Inert CD30-positive extranodal NK/T cell lymphoma with large cell transformation: a case report

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Case Report

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Abstract

Background Extranodal natural killer (NK)/T-Cell Lymphoma is a rare type of cytotoxic lymphoma associated with Epstein-Barr virus infection, highly invasive and relatively resistant to chemotherapy. Inert CD30-positive extranodal NK/T cell lymphoma with large cell transformation is very rare.

Case presentation A married 55-year-old male was admitted to hospital in February 2017, because of “diagnosis of malignant lymphoma for about 12 years with high fever and a left neck mass present for about 3 weeks". The patient was diagnosed to NK/T Cell Lymphoma as early as 2006, repeated relapses in June 2010 and April 2013. The patient was biopsied again in February 2017, lymph node, about 2.5×2×1.3cm.The section was off-white and tender. Microscopic examinations showed a diffuse proliferation of small and atypical lymphoid cells, admixed with large lymphoid cells. Immunohistochemically, the tumor cells exhibited positivity for CD30, CD3, CD43, CD2, CD56, TIA, negativity for CD4, CD8, AE1/AE3, CD20, ALK, EMA staining. In situ hybridization for EBER was strongly positive in the specimens.

Conclusions Herein, we report a case of CD30-positive extranodal NK/T Cell Lymphoma with large cell transformation, nasal type, in indolent course over a period of 12 years. The accurate diagnosis of NK/T-cell lymphoma with CD30 expression and large cell transformation is very important. The disease usually has a poor prognosis related to several factors, but the indolent behavior of the present case is more unusual. A long-term follow-up is suggested to be performed to inspect the progression for this tumor.

Background

Extranodal natural killer (NK)/T-cell lymphoma involve mainly the nose, facial midline, waldeyer's ring. Other sites of involvement are the gastrointestinal system, soft tissue, brain, liver, spleen, bone marrow and testis(1). Extranodal NK/T Cell Lymphoma is considered as an aggressive form of non-Hodgkin’s lymphoma associated with Epstein-Barr virus infection. Serious patients accompanied by Haemophilus syndrome severe and clinical manifestations such as high fever, hepatosplenomegaly, hemocytopenias. Under a microscope, the mass showed extensive necrosis and inflammatory exudation, Tumor cells were medium to large in size with irregular nuclei; some can see anaplastic cells, showed round or ovoid, and a moderate amount of cytoplasm which characteristically showed peculiar coarse eosinophilic granules, and eggplant-like kidney-like irregular nuclei, unobvious nucleoli(2). The lesion was mainly infiltrated by small- to middle-size atypical lymphoid cell, histiocytes and eosinophils. Perivascular infiltrating and local angioinvasion were noted in the lesion. Immunohistochemical staining showed that tumor cells were strongly positive for T cell markers CD2, positive for CD56 and cytotoxic molecules (perforin, GrB, TIA1), but negative for CD3. In situ hybridization for EBER was strongly positive in specimens.

Inert extranodal NK/T-Cell lymphoma is a rare type of cytotoxic lymphoma. Seok Jim Kim et al(3) studied 140 cases of NK/T cell lymphoma, only found 6 cases with long-term survivors (surviving for more than 5 years). Herein, we reported a case of primary NK/T cell lymphoma in spinal canal with initial

manifestation of diffuse growth of small cells, survival and recurrence after 12 years follow-up with CD30 positive large cells transformation. After treatment, the patien’s condition improved and was currently doing well (November, 2017).

