Successful Use of Ruxolitinib for Refractory Haemophagocytic Lymphohistiocytosis: A Case Report

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Introduction

Haemophagocytic lymphohistiocytosis (HLH) is a life-threatening syndrome of immune activation resulting in cytokine-mediated inflammation, occurring in 17% of patients with subcutaneous panniculitis-like T-cell lymphoma (SPTCL).[1]

Initial HLH treatment involves addressing underlying drivers.[2] The HLH-94 protocol is an established HLH-directed therapy developed by the Histiocyte Society, which consists of corticosteroids, cyclosporine, intrathecal therapy and etoposide to treat hyperinflammation.[2]

Ruxolitinib is a Janus kinase inhibitor that abrogates JAK-STAT inflammatory cytokine signal transduction and has reported use for relapsed/refractory HLH in one case-series and two case-reports.[3] Ruxolitinib use in adults with refractory HLH and SPTCL specifically, has not been described.

This case report describes successful use of ruxolitinib in refractory HLH secondary to SPTCL.

Case Progress

A 27-year-old male presented with fevers, constitutional symptoms, and hyperferritinaemia (17,825microg/L). He had a past medical history of asthma, childhood pulmonary tuberculosis (TB) and dyslipidaemia.

He was diagnosed with secondary HLH and was initially treated with dexamethasone (2-6 mg/day) only, for 26 days in the setting of an undiagnosed driver.

With fever resurgence and increasing inflammatory markers, anakinra was trialled for 4 days unsuccessfully. A decision was also made on day 3 of anakinra to treat empirically for TB, as a potential HLH driver. Empiric quadruple TB therapy (moxifloxacin, rifampicin, ethambutol and pyrazinamide) was commenced.

Anakinra was then switched to HLH-94 (tapering etoposide 150mg/m^2 twice a week and dexamethasone 10mg/m^2 daily) with ongoing pursuit of aetiology.

Four days later, germline-associated SPTCL was diagnosed on skin biopsy and treatment was altered to CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisolone).

Fevers and biochemical abnormalities persisted hence ruxolitinib 15mg twice daily was initiated the next day.

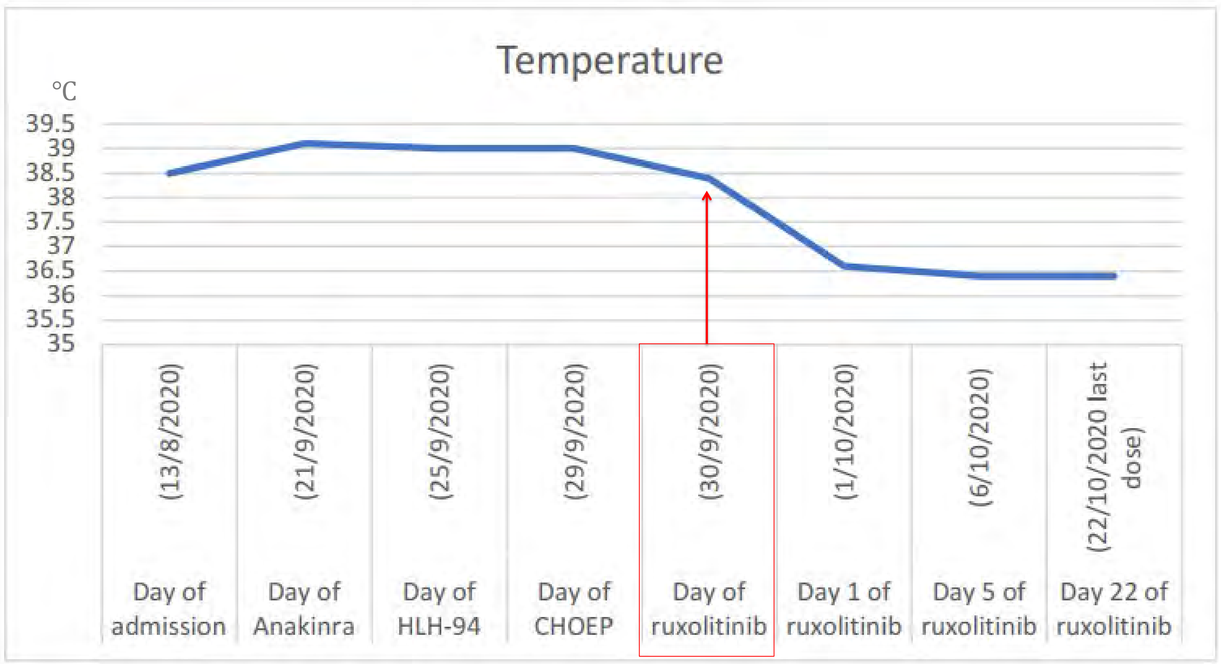

Figure 1. Temperature trend during admission.

