Management of Human T-Cell Lymphotropic Virus Type-1-Associated Adult T-Cell Leukaemia (HTLV-1 ATL) & Pharmacist Involvement in Rare Malignancies

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Aim:

This case outlines a treatment approach for HTLV-1 ATL based on literature, and the role of the pharmacist in the treatment of rare malignancies where no formal guidelines are available.

Background:

HTLV-1 ATL is an aggressive, chemotherapy-resistant malignancy, rare in Australia.[1,2,3]
The HTLV-1 virus is endemic in Central Africa, South America, the Caribbean, Iran and South-Western Japan, with between 10-20 million people infected worldwide. (figure 1).[1] It has a 50-year mean latency period and can transform to cause clonal expansion of T-cells, resulting in ATL in 1% to 4% of hosts.[3]
Clinical expression of HTLV-1 ATL is classified into 4 subtypes (figure 2), the aggressive subtypes requiring early treatment.[1]
The available evidence for treatment is limited to case-reports and small studies. In recent years, literature has increasingly suggested the antiviral regimen of zidovudine (AZT) and interferon alfa (IFN) as standard treatment for the aggressive leukaemia subtypes.[1,2,3]
Alternatively, chemotherapy protocols such as VCAP-AMP-VECP and CHOP can be used, the former not available in Australia due to lack of access to ranimustine.[1] Allogenic stem cell transplantation can be considered if there is a response to first-line treatment.[1]
Given the rare nature of HTLV-1 ATL in Australia and lack of formal treatment guidelines, cases require careful consideration of literature and extensive consultant discussion.

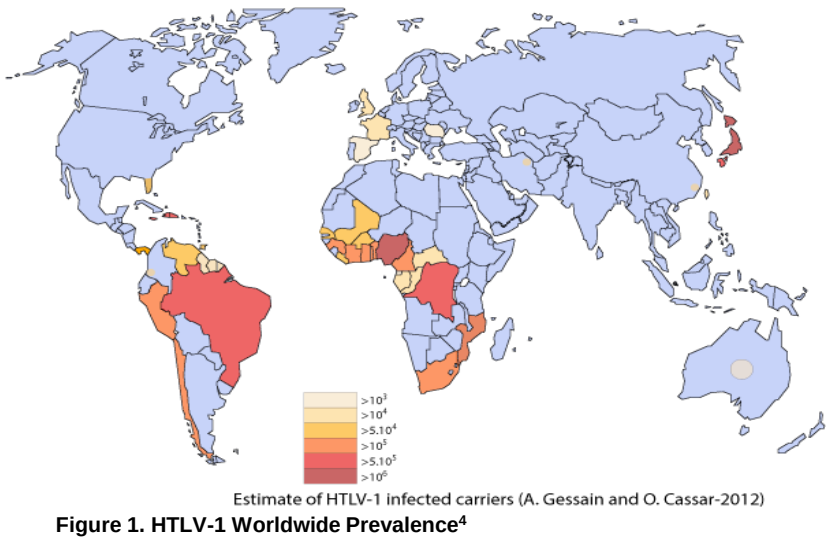

Figure 1. HTLV-1 Worldwide Prevalence[4]

Clinical Features:

A 56 year old female presented to hospital with 3-week history of intermittent dizziness, back pain of unknown trigger, poor appetite, weight loss and lethargy with general functional decline.
Upon investigation, an elevated white cell count (WCC) and abnormal T-cell population on bone marrow biopsy were consistent with mature T-cell lymphoprolipherative disorder.[1] Positive HTLV-1 serology and Western blot test both confirmed the diagnosis of acute subtype HTLV-1 ATL.[1]

Interventions:

The haematology team conducted a literature review and consulted medical counterparts from overseas to determine the most appropriate treatment option for this patient. Available evidence and expert advice from endemic areas both suggested first line treatment with an antiviral regimen.[1,2,3] Figure 2 outlines this suggested therapeutic strategy, based on a summary of available literature.[1]

