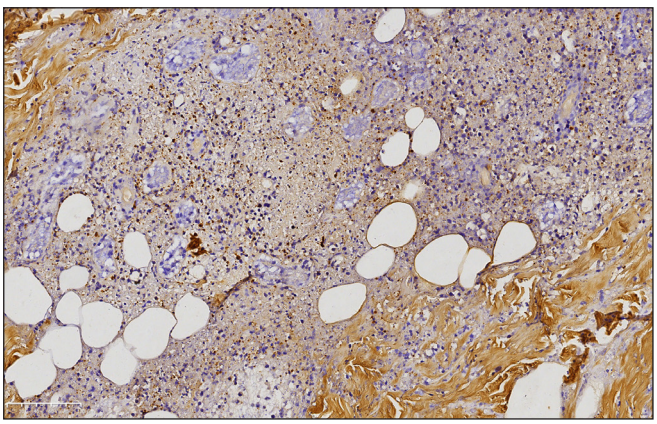

Figure 4f: Atypical lymphoid cells positive for Epstein–Barr encoding region in the biopsy (Epstein–Barr encoding region, ×200)

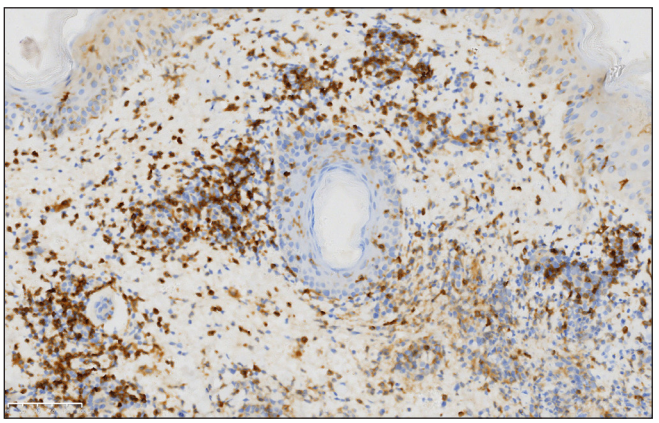

Figure 4g: Atypical lymphoid cells positive for clusters of differentiation 4 in the biopsy (clusters of differentiation 4, ×200)

regional and ethnic differences, high recurrence and poor prognosis. It is mainly prevalent in East Asia and parts of Central and South America.[1] The median survival time is only 5.3 months, and the 5-year overall survival rate is 49.9 ± 12.5%.[2] Extranodal NK/T-cell lymphomas involving the skin and digestive tract are rare.

Extranodal NK/T-cell lymphoma mainly involves the lower limbs when it affects the skin. Patients often exhibit cellulitis, nodules, skin ulcers and vasculitic lesions.[3] Extranodal NK/T-cell lymphoma mainly invades the colon when affecting the digestive tract, with atypical clinical features. Evident symptoms include abdominal pain, bloody stool, abdominal mass, weight loss, intestinal obstruction and intestinal perforation,

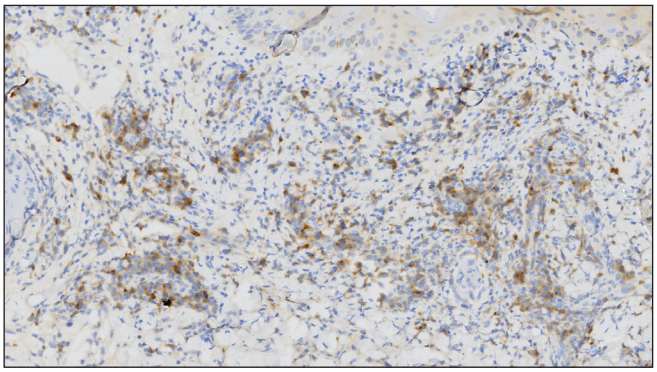

Figure 4h: Atypical lymphoid cells positive for clusters of differentiation 30 in the biopsy (clusters of differentiation 30, ×200)

