Clinical Case Report

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T-cell lymphoma with abundant CD20 expression showing a good response to rituximab with gemcitabine, oxiplatin, and L-asparaginase (R-pGEMOX)

A case report

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Abstract

Rationale: T-cell lymphoma is a neoplasm that expresses markers of T-cell or natural killer cell (NK)-origin but not those of B-cell origin. Although B-cell lymphoma with abundant expression of T-cell markers exist, the opposite is very rare. Therefore, little is known about this subtype of lymphoma, including its treatment and prognosis.

Case report: A 65-year-old man was diagnosed with T-cell lymphoma with abundant CD20 expression. He was refractory to cyclophosphamide + epirubicin + vincristine + prednisone + etoposide (CHOPE), ifosfamide + cisplatin + etoposide + dexamethasone (DICE), and hyper-cyclophosphamide + vincristine + epirubicin + dexamethasone (CVAD) chemotherapy. The patient was also treated with prednisone + thalidomide + chidamide, which was also not effective. Upon admission to our department, he was administered a rituximab + gemcitabine + oxiplatin + L-asparaginase (R-pGEMOX) regimen and achieved partial remission.

Lessons: CD20-positive T-cell lymphoma is a very rare type of lymphoma that is refractory to CHOP-like regimens alone. Rituximab may be effective in patients showing abundant CD20 expression, and an R-pGEMOX regimen will likely be effective, even in refractory/recurrent patients.

Abbreviations: CHOP = cyclophosphamide + epirubicin + vincristine + prednisone, CHOPE = cyclophosphamide + epirubicin + vincristine + prednisone + etoposide, CR = completely remission, CT = computed tomography, CVAD = cyclophosphamide + vincristine + epirubicin + dexamethasone, DICE = ifosfamide + cisplatin + etoposide + dexamethasone, GEMOX = gemcitabine + oxiplatin, HE = hematoxylin and eosin, NK = natural killer cell, PD = progressive disease, PLT = platelet, PR = partial remission, RECIST = response evaluation criteria in solid tumors, R-pGEMOX = rituximab + gemcitabine + oxiplatin + L-asparaginase, WBC = white blood cell.

Keywords: CD20-positive, chemotherapy, rituximab, T-cell lymphoma

1. Introduction

T-cell lymphomas comprise a heterogeneous group of neoplasms that are highly diverse, but they share a common characteristic regarding the clusters of differentiation: positive expression of T-cell antigens (CD2, CD3, CD5, and CD7) and negative expression of B-cell antigens (CD19, CD20, CD79α, and PAX5). While there are cases of B-cell lymphoma with significant expression of T-cell antigens,[1] the opposite is rarely found. Because of its rarity, little is known about this subtype of disease, particularly regarding its treatment and prognosis.

T-cell lymphoma is characterized by a poor prognosis. Moreover, it is refractory to traditional chemotherapy regimens, and no standard treatment exists to date. The response rate of T-cell lymphoma to cyclophosphamide + epirubicin + vincristine + prednisone (CHOP) was reported as 50% to 70%,[2] which is much lower than that of B-cell lymphoma. In the past few years, a gemcitabine-based regimen plus L-asparaginase was shown to be effective for the treatment of T-cell lymphoma.[3] However, due to the rarity of the disease (only few cases have been reported), there has been no clinical trial for T-cell lymphoma with abundant CD20 expression.

Herein, we report a case of T-cell lymphoma with abundant CD20 expression; the patient showed a good response to treatment with rituximab + gemcitabine + oxiplatin + L-asparaginase (R-pGEMOX).

2. Case report

2.1. Patient information

A 65-year-old man found that he had enlarged neck lymph nodes in January 2015. He was initially diagnosed with inflammation,

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Table 1

Important dates in the case.