Case Presentation

A married 55-year-old male was admitted to the Third Affiliated Hospital of Soochow University in February 2017, because of “diagnosis of malignant lymphoma for about 12 years with high fever and a left neck mass present for about 3 weeks". Medical history showed the patient underwent sacral tumor resection at the Third Affiliated Hospital of Soochow University in April 2006, because of abdominal pain and right lower limb pain. The postoperative pathological diagnosis was NK/T cell lymphoma (stage II). After two courses of CHOP and MEOP regimen chemotherapy, the patient was remission. Four years later, In June 2010, the patient was admitted to the Third Affiliated Hospital of Soochow University for "high fever with body temperature of 39℃and shoulder pain for more than 1 month". CT displayed the mass involving the right adrenal gland and retroperitoneal lymph nodes, considered recurrence. The patient received ESHAP regimen chemotherapy on July 3rd 2010. On July 6th 2010, the patient developed high fever with body temperature of 40℃ and pain and discomfort, treated with meropenem for anti-infection. B-ultrasound showed left adrenal mass; the patient received ESHAP regimen chemotherapy again On July 31st 2010, and discharged after improvement and remission. In April 2013, the patient developed a lump behind the retroperitoneal left renal vein (Figure 1A), considered recurrence, and clinical remission after local radiotherapy. In February 2017, the patient with fever without obvious cause found swelling of lymph nodes in the left neck and lymph node biopsy after hospitalization (the Third Affiliated Hospital of Soochow University) (Figure 1B). Physical examination revealed the left neck lymph node of 2.5×2cm; other superficial lymph nodes were non-enlargement, no involvement in liver and spleen. Biopsy pathology showed NK/T cell lymphoma, nasal type, giving the GDP plus pembellase regimen chemotherapy, the patient's condition improved and discharged.

Figure 1 Computed tomography examination

A, T showed a small lymph node was behind the retroperitoneal left renal vein in April 2013; B, CT showed an enlarged lymph nodes was behind the retroperitoneal left renal vein, evenly enhanced, compared to the previous piece (in April 2013) significantly increased in February 2017

Pathological examination: The first biopsy tissue (July 2006), intra-spinal mass was off-white, about 5×5×3cm. Microscopic examinations microscopic examinations showed diffuse and small lymphoid cell hyperplasia, common cytoplasm, irregular nucleus, granular chromatin, unobvious nucleolus, frequent mitosis, focal necrosis (Figure 2A, 2B, 2C). According to the immunohistochemical staining, the tumor cells were positive for CD43, CD2, CD56, TIA, GrB, with positive in situ hybridization for EBER, negative for CD20, CD3, ALK, CD30, CD4, and CD8. The clinical and histopathological finding of this case was in accord with the extranodal NK/T cell lymphoma, nasal type. The second biopsy (left cervical lymph node with the same people, February 2017), lymph node, about 2.5×2×1.3cm.The section was off-white and

tender. Microscopic examinations showed a diffuse proliferation of small and atypical lymphoid cells, admixed with large lymphoid cells (Figure 2D). The large lymphoid cells showed irregular nuclear borders and had amounts of cytoplasm, large nuclear, obvious nucleolus, part of nuclear folding, multiple mitotic figures, visible intravascular tumor suppository (Figure 2E). Small lymphocytes were uniform in size and regular in shape, less cytoplasm, nuclear folding, rarely mitotic figures (Figure 2F).

Figure 2: Tumor patterns, hematoxylin eosin staining.

A, necrotic tumor cell clusters (×5). B, tumor cells diffuse into pieces, infiltrating adipose tissue (×5). C, tumor cells are relatively uniform in size, nuclear round, oval, partial nuclear irregular, abundant cytoplasm (×10). D, a diffuse proliferation of small and atypical lymphoid cells, admixed with large lymphoid cells (×10).E, large nuclear, binuclear, multinuclear, visible intravascular tumor suppository (×20). F, Small lymphocytes were uniform in size and regular in shape, less cytoplasm, nuclear folding, rarely mitotic figures (×20). (A/B/C were the first biopsy organization in April 2006, and D/E/F were the biopsy organization in February 2017)

Histologically, extranodal NK/T-cell lymphoma was difficult to differentiate from metastatic carcinoma and intervariable large cell lymphoma. According to the immunohistochemical staining, the tumor cells were positive for CD3 (Fiugre 3A), CD30 (Figure 3B), CD43, CD2, CD56, TIA (Figure 3C), GrB (Figure 3D), negative for CD4, CD8, AE1/AE3, CD20, ALK, EMA. In situ hybridization for EBER was strongly positive in both specimens (Figure 3E). The proliferation index of Ki-67 was about 70% (Figure 3F). After inquiring medical history, the case was diagnosis to extranodal NK/T-cell lymphoma, nasal type, and recrudescence.