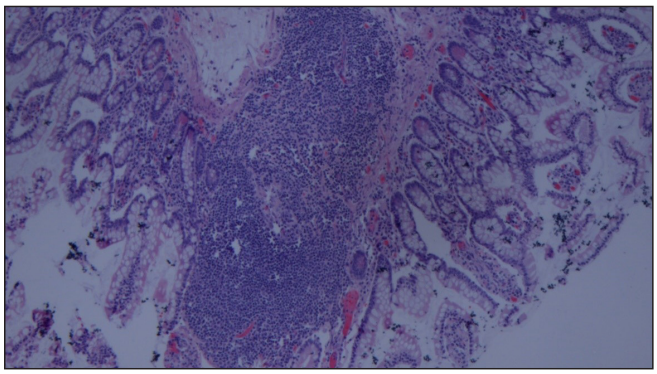

Figure 5a: Biopsy scan of the small intestine tissue (H and E, × 40)

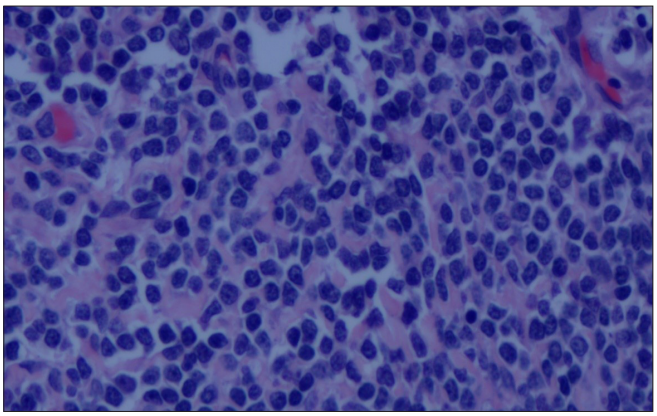

Figure 5b: Biopsy of the small intestine tissue, showing atypical lymphoid cells mixed with inflammatory cells (H and E, ×100)

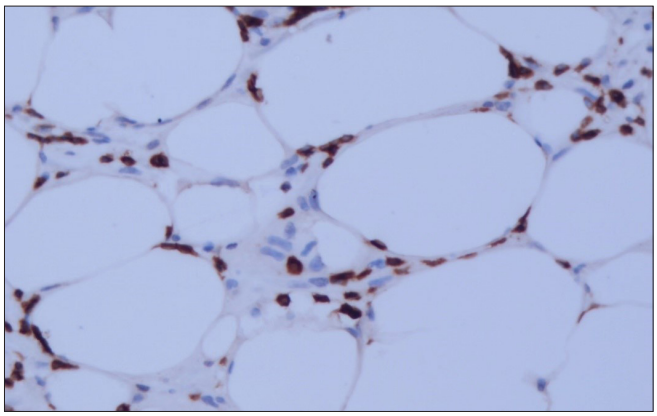

Figure 5c: Atypical lymphoid cells partial positive for CD3 in the biopsy (CD3, ×200)

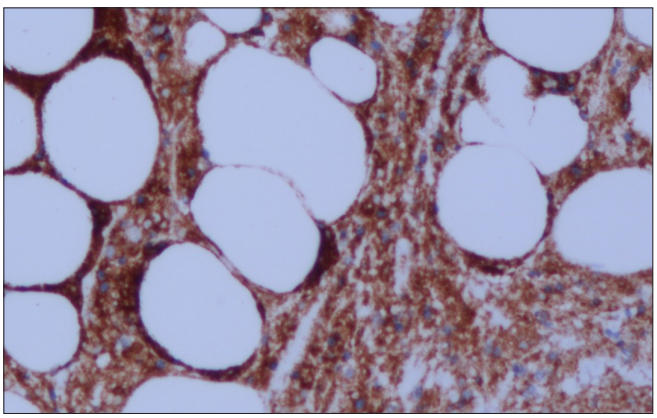

Figure 5d: Atypical lymphoid cells partial positive for CD56 in the biopsy (CD56, ×200)

