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## CASE REPORT

# Case Sharing in T-cell Lymphomas and Review of Angioimmunoblastic T-cell Lymphoma

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## ABSTRACT

*Mature T-cell and natural killer–cell neoplasms can be classified into four categories based on site: cutaneous, extranodal, nodal, and leukaemic. Subtypes within these categories may be aggressive or indolent, with some indolent cases potentially undergoing aggressive transformation. However, both indolent and aggressive cases are potentially manageable with appropriate therapy. In this report, four patients, representing the four sites of disease, are described: cutaneous — mycosis fungoides; extranodal — natural killer/T–cell lymphoma nasal type; nodal — angioimmunoblastic T-cell lymphoma; and leukaemic — adult T-cell leukaemia/lymphoma. The published literature on potential therapeutic options for angioimmunoblastic T-cell lymphoma is reviewed.*

***Key Words:*** *Immunoblastic lymphadenopathy; Lymphoma, non-Hodgkin; Lymphoma, T-cell, peripheral; Mycosis fungoides; Treatment outcome*

## 中文摘要

### T細胞淋巴癌的病例分享及血管免疫母細胞T細胞淋巴瘤的回顧

**林炎坤**

成熟的T細胞和自然殺手細胞腫瘤可按其病發位置分為以下四類：皮膚、淋巴結外、結節和類白血病。這些類別中可再分為侵襲型或緩慢型，但部分的緩慢型有可能會演變為侵襲型。然而，無論是侵襲型或緩慢型，均可施以適當治療以治病癒。本文報告四宗分別在不同位置的病例：皮膚（蕈樣肉芽腫）、淋巴結外（自然殺手/T細胞淋巴瘤—鼻腔型）、結節（血管免疫母細胞性T細胞淋巴瘤），以及類白血病（成人T細胞白血病/淋巴瘤）。此外，本文會回顧文獻中有關血管免疫母細胞性T細胞淋巴瘤的治療選擇。

## INTRODUCTION

In 2009, there were 730 new cases of non-Hodgkin lymphoma (NHL) in Hong Kong, accounting for 2.8% of all new cancer cases.[1] T-cell lymphomas comprise around 15 to 25% of NHL cases in Hong Kong.[2] The mature T-cell and natural killer (NK)–cell neoplasms include more than a dozen subclassifications,[3,4] which can be grouped according to site and cause, and may be aggressive or typically indolent in nature (Table).[4]

## CASE REPORTS

### Patient 1: Mycosis Fungoides

A 55-year-old woman presented in 2004 with a facial erythematous rash of four to five years' duration.

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**Table.** Subclassification of mature NK- / T-cell neoplasms. Aggressive subtypes are indicated in dark shading and indolent forms in light shading.*

| Mature T/NK-cell neoplasms | | | |
|---|---|---|---|
| Cutaneous | Extra-nodal | Nodal | Leukaemic |
| Mycosis fungoides | NK/TCL nasal type | Angioimmunoblastic TCL | Adult T-cell leukaemia/ lymphoma |
| Sézary syndrome | Enteropathy-associated TCL | Anaplastic large cell lymphoma (ALK+/-) | Aggressive NK-cell leukaemia |
| Primary cutaneous CD30+ T-cell disorder | Hepatosplenic TCL | Peripheral TCL-NOS | T-cell prolymphocytic leukaemia |
| Primary cutaneous gamma/ delta TCL | Subcutaneous panniculitis-like TCL | - | T-cell large granular lymphocytic leukaemia |

Abbreviations: TCL = T-cell lymphoma; NK = natural killer; ALK+/- = anaplastic lymphoma kinase positive or negative; NOS = not otherwise specified.
* Adapted from Rodríguez et al.[4]

Skin biopsy confirmed mycosis fungoides. Physical examination and computed tomography (CT) scans showed no evidence of lymphadenopathy in the cervical, thoracic, abdominal, or pelvic areas, and her bone marrow was normal. As the disease displayed a stable course, the patient was managed with ultraviolet light therapy and topical steroids only. Follow-up CT scans in 2007 showed no change.

However, in 2008, the disease became aggressive and the patient presented with fever and generalised lymphadenopathy. Physical examination showed diffuse reticulated infiltration of the skin and CT scans revealed lymphadenopathy in the bilateral groin, external iliac, left common iliac, left para-aortic, and bilateral axillary lymph nodes. Biopsy confirmed reactive changes to lymphoma only. Chemotherapy with cyclophosphamide, epirubicin, vincristine, and prednisone and, later, with ifosfamide, methotrexate, and etoposide failed; however, resolution of lymphadenopathy was achieved with cisplatin, cytosine arabinoside, and dexamethasone. In 2012, the disease continues to be stable, with only an erythematous rash over the left forearm and back evident; this is adequately managed with intermittent dexamethasone.