Figure 3: Assessment of CD3, CD30, TIA, GrB, EBER and Ki-67

A, positive CD3 staining in the tumor cells (×10). B, positive CD30 staining in large cells (×20). C, positive TIA-1 staining in of large cells (×20).D, positive GrB staining in large cells (×20). E, EBER positive of large cells (×20). F, the proliferation index of Ki-67 was about 70%(×20)February 2017 biopsy organization)

Discussion

Extranodal NK/T-cell lymphoma, nasal type, is a disease with an aggressive course, considered as an aggressive form of non-Hodgkin's lymphoma associated with Epstein-Barr virus infection, vascular infiltration, extensive necrosis and inflammatory exudation, expression of cytotoxic markers. The tumor is more common in adult men. The skin is the second commonest site of involvement after the upper respiratory tract. Other sites of involvement are the gastrointestinal system, soft tissue, brain, liver, spleen, bone marrow, and testis.

The survival rate of NK/T cell lymphoma is usually low (30-40%). The disease usually has a poor prognosis related to factors such as clinical stage, international classification index, bone marrow recidivism, and high level of circulating EBV DNA(3). In our case, the disease primary fistula is very rare and repeated recurrence within 11 years. The recurrence site appeared around the kidneys, adrenal glands, and in the cervical lymph node, showed local lesions. The patient treated with chemotherapy and radiotherapy, and remission.

Seok Jin Kim et al(3) observed 140 patients with NK/T cell lymphoma, of whom 6 patients had long-term survival, median overall survival was 66 months (range, 42-89 months). Two patients were located in the nasal cavity, two tonsils, one gastrocnemius muscle and one gums. Au WY et al(4) observed 40 patients with NK/T cell lymphoma in stage I. 9 patients had prolonged recurrence (10-29 years), after the first treatment. 7 cases were located in the nasopharynx, one case in tonsils, one case occurred in the ileum. All recurrence cases were confirmed by biopsy. The patient's prognosis was inferred from the cell morphology, because of histological morphology was consistent with the primary manifestation. The review of the literature showed that patients with long-term survival had limited lesions and early clinical stages. However, our case was in clinical stage II, focal lesions were a good factor for prognosis. Our case found large cell transformation in tumor recurrence in February 2017. Large cells with abundant cytoplasm in the background of small lymphocytes, accompanied with vascular tumor emboli, difficult to differentiate between histological and metastatic cancer, anaplastic large cell lymphoma, and tumor cells significantly express CD30. It is difficult to diagnose without a medical history.

In recent years, there have been a few reports with CD30 positive phenotypes of NK/T cell lymphomas. One case occurred in the skin with $CD30^+$ etranodal NK/T cell lymphoma died after eight months of diagnosis(5). Another case occurred in adrenal with $CD30^+$ etranodal NK/T cell lymphoma died after 7 days of diagnosis. The prognosis was also very poor occurred in prostate(6). Some studies have found that nucleus diameter and $CD30^+$ can be used as indicators of poor prognosis in extranodal NK/T lymphocytes(7). However, some researches found that $CD30^+$ has nothing to do with the prognosis(8). NK/T cell lymphoma is associated with Epstein-Barr virus infection. EBV can transform human lymphocytes through a multi-gene, multi-path participation process Such as driving the cell cycle, promoting cell cycle and mitosis, inhibiting apoptosis and other ways to transform human lymphocytes. EBV episomes have been employed to determine the association of the virus with various aggressive types of lymphomas, indicating that it is likely involved in tumor progression, but not tumor initiation(9). Therefore, it is speculated that this may be one of the mechanisms for the indolent lymphomas. In our case the tumor was small cells in the primary manifestation. After repeated chemotherapy, the tumors turned into large cells, and expressed CD30 that was the value-added activity but There are no similar reports in the literature. We speculated that it may be related to disease progression. Au WY et al(4) researched found that most of the patients with relapse had a poor prognosis. However, our case had multiple relapses, is currently in good condition. It still needs further observation and study the effect of large cell transformation on its prognosis. Molecularly, NK/T cell lymphomas are associated with activation of the JAK/STAT pathway and are over-expressed NK-κB and photokinase A(10). In addition,

the DDX3X mutation was found in approximately 20% of cases. Other mutations included TP53, approximately 13% and 4–18% of MLL, ASXL1, ARID1A, and EP300 mutations JAK/STAT pathway can be used as target for molecular targeted therapy(11). In addition, it have been shown that EBV-encoded proteins, such as LMP-1, EBNA-1, and EBNA-3 were interact with E2F1 to influence cell growth(12). These are expected to become new therapeutic targets for EBV-related malignancies.