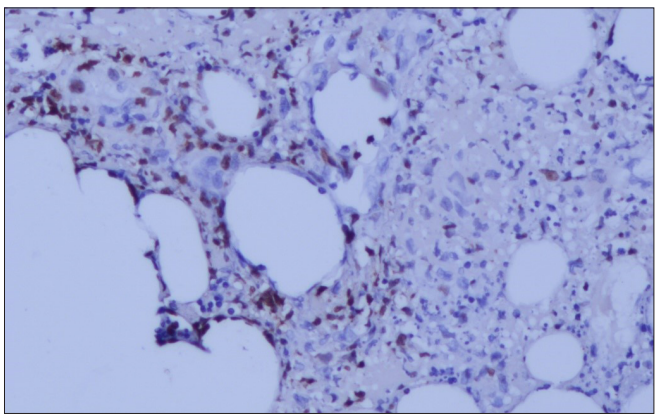

Figure 5e: Atypical lymphoid cells partial positive for Epstein-Barr encoding region (EBER) in the biopsy (EBER, ×200)

of which intestinal perforation occurs in only 8.7% (92/1062) of cases.[4] Early diagnosis is nearly impossible without specific symptoms and examinations and most patients undergo emergency surgery for intestinal perforation. Moreover, anticancer treatment is delayed in patients with intestinal perforation with severe peritonitis, gastrointestinal bleeding, septic shock and multiple organ failure, resulting in an extremely poor prognosis. Therefore, early diagnosis and surgical treatment of patients with extranodal NK/T-cell lymphoma are crucial before intestinal perforation occurs.

The diagnosis depends on histopathological and immunohistochemical findings. The examination of Epstein-Barr virus-encoded small RNAs *in situ* hybridisation is often used in diagnosing Epstein–Barr virus-related infections and is an important auxiliary method for diagnosing extranodal

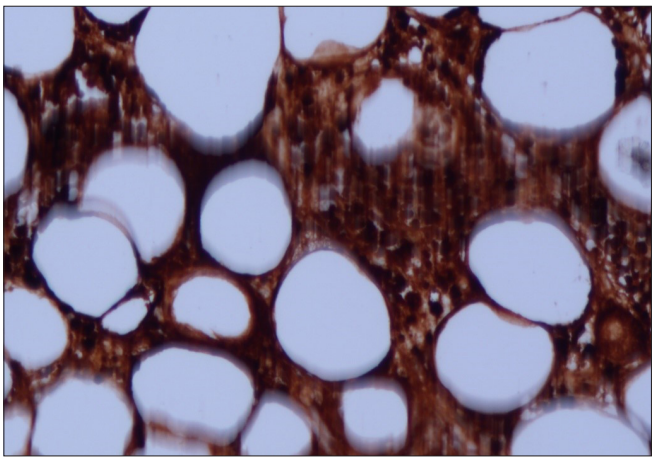

Figure 5f: Atypical lymphoid cells partial positive for Granulase B in the biopsy (Granulase B, ×200)

NK/T-cell lymphoma. Li *et al*. reported that the expression rate of Epstein-Barr virus-encoded small RNAs in patients with extranodal NK/T-cell lymphoma in Xinjiang was 94.2% (97/103).[7] The prognosis of patients with extranodal NK/T-cell lymphoma is closely associated with disease location also. The median survival of patients presenting with the skin-limited disease is 27 months (95% confidence interval 9–45) and only 4 months (95% confidence interval 3–5) for those presenting with both cutaneous and extracutaneous involvement.[8] A study found that the median survival time of patients with intestinal extranodal NK/T-cell lymphoma was 2.8 months (95% confidence interval 0.3–29), while that of patients with intestinal perforation was only 1.5 months (95% confidence interval 0.3–2.7).[9] Other adverse prognostic factors include B symptoms, elevated lactate dehydrogenase levels, decreased albumin levels, advanced disease, extranodal involvement, and Epstein–Barr virus load in the tissues. Our patient had typical B symptoms, an increased lactate dehydrogenase level and a decreased albumin level.

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Declaration of patient consent

The authors certify that they have obtained the patient's consent.

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Conflict of interest

There are no conflicts of interest.

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