JANUS KINASE (JAK) INHIBITION FOR POST-INFECTIOUS INFLAMMATORY RESPONSE SYNDROME IN PREVIOUSLY HEALTHY PATIENTS WITH CRYPTOCOCCAL MENINGITIS (CM)

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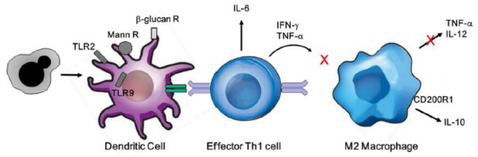
Abstract

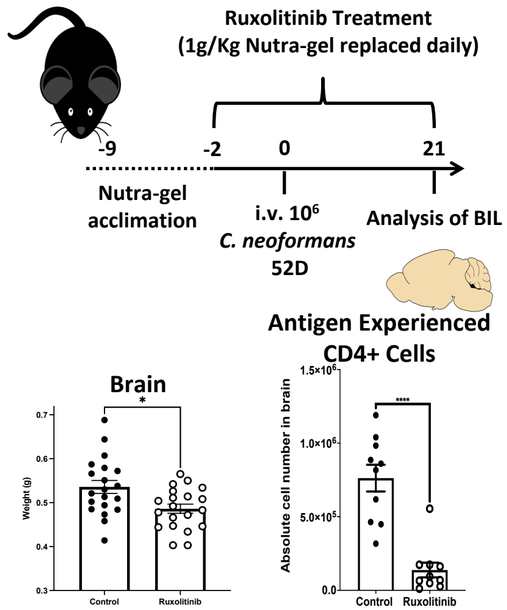
- Post-infectious inflammatory response syndrome (PIIRS) is a previously reported complication of non-HIV cryptococcal meningitis involving a pathological T cell-mediated neuroinflammatory response post infection. [1]



C neoformans non-HIV PIIRS

- Although corticosteroids have been successfully used as therapy[2], side effects preclude prolonged use and alternative agents may be required for steroid - refractory PIIRS.
- Janus Kinase (JAK) inhibitors such as ruxolitinib have shown to attenuate neuro-inflammation in animal models of multiple sclerosis and patients with neurotuberculosis. [3,4]
- We report outcomes of JAK inhibitor use in 1) CM-PIIRS mouse model and 2) 3 patients with CM-PIIRS in conjunction with corticosteroids.

Ruxolitinib attenuates neuro-inflammation in CM-PIIRS mouse model



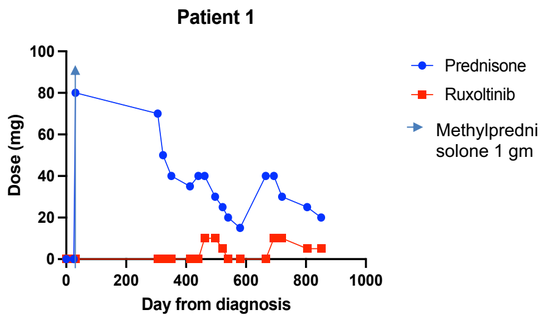
Methods

Medical records of three previously healthy CM-PIIRS patients admitted between January to December 2021 were analyzed.

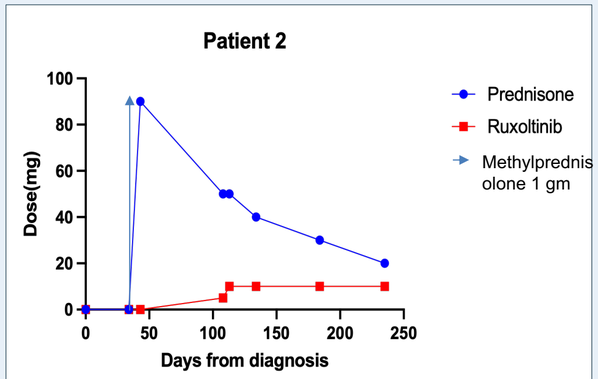
All were transferred from another facility due to worsening neurological status.

Neurological exam and radiological findings were compared at baseline and one month after ruxolitinib initiation.

