中文題目：JAK 抑製劑 Ruxolitinib 在復發性吞噬性淋巴細胞組織細胞增多症成人中的成功搶救和持久療效：一例報告

英文題目：Successful rescue and durable response of Ruxolitinib, a JAK inhibitor, in the adult with recurrent hemophagocytic lymphohistiocytosis: a case report

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Abstract:

Hemophagocytic lymphohistiocytosis (HLH) is a notorious and life threatening syndrome, in which the dysregulation of macrophages and cytotoxic T cells causes hyper-activation of the immune system. In adults, it is usually secondary which is triggered by infection, malignancy, or autoimmune disease. In severe case, multiple organ failure may be presented. The treatment of HLH is mainly focus on its underlined disease. However, of some adult patient, clear etiology causing the HLH may not be identified. HLH2004 protocol, which is commonly applied to pediatric primary HLH, may be applied to these patients, though it is not validated in the adult population. The prognosis of adults with recurrent HLH is extremely poor. We hereby reported the 46 year-old female whose HLH was idiopathic and rapidly complicated with multiple organ failure. Although initially responsive to HLH2004 protocol treatment, there was a rapid recurrence which was successfully controlled by Ruxolitinib, a JAK inhibitor.

Case report: The 46 year-old female presented to our hospital for fever with multiple skin rash for 4 days. After admission, persistent fever was noted despite of adequate antibiotic treatment. Ten days later after admission, fever with hypotension, acute kidney injury and respiratory failure developed despite of adequate antibiotic treatment. The lab data were notable for worsening leukocytosis, normocytic anemia and thrombocytopenia, higher serum levels of procalcitonin, uric acid, LDH, and declining fibrinogen level. Additional blood tests revealed an elevated triglyceride (221 mg/dL) and ferritin levels (>40000 ng/mL). The bone marrow showed hemophagocytosis, and the diagnosis of HLH was made. The patient was soon transferred to ICU due to shock and multiple organ failure including lung, renal, and liver. Supportive care including mechanical ventilation and continuous venovenous hemofiltration were applied. No definite cause was identified after evaluations of infections (EBV, CMV, and TB), autoimmune diseases, and hematological malignancies including lymphoma. The treatment based on HLH2004 protocol was first administrated on day 20 since admission. Her clinical condition improved gradually and the endotracheal tube, hemodialysis was disconnected gradually. After the one-month stay in ICU, she was then transferred to the ordinary ward. Unfortunately, intermittent fever with high triglyceride and ferritin levels was noted again one month later. Fever progressed despite of strictly followed the

protocol. However, fever and pancytopenia persisted. Considering the extremely poor prognosis of recurrent and refractory HLH in the adult, the patient began to receive Ruxolitinib at the initial dose of 2.5mg BID and then escalated to 5 mg BID. The fever subsided gradually, and, in addition, the followed-up laboratory data including ferritin, LDH, and triglyceride also improved. The patient was finally discharged 3 months since admission. Ruxolitinib was continuously given as the maintenance, and successfully tapered off 6 months later (November 2018). The patient returns to her normal work and, in the last follow up in October 2019, there is no recurrence of HLH noted, 11 months later since discontinuation of Ruxolitinib.

Conclusion: To our knowledge, there is no report regarding adult patients with recurrent and refractory HLH who did not be rescued by allogeneic hematopoietic stem cell transplantation, but was successfully recused and controlled by a JAK inhibitor, with no subsequent recurrence.