This case shows that, although mycosis fungoides typically follows an indolent course, it can undergo aggressive transformation, requiring intervention with intensive chemotherapy.

## Patient 2: Natural Killer– / T-cell Lymphoma, Nasal Type

A 70-year-old man presented with a non-specific complaint of epistaxis in February 2006. Examination revealed maggot infestation of his nasal cavities, and CT scans showed some masses in the nasopharyngeal area. The histological diagnosis was nasal NK/T-cell lymphoma (NKTCL) complicated by a maggot infestation. After discharge, the patient failed to attend for follow-up treatment. He presented again after three weeks with an acute exacerbation of chronic pulmonary obstructive disease. By then, his nasal condition had advanced rapidly with extensive tumour infiltration and necrosis affecting his nose and face. As this patient illustrates, NKTCL is highly aggressive and needs prompt intervention to prevent the type of rapid and extensive disease progression seen in this patient.[5]

## Patient 3: Adult T-cell Leukaemia / Lymphoma

A 61-year-old man presented with exudative left pleural effusion during a health check in 2011. No peripheral lymphadenopathy was found and pleural biopsy resulted in a diagnosis of T-cell lymphoblastic leukaemia / lymphoma. Bone marrow staging was negative, although the condition was treated as stage IV because of the pleural effusion. In view of the patient's good performance status (Eastern Cooperative Oncology Group 1), he received eight cycles of hyper-fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone, with complete resolution of the pleural effusion and disappearance of the tissue mass (Figure). Thus, even an aggressive subtype such as T-cell lymphoblastic leukaemia / lymphoma can be markedly improved with intensive chemotherapy.

## Patient 4: Angioimmunoblastic T-cell Lymphoma

A 74-year-old man presented with B symptoms (systemic symptoms of fever, night sweats, and weight loss) in May 2011. Very aggressive multiple lymphadenopathies were discovered in the cervical, supraclavicular, and groin regions. Diagnostic