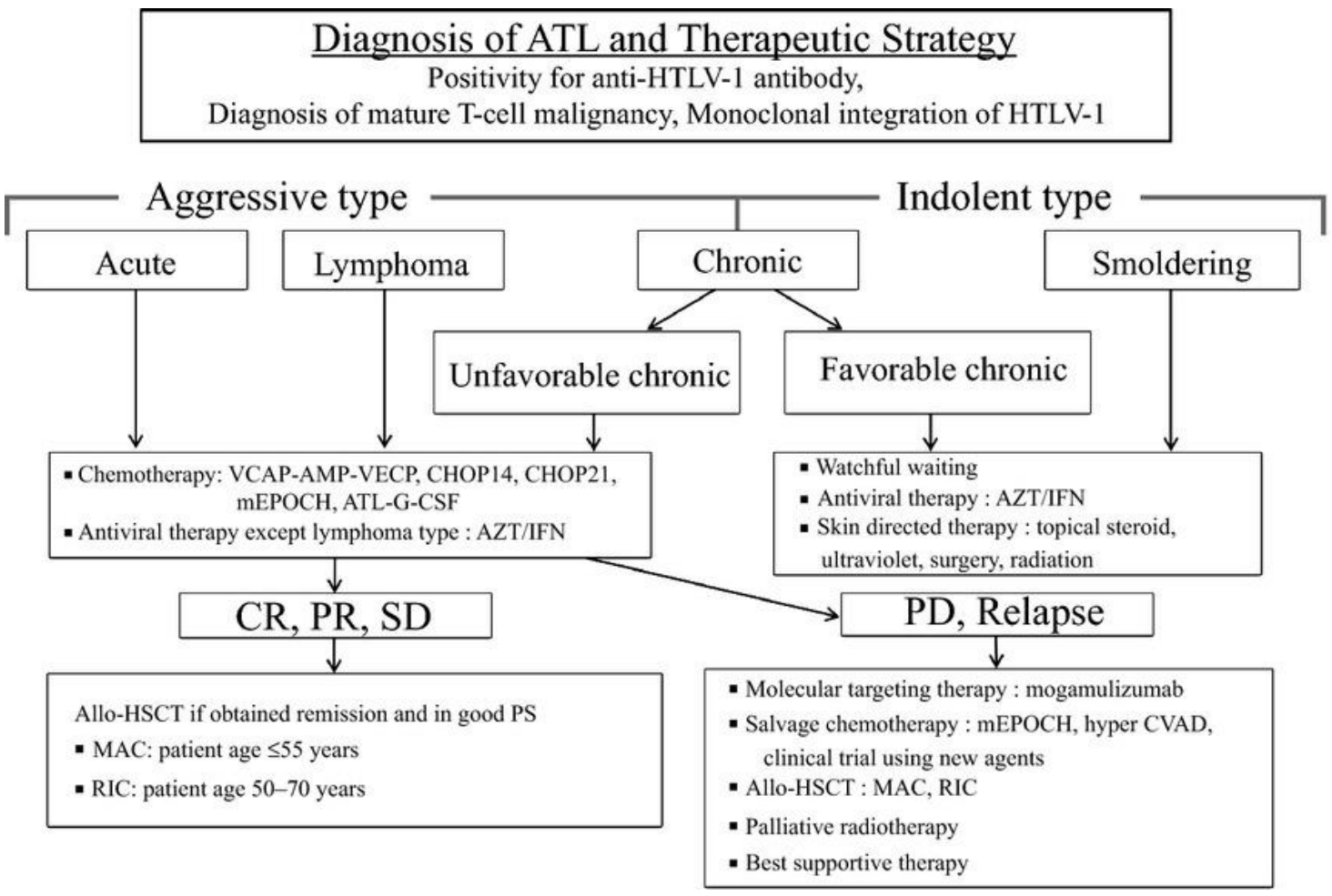

Figure 2. Therapeutic strategy for various types of HTLV-1 ATL[1]