Time	Event
January 2015	Neck lymph node enlargement
March 2016	Biopsy
April 2016	1 cycle of CHOPE regimen
May 4, 2016	1 cycle of DICE+chidamide regimen
May 31, 2016	1 cycle of hyper-CVAD+ chimamide regimen
June 2016	Thalidomide, predisione, and chidamide regimen
July 20, 2016 September 7, 2016 October 11, 2016	3 cycles of R-pGEMOX regimen
Nov 2016~Dec 2016	Radiation to neck and nasopharynx
February18, 2017 April 7, 2017	2 cycles of Pemtrexe, topotecan, dexamethasone regimen
May 9, 2017	Died

CHOPE = cyclophosphamide + epirubicin + vincristine + prednisone + etoposide, CVAD = cyclophosphamide + vincristine + epirubicin + dexamethasone, R-pGEMOX = rituximab + gemcitabine + oxiplatin + L-asparaginase.

but a chest computed tomography (CT) scan that was conducted two months later revealed multiple enlarged lymph nodes in the mediastinum, fossa ancillaris, inguinal region, and pelvic cavity. The patient underwent a biopsy of the neck lymph nodes at a local hospital in March 2016. Pathological examination revealed, "angioimmunoblastic T-cell lymphoma, CD20 diffusely positive."

In April 2016, the patient underwent 1 cycle of cyclophosphamide + epirubicin + vincristine + prednisone (CHOPE) (cyclophosphamide, 1200 mg d1; etoposide, 100 mg d1–3; epirubicin, 70 mg d1; vincristine, 2 mg d1; and prednisone, 100 mg po d1–3) at a cancer hospital. However, he was quickly found to have progressive disease (PD) with larger neck lymph nodes. On May 4, 2016, he received ifosfamide + cisplatin + etoposide + dexamethasone (DICE; ifosfamide, 2 g d1–4; cisplatin, 50 mg d1–3; etoposide, 100 mg d1–3 and 200 mg d4; and dexamethasone 9 mg po d1–4) + chidamide 20 mg twice weekly. However, the patient still had PD one month later. On May 31, 2016, he underwent one cycle of a hyper-cyclophosphamide + vincristine + epirubicin + dexamethasone (CVAD) regimen (cyclophosphamide, 500 mg q12h iv d1–d3; vincristine, 2 mg iv d4; epirubicin, 60 mg iv d4 and 60 mg d5; and dexamethasone, 20 mg iv d1–d5) + chidamide 20 mg po twice weekly, after which he achieved stable disease.

Thereafter, the patient discontinued the chemotherapy and was transferred to oncology clinic of our hospital where he was given cyclosporine plus thalidomide (100 mg po qd) + prednisone (50 mg po qd) + chidamide (twice weekly) starting in June 2016. When he was admitted to our department on July 17, 2016, he showed rapid enlargement of his neck lymph nodes and developed a fever as well as difficulty breathing. The patient denied a lasting fever, night sweats, and weight loss. His past medical history included hypertension and obstructive sleep apnea syndrome.

Table 1 depicts the clinical timeline of this case.

2.2. Clinical findings

A physical exam upon admission showed stable vital signs, obvious swelling of the pharyngeal tissue, inflammation of the tonsils with purulent secretion, and a small pharyngeal cavity. Enlarged lymph nodes were observed bilaterally in the neck, with some fusing to form big masses.

2.3. Diagnostic assessment

Laboratory examinations showed the following: hemoglobin, 95 g/L; lactose dehydrogenase, 688 U/L; as well as normal white blood cell (WBC) and platelet (PLT) counts. Liver and kidney function tests were also normal. A bone marrow biopsy showed findings of anemia; no abnormal cells were found.

A pathology consult revealed T-cell lymphoma with diffuse positive CD20 expression, not specified as a certain subtype. Immunohistochemical analyses showed the following: CD20 (+), CXCL-13 (−), PAX-5 (−), CD3 (+), Bcl-2 (+), CD56(NK-1) (−) (Fig. 1). Molecular pathology showed EBER (scattered+), and a gene rearrangement analysis indicated T-cell clone rearrangement.