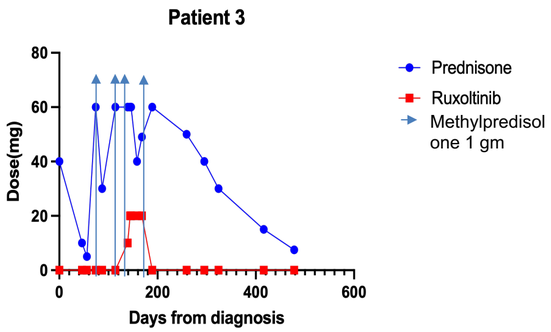
CSF parameters including cellular markers of T-cell inflammation and soluble cytokines were included in the comparison.



- 44 y/o male with a history of alcohol abuse who was started on corticosteroids for PIIRS one month after CM diagnosis.
- Experienced persistent headaches and hearing loss for 9 months despite taking prednisone 80 mg PO daily and VP shunt placement.
- On repeat LP, he was noted to have persistent neuro-inflammation and started on ruxolitnib 5 mg PO BID. Later, this was held due to abnormal liver enzymes and improved headaches.
- Prednisone was tapered to 15 mg daily but 22 months post diagnosis, he experienced worsened headaches and with repeat LP confirming ongoing PIIRS. He was restarted on ruxolitinib and prednisone dose was increased with clinical improvement.

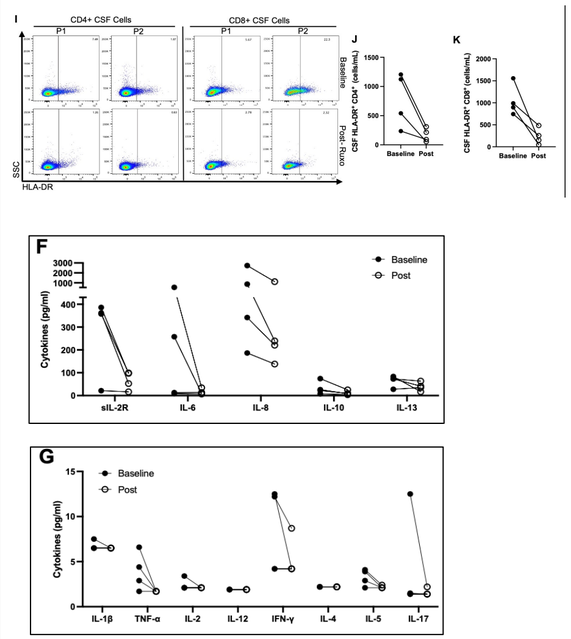


- 61 y/o healthy male diagnosed with cryptococcal meningitis who presented for worsening tinnitus and severe headaches 3 weeks after diagnosis.
- Diagnosed with PIIRS based on CSF analysis and MRI brain showing right frontal lobe, ependymal and meningeal enhancement, started on methylprednisolone 1 gm IV pulse x 1 week.
- Also started ruxolitinib 3 months post diagnosis with ability to taper steroids based on improved symptoms and CSF parameters.



- 59 y/o male diagnosed with sarcoidosis based on granulomas found on neck lymph node biopsy, stated on prednisone.
- Developed worsened headaches 5 months later and diagnosed with cryptococcal meningitis at outside facility. Found to have anti-NMDA receptor antibodies in CSF and treated with brief pulse corticosteroids.
- Transferred to NIH 4 months after diagnosis for deteriorating mental status. Received 3 pulses (methylprednisolone 1 gm daily) one month apart and ruxolitinib with significant clinical improvement.
- Course complicated by shingles and renal failure temporarily requiring dialysis
- Discharged to rehab

Ruxolitinib attenuates T cell responses and pro-inflammatory cytokines in CM-PIIRS patients



Summary:

- All three patients were started on ruxolitinib as an adjunct to prednisone with significant improvement in their neurological status, CSF and radiological findings.
- CSF fungal cultures remained negative with no occurrence of adverse effects.
- Therapy with ruxolitinib allowed continued corticosteroid taper without neuroinflammatory flairs in each patient.

Conclusions

- Ruxolitinib was safe in a small group of HIV-negative patients with cryptococcal meningitis and PIIRS.
- This agent may offer promise in conjunction with corticosteroids in the treatment of non-HIV CM patients with refractory PIIRS who are at risk for adverse side effects related to prolonged steroid use.

References

1. Elsegeiny et al. Front Immunology.2018
2. Anjum et al. Clin Infect Dis. 2021
3. Ms. Hosseini et al. Like. Sci 2021
4. YL Xie et al. Open forum Infect. Dis. 2019