Allo-HSCT- allogenic haematopoietic stem cell transplantation; **ATL-G-CSF-** vincristine, vindesine, doxorubicin, mitoxantrone, cyclophosphamide, etoposide, ranimustine, and prednisone with granulocyte colony stimulating factor support; **AZT-** zidovudine; **CHOP-** cyclophosphamide, doxorubicin, vincristine and prednisone; **CR-** complete remission; **HyperCVAD-** cyclophosphamide, vincristine, doxorubicin, and dexamethasone; **IFN-** interferon alfa; **MAC-** myeloablative conditioning; **mEPOCH-** etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin; **PD-** progressive disease; **PR-** partial remission; **PS-** performance status; **RIC-** reduced intensity conditioning; **SD-** stable disease; **VCAP-AMP-VECP-** (VCAP- vincristine, cyclophosphamide, doxorubicin and prednisolone; AMP- doxorubicin, ranimustine and prednisolone; VECP- vindesine, etoposide, carboplatin prednisolone)

After discussion within multidisciplinary team, AZT 900mg daily and IFN 5million IU/m^2/day were started, with the addition of intrathecal hydrocortisone, methotrexate and cytarabine for potential central nervous system (CNS) disease involvement, as also suggested in literature.[1,3]
Informed of the treatment plan, the pharmacist also conducted a literature review, assessing the selected treatment against evidence, and confirming the proposed dosing regimen was appropriate.
Given the lack of formal guidelines available, the pharmacist was particularly important in recommending the supportive medication necessary based on literature.
After reviewing the available evidence, the pharmacist recommended a supportive treatment plan including antiviral, anti-pneumocystis jiroveci pneumonia, antifungal and tumour lysis prophylaxis.[1,3] Strongyloides prophylaxis was also suggested based on a case report in the literature.[5] However, upon further discussion with the consultant it was decided to omit this due to absence of risk factors.
As treatment commenced, monitoring included viral load, full blood count, urea, electrolytes and lactate dehydrogenase (LDH).[1]

Case Progress and Outcomes:

Within one week, increasing WCC and LDH levels indicated rapid disease progression.[1] The medical team decided to urgently start the CHOP chemotherapy protocol. The antiviral regimen was withheld due to causing thrombocytopaenia.
Though WCC and LDH levels transiently decreased, CHOP caused significant haematological toxicity, requiring support with granulocyte colony stimulating factor and cessation of chemotherapy after only one cycle. Antivirals were then re-started at lower doses due to cytopaenias, continuing until the patient's death from infective complications 3 months after treatment initiation.

Conclusions:

Treatment of rare malignancies such as HTLV-1 ATL requires careful consideration of available literature.
In Australia, options for acute HTLV-1 ATL include an antiviral regimen and the CHOP chemotherapy protocol, with potential for allogenic stem cell transplantation if there is a response to treatment.[1]
Unfortunately, treatment can often be limited by toxicities and infective complications.[1]
Cancer pharmacists have an important role in the setting of rare malignancies, to evaluate proposed treatment plans against evidence and provide advice relating to supportive treatment where no guidelines are present and only limited literature available.

References:

1. Utsunomiya A, et al. Recent advances in the treatment of adult T-cell leukemia-lymphomas. Cancer Sci. 2015 Jan 25; 106(4):344-355
2. Bazarbachi A, et al. Meta-analysis on the use of zidovudine and interferon-alfa in adult T-cell leukemia/lymphoma showing improved survival in leukemic subtypes. J Clin Oncol, 2010 Sep 20; 28(27): 4177-4183
3. Bazarbachi A, et al. How I treat adult T-cell leukemia/lymphoma. Blood. 2011 Aug 18; 118(7): 1736-1745
4. Gessain A, et al. Epidemiological aspects and world distribution of HTLV-1 infection. Front Microbiol. 2012 Nov 15; 3:388
5. Peters L, et al. Secondary strongyloides stercoralis prophylaxis in patients with human T-cell lymphotropic virus type-1 infection report of two cases. Int J Infect Dis. 2009 Feb 6; 13:e501-e503

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