Abbreviations

extranodal NK/T-cell lymphoma: Extranodal natural killer (NK)/T-Cell Lymphoma;

CT: computed tomography

EBV: Epstein-Barr virus.

Declarations

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Contributions

HW performed t the histological and immunohistochemical examination, collected imaging data, and wrote the manuscript. QL made the final diagnosis of this disease. PY collected the clinical data and wrote the manuscript.. All authors have read and approved the final manuscript.

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Ethics declarations

Ethics approval and consent to participate

This study was approved by the biomedical ethics committee of the third affiliated hospital of Soochow University, Changzhou, China.

Consent for publication

Written informed consent was obtained from the patient for the publication of this case report.

Competing interests

The authors declare that they have no competing interests.

Additional information

Publisher's Note

Availability of data and materials Not applicable.

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Figures

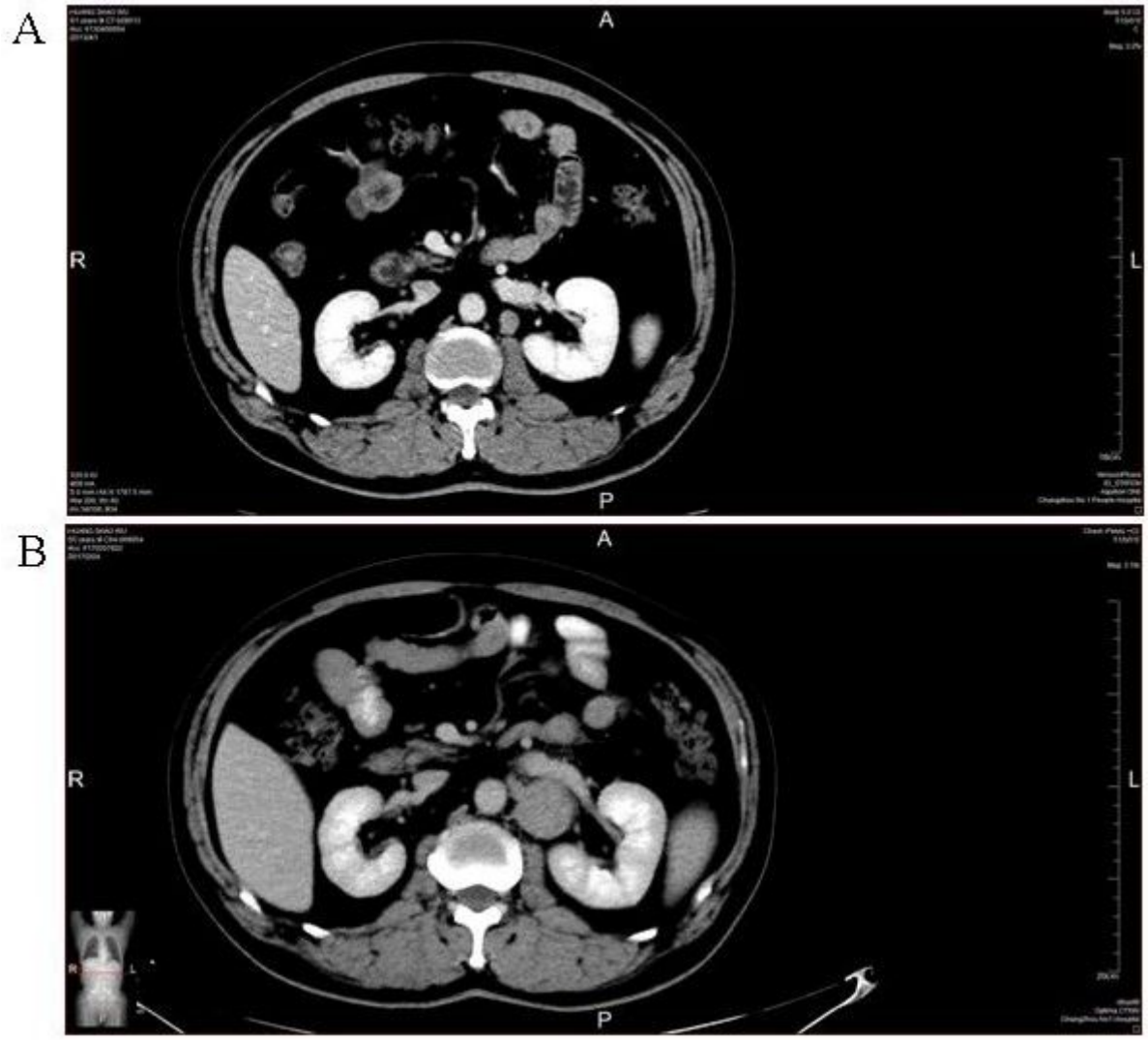

Figure 1

Computed tomography examination.

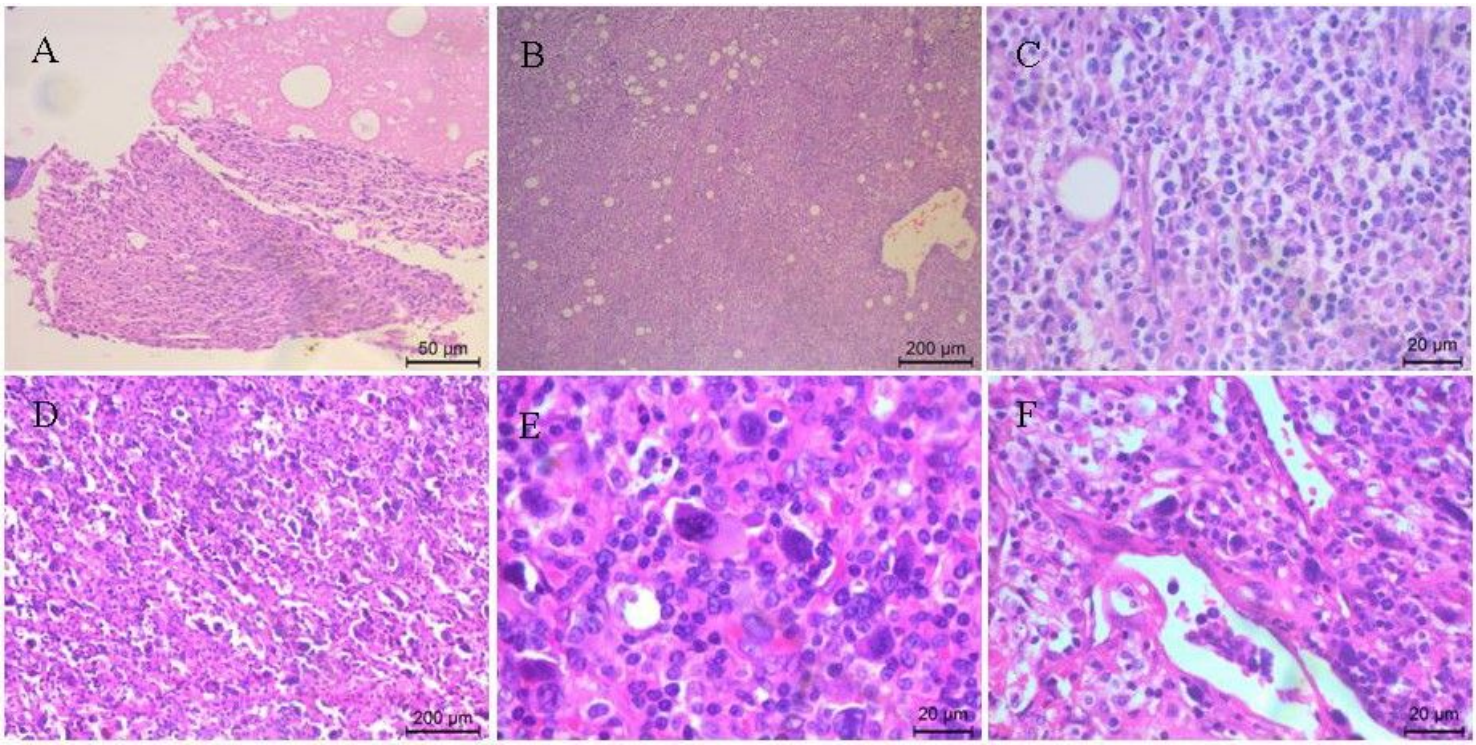

Figure 2

Tumor patterns, hematoxylin eosin staining.