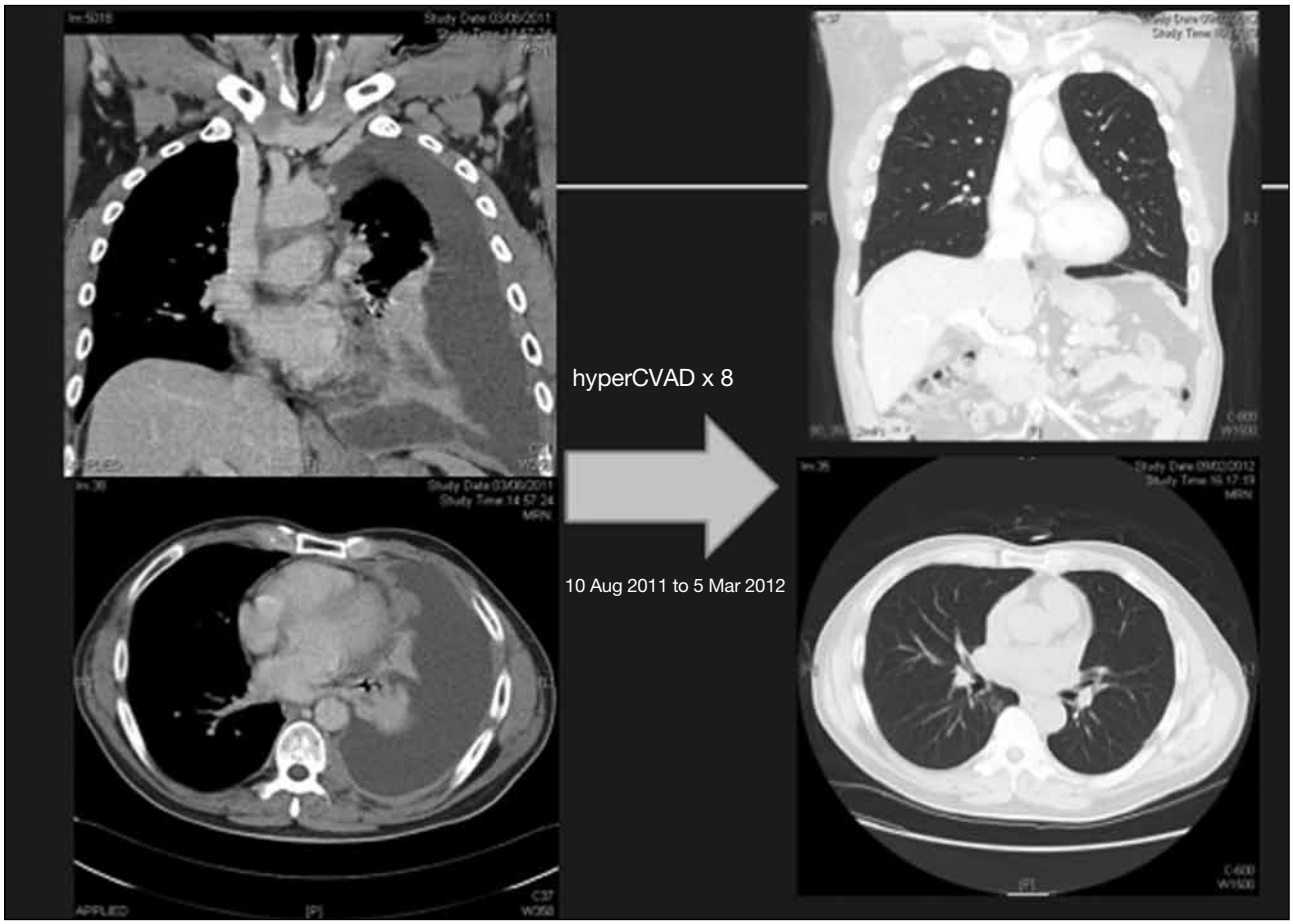


**Figure.** Thoracic computed tomography images of a patient with T-cell lymphoblastic leukaemia / lymphoma before and after eight cycles of hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone (hyperCVAD).

imaging also suggested the presence of left adrenal metastases. Histology indicated a diagnosis of angioimmunoblastic T-cell lymphoma (AITL) with Epstein-Barr encoded RNA–positive cells. The patient refused chemotherapy in Hong Kong, and was treated in China with cyclosporin A (CsA), which caused regression of the cervical and groin lymphadenopathies for about five months. Despite subsequent treatments in China, the disease progressed in early 2012 and the patient developed progressive pancytopenia. In April, he presented with refractory thrombocytopenia and neutropenic fever, and developed a left intracerebral haemorrhage. After admission to a private hospital, the patient wanted to try a novel treatment, but died before therapy could be commenced.

## DISCUSSION

### What treatments are of benefit in Angioimmunoblastic T-cell Lymphoma?

The US National Comprehensive Cancer Network (NCCN) guidelines on treatment of peripheral T-cell lymphoma (PTCL) recommend chemotherapy as first-line therapy for AITL, including cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP)–based regimens.[6] Available evidence suggests that more intensive chemotherapy is not superior to CHOP in terms of survival in patients with T-cell NHL,[7] including AITL.[8]

In the NCCN guidelines, CsA is indicated as second-line therapy for AITL in patients unsuitable for transplant.[6] Published data for CsA in AITL are largely confined to case reviews,[9,10] and suggest that it could be beneficial for some patients with AITL.

There is interest in adding monoclonal antibody agents to CHOP regimens to improve clinical outcomes in patients with PTCL, including AITL. A small Italian study obtained encouraging results with alemtuzumab plus CHOP, with a 70% one-year overall survival rate

in AITL patients[11]; further phase III trials are ongoing. Rituximab plus CHOP has also been studied in small numbers of AITL patients,[12,13] but with so few data available, it remains unclear whether this provides a benefit over CHOP alone.

Autologous stem cell transplantation (ASCT) should be considered for patients with PTCL who attain a good clinical response to chemotherapy, according to the NCCN guidelines.[6] A retrospective study of AITL patients receiving high-dose therapy followed by ASCT showed that disease status at transplantation was the major factor influencing outcome; patients who received a transplant during the first complete remission had significantly superior progression-free and overall survival.[14] The findings of a prospective multicentre study of upfront ASCT in PTCL patients, including AITL cases, suggested that this approach could have a considerable impact on clinical outcome in AITL,[15] although randomised clinical trial data are still needed.

## CONCLUSION

Mature T and NK-cell neoplasms can be indolent and aggressive, with both types potentially manageable with appropriate therapy. Conventional cytotoxic chemotherapy continues to be the first-line therapy for AITL, although CsA may be an alternative for AITL as a second-line therapy. The benefit of alemtuzumab plus chemotherapy in untreated PTCL remains under investigation.

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