Based on the above findings, the patient was diagnosed with peripheral T-cell lymphoma, unspecified, stage IIIA, group 4.

2.4. Therapeutic interventions

On July 20, September 7, and October 11, 2016, the patient was given 3 cycles of the R-pGEMOX regimen (rituximab, 700 mg iv d0; gemcitabine, iv 1.6 g d1 and 1.4 g d8; oxaliplatin, 100 mg d2 and 50 mg d8; and L-asparaginase, 3,750 u im d15). He developed a fever on the day on which he received gemcitabine and L-asparaginase. Moreover, he suffered from grade 2 WBC and PLT deficiencies as well as grade 3 anemia during the course of the chemotherapy. After 2 cycles of R-pGEMOX, the patient experienced an improvement in his breathing, and a CT scan showed partial remission (PR) according to the Response Evaluation Criteria in Solid Tumors (RECIST). The size of the target tumor decreased by 60% (Figs. 2A–D and 3).

On November 2, 2016, after 3 cycles of R-pGEMOX, a repeat CT scan showed a tumor in the enlarged nasopharynx (Fig. 4). At this time, the patient also developed pneumonia and therefore had to discontinue the chemotherapy; instead, he received radiation therapy targeting the nasopharynx and neck region. The pneumonia improved after antibiotics treatment. After the completion of radiation therapy, a CT scan conducted on January 15, 2017, showed another obvious decrease in tumor size (Fig. 2E and F), but new lymph nodes were found in his right arm. On February 18 and April 7, 2017, the patient received pemetrexed, topotecan, and dexamethasone for 2 cycles as well as radiation therapy of the right arm and right fossa axillary; however, he still had gradual PD.

2.5. Follow-up and outcomes

Because the pneumonia persisted and worsened intermittently, the patient's relative decide to discontinue the chemotherapy; instead, the patient underwent treatment using Chinese herbal medicine. On May 3, 2017, a routine blood analysis conducted at a local hospital showed a WBC of 168×10 e9/L, 11% neutrophils, 64.5% monocytes, 10.2% lymphocytes, 13.6% eosinophils, and 0.3% basophils. Leukemia was not excluded, and the patient died on May 9, 2017, before a bone marrow biopsy could be conducted.