Pharmacist Interventions

The pharmacist played a pivotal role in reviewing for potential drug interactions and monitoring treatment efficacy and adverse effects.

- A literature review guided the initial ruxolitinib dosing.
- An interaction with posaconazole was identified: posaconazole as a strong CYP3A4 inhibitor, may increase the serum concentration of ruxolitinib and the risk of toxicities.[4] The pharmacist recommended reduction of ruxolitinib to 10mg twice daily with close blood count monitoring.
- Throughout admission, the pharmacist recommended co-trimoxazole (prolonged corticosteroid use), posaconazole (for prolonged neutropenia), and valaciclovir (for viral prophylaxis).

Outcome

Upon ruxolitinib initiation :

- A brisk response was observed with fever termination within 2 hours (16 continuous days of fevers prior) (Figure 1).
- The patient remained afebrile thereafter, with improving inflammatory markers including ferritin, allowing weaning of dexamethasone (Figure 2).

The timing of this rapid response was consistent with a paediatric case report.[5] Ruxolitinib was weaned and ceased after 22 days and CHOEP continued alone. Grade 4 neutropenia and thrombocytopenia developed, however pre-dated ruxolitinib and resolved post CHOEP nadir (14 days).

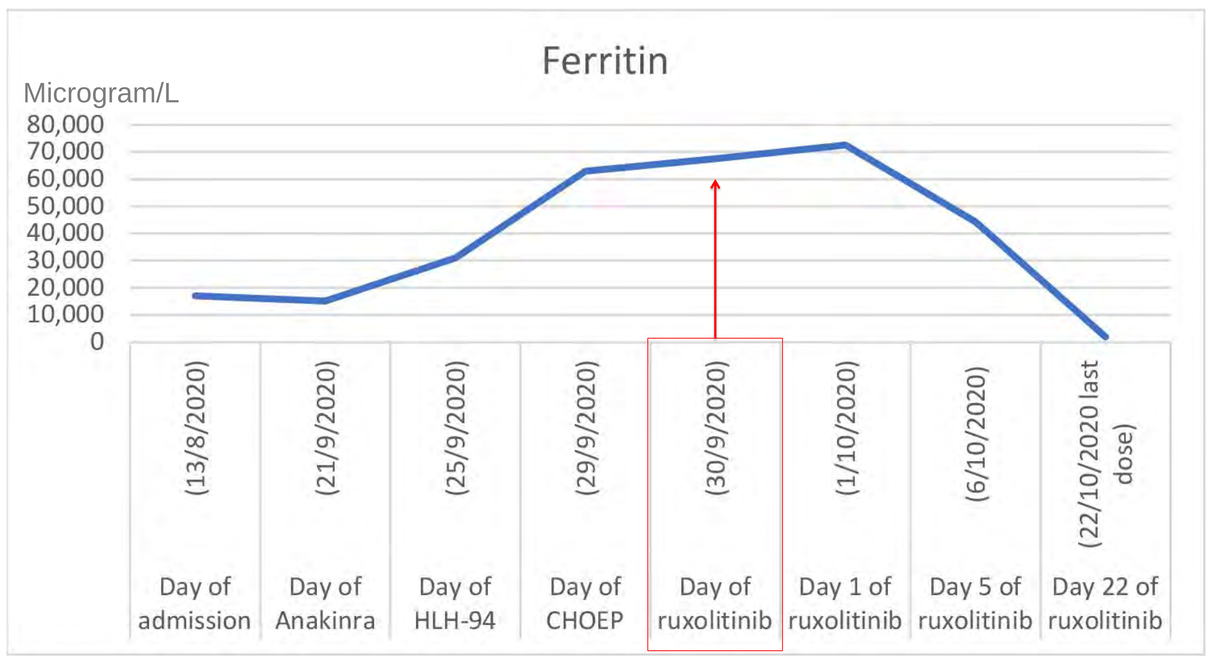

Figure 2. Ferritin level trend during admission.

Conclusion

While temporally related to CHOEP, the rapid symptomatic and biochemical recovery upon initiation of ruxolitinib provides additional evidence to supports its use in abrogating cytokine storm in refractory HLH.

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