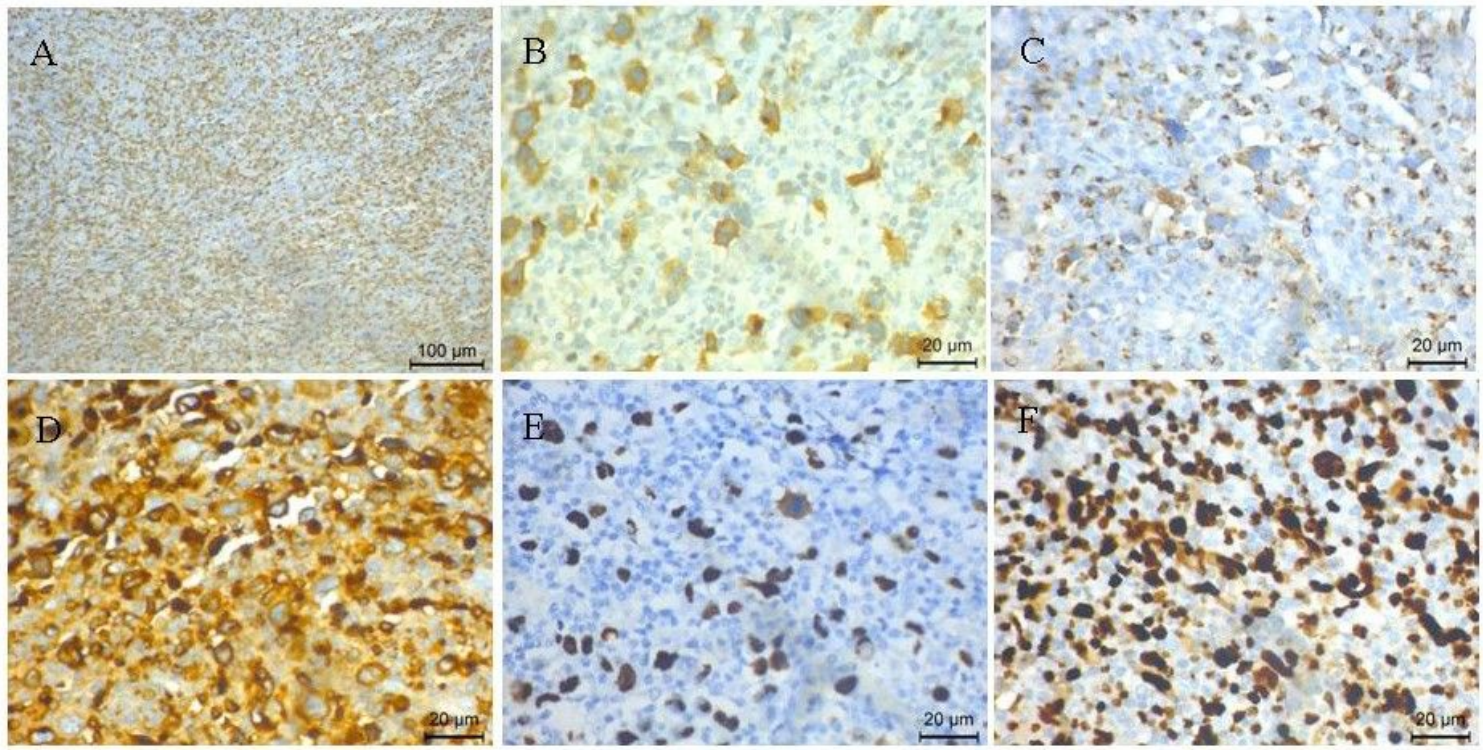

Figure 3

Assessment of CD3, CD30, TIA, GrB, EBER and Ki-67

Supplementary Files

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