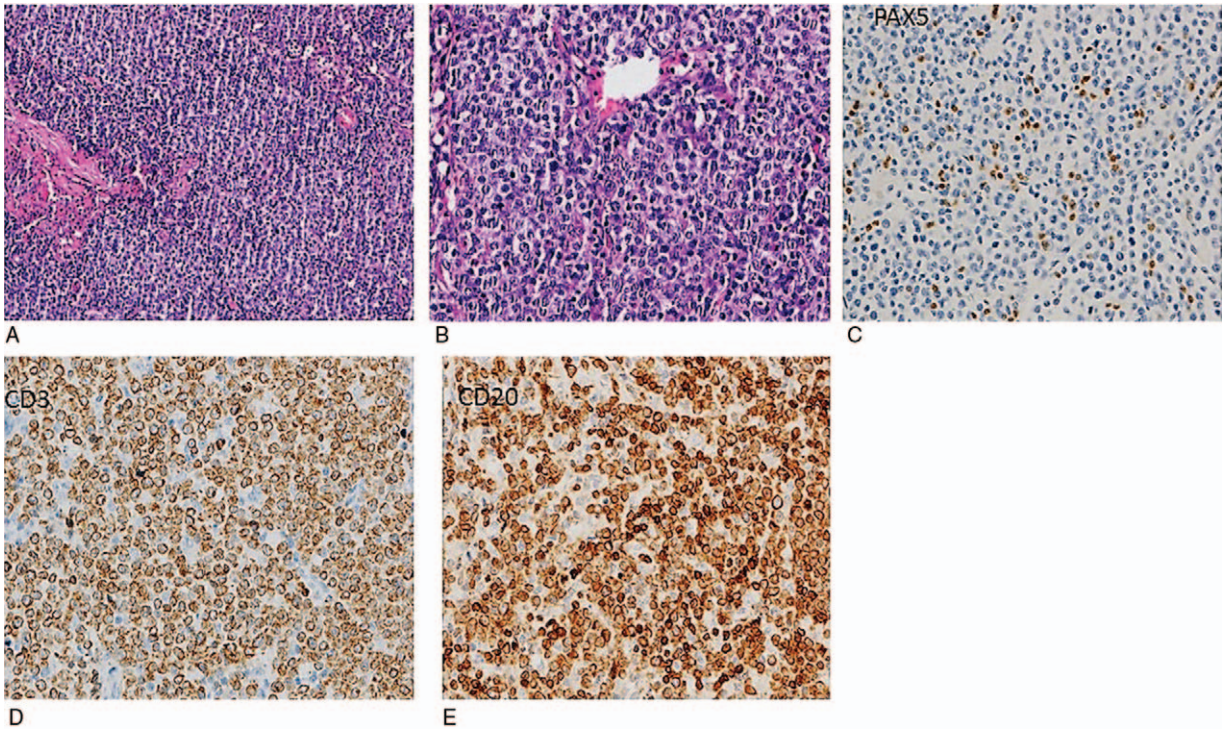


Figure 1. (A) Parts of the lymph node were replaced by diffuse tumor cells (low power microscope, hematoxylin and eosin [HE] stain). (B) The tumor cells were of medium size and were of medium and slightly large size, with irregular nuclei and small nucleoli (low power microscope, HE stain). (C) The tumor cells were negative for PAX5. (D) The tumor cells showed positive CD3 staining. (E) Diffuse positive staining of the tumor cells for CD20 was observed. HE = hematoxylin and eosin

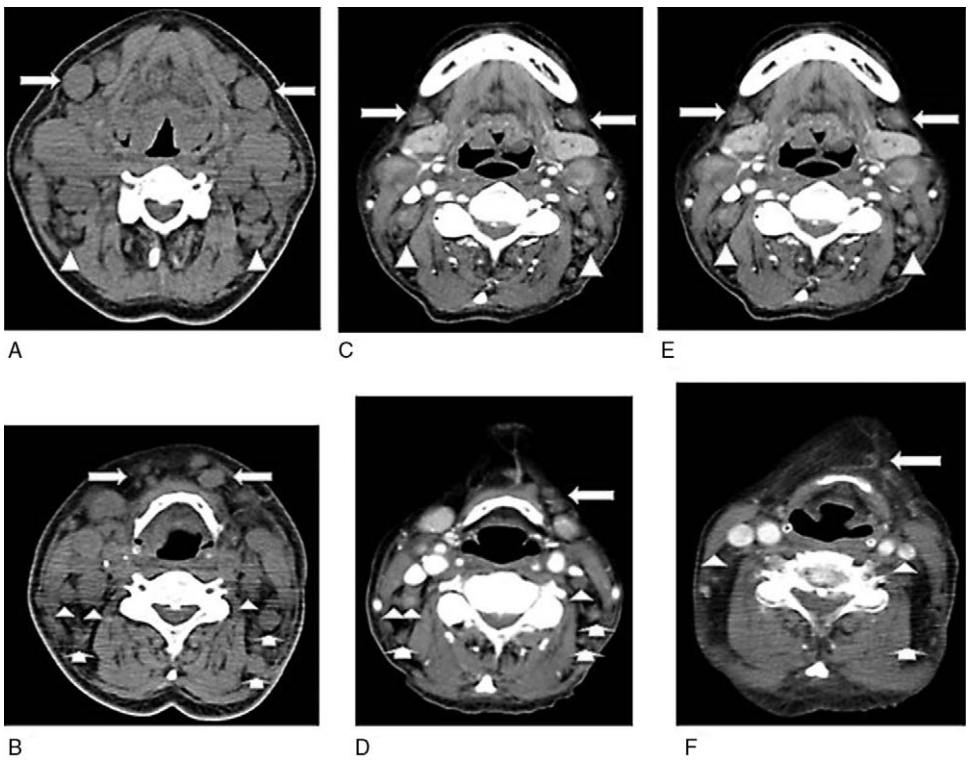
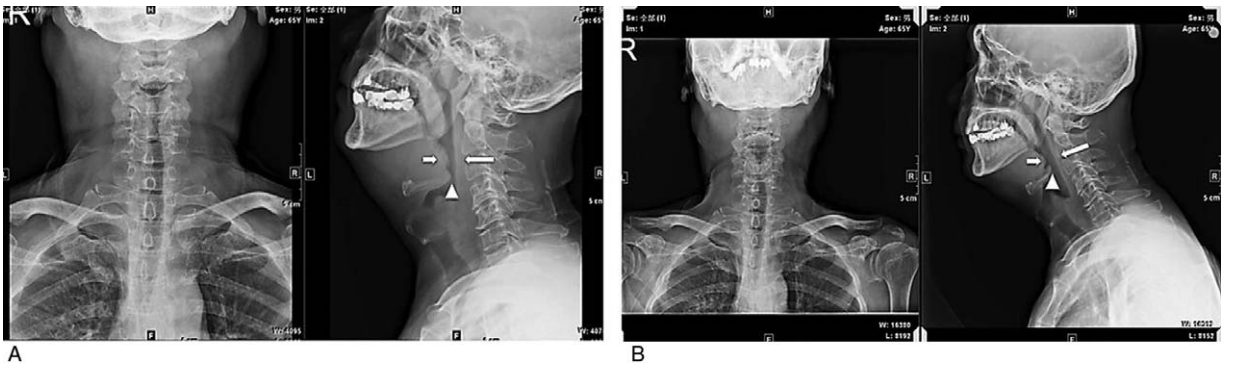


Figure 2. Neck computed tomography scan before (A, B) and after (C, D) 2 cycles of rituximab + gemcitabine + oxiplatin + L-asparaginase (R-pGEMOX) chemotherapy and after radiation therapy (E, F). (A, B) Lymph nodes enlarged in bilateral submandibular (IB) area (long arrow), carotid sheath (II) area (arrowhead), and accessory nerve lymphatic chain (VA) area (short arrow); (C, D) lymph nodes significantly decreased in size after the chemotherapy. (E, F) After radiation therapy, another decrease in the size of the lymph nodes was observed. R-pGEMOX = rituximab + gemcitabine + oxiplatin + L-asparaginase.



A B

Figure 3. Tracheal phase before (A) and after (B) rituximab + gemcitabine + oxiplatin + L-asparaginase (R-pGEMOX) chemotherapy. The swelling of the anterior and posterior oropharynx (arrowhead) obviously improved, and the stricture of the pharynx improved (triangle). R-pGEMOX = rituximab + gemcitabine + oxiplatin + L-asparaginase.

3. Discussion

T-cell lymphoma is a group of heterogeneous malignancies originating from T-cells or NK cells; thus, these tumors typically express markers of T- but not B-cell origin. T-cell lymphoma has a poor prognosis, does not respond to CHOP-like regimens, and no standard treatment regimen exists to date. Our case was also refractory to the CHOP, DICE, and hyper-CVAD regimens but showed a very good response to R-pGEMOX.

As a CD20 antibody, rituximab has been important in the treatment of B-cell lymphoma since its introduction in 1997. It has greatly improved the response rate and overall survival of patients with B-cell lymphoma.[4–6] The rationale for using rituximab in this case was based on the abundant expression of CD20, similar to B-cell lymphoma. The patient also received other chemotherapy regimens, including CHOP, DICE, and hyper-CVAD, none of which were effective. Therefore, we chose a GEMOX regimen, which was reported to be effective for the treatment of NK/T-cell lymphoma in recent years.[7,8] A clinical trial of its role in the treatment of T-cell lymphoma is ongoing (clinicaltrials.gov: NCT01626664). L-asparaginase was the first drug that was found to be effective for the treatment of NK/T-cell lymphoma[9] and T-cell lymphoma.[10] Therefore, we combined GEMOX with L-asparaginase and rituximab in the current case and found this regimen to be remarkably effective.

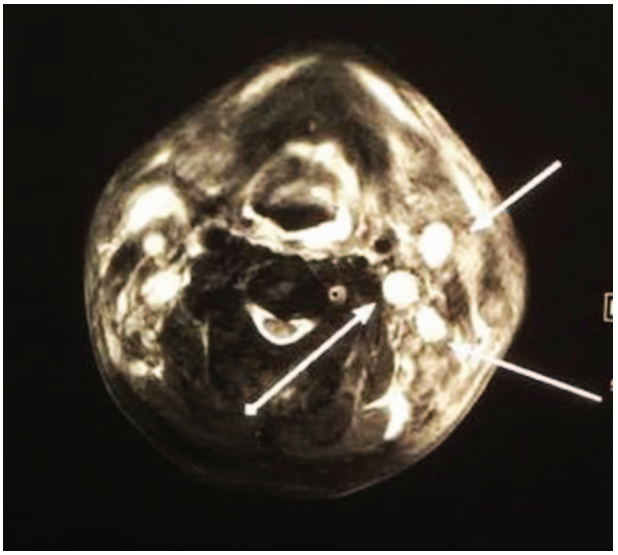


Figure 4. Enlargement of the lymph nodes in the left cervical and common carotid arteries bifurcation (arrows).

Kakinoki et al[11] reported the successful treatment of 11 patients with CD20-positive T-cell lymphoma with rituximab alone or with rituximab plus chemotherapy. Of these patients, 3 showed strong CD20 staining and 2 showed weak CD20 staining; all were treated with RCHOP. The remaining 6 patients exhibited variable CD20 staining; of these, 2 were treated with rituximab only. The study further showed that all patients with strong CD20 staining achieved complete remission (CR)/PR; in contrast, only 2 patients with variable staining achieved CR/PR, and 1 patient with weak staining achieved PR. This indicates that patients with abundant CD20 expression will benefit the most from treatment with R-CHOP.

In this case, the patient had PD although he was repeatedly and heavily treated with high-intensity chemotherapy regimens. However, he achieved PR that was maintained for 4 months with R-pGEMOX. Due to his worsening condition, he did not receive the chemotherapy according to the planned regimen; rather, it was delayed for 1 to 3 weeks. If the regimen could have been initiated earlier, it is likely that a better effect would have been seen. The most severe chemotherapy-related toxicity seen in this case was grade 3 anemia as well as pneumonia, the latter of which became an obstacle to the chemotherapy. Pneumonia was previously reported during rituximab treatment; it is thought to be induced by B-cell deficiency or a yet undetermined mechanism of rituximab.[12,13] No new adverse reactions were observed in this case. The pneumonia improved after antibiotics treatment.

In conclusion, CD20-positive T-cell lymphoma is a very rare type of lymphoma, which is refractory to treatment with a CHOP-like regimen alone. Rituximab may be effective in these patients, and a p-GEMOX regimen is likely effective, even in refractory/recurrent patients.

4. Ethics approval and informed consent

All clinical specimens were obtained with the approval of the institutional ethics committee, and the research was performed in accordance with the Declaration of Helsinki. Written informed consent for the publication of the patient's clinical details and images was obtained from the relative of the patient.

5. Availability of data and materials

The datasets used and analyzed in this report are available from the corresponding author upon reasonable request.

6. Authors' contributions

YJS drafted the paper, CMB reviewed, and edited the manuscript. JS interpreted the pathological imaging and XG interpreted the radiological image. All authors contributed equally to the manuscript. All authors read and approved the final manuscript.

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