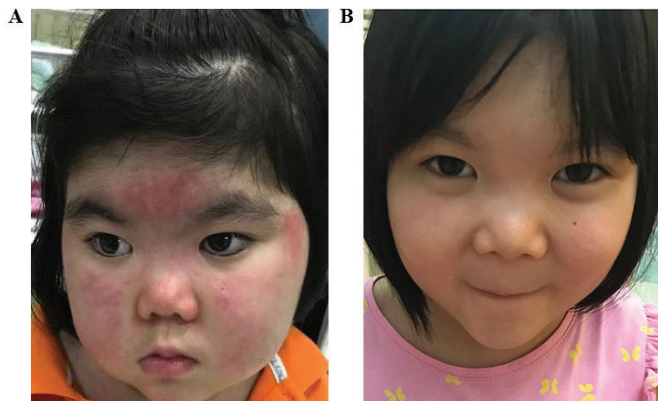


## Janus kinase inhibitor significantly improved rash and muscle strength in juvenile dermatomyositis

Juvenile dermatomyositis (JDM) is a rare systemic autoimmune vasculopathy characterised by weakness in proximal muscles and pathognomonic skin rashes.<sup>1</sup> Clinically, some patients are refractory to any available treatments or became steroids dependent.<sup>2</sup> The adverse reactions of long-term use of steroids are severe; therefore, more effective and safer medications are urgently needed. JAK inhibitors (JAKi) can reduce interferon (IFN)-induced STAT1 phosphorylation and block the JAK-STAT pathway, demonstrating a therapeutic potential of inflammation control in JDM.<sup>3</sup> The successful uses of JAKi were reported in adult dermatomyositis (DM) and two patients with JDM.<sup>3–5</sup> Here, we want to share the JAKi using experiences of 25 refractory JDM cases who were diagnosed and classified according to Bohan and Peter's criteria and treated between November 2017 and May 2019. Written informed consents were obtained from the guardians of all patients before starting the treatment.

Among 25 cases, 44% (11/25) patients were female, the mean age of onset was  $4.6 \pm 3.3$  years and the mean age to start add-on JAKi treatment was  $7.2 \pm 4.0$  years. The mean disease course of the 25 JDM patients before JAKi treatment is 21.0 months (range: 14.0–36.5). All cases are refractory JDMs, including 32% (8/25) ineffective patients and 68% (17/25) glucocorticoid-dependent cases. After routine treatment fails, they received JAKi for 3–18 months as an off-label use. In subsequent JAKi treatment, 28% (7/25) used tofacitinib, and 72% (18/25) used ruxolitinib. In patients of  $<25$  kg ( $n=11$ ), the initial dosage was 2.5 mg twice daily, and in patients of  $\geq 25$  kg ( $n=14$ ), the initial dosage was 5 mg twice daily, and one patient required the maximum dosage of 7.5 mg twice daily.

The 25 patients were followed for a median of 7.0 months (range: 3–21 months). Ninety-six per cent (24/25) had rash when



**Figure 1** A typical case of a girl >25 kg who received an initial dose of 5 mg twice daily of Janus kinase inhibitor (JAKi) but required the maximum dose of 7.5 mg twice daily. She received this dose for 6 months, and the dose was gradually tapered. In the meantime, glucocorticoids were also tapered, and the patient showed an increased growth rate. (A) The typical skin lesions before treatment with JAKi. (B) Those lesions had mostly disappeared after treatment.

JAKi was added, and all showed improved rashes, including 66.7% (16/24) cases of complete resolution. In patients with rash, rashes started to improve after 1.0 (0.6–2.0) weeks of JAKi and showed obvious improvement after 2.5 (2.0–4.0) weeks of JAKi. No clinically observable rash could be seen after 12.0 (8.0–24.0) weeks of JAKi. The Cutaneous Assessment Tool Binary Method score decreased dramatically from 7.0 (3.0–10.0) to 0.0 (0.0–1.0) ( $p < 0.001$ ). **figure 1** shows a girl with a long-term refractory rash that disappeared after gradually increasing the JAKi dose to 7.5 mg twice daily. Up to the last follow-up in August 2019, 28% (7/25) patients discontinued glucocorticoids including this girl. There is currently only one case relapsed, the rash disappeared after 8 weeks of JAKi but recurred 4 weeks later and JAKi was stopped at 12 weeks.

Additionally, 10/25 (40%) patients had decreased muscle strength, and 4% (1/25) had continuous high levels of muscle enzymes. After treatment, seven cases improved in childhood myositis assessment scale (CMAS) score (from  $18.6 \pm 15.0$  to  $35.7 \pm 6.3$ ,  $p = 0.018$ ). Two patients did not change in CMAS score (pretreatment/post-treatment score=47) but reported improvement in fatigue and activity tolerance. One patient was unevaluable for CMAS score before JAKi treatment due to joint contracture. As for biochemical indicators, CK and/or LDH were abnormal in 12 patients when JAKi was added. Median CK levels were normal before and after treatment. LDH decreased from 361.5 (306.3–463.3) U/L to 291.0 (275.8–394.8) U/L ( $p = 0.034$ ) in 12 patients, but two patients showed LDH increase, from 340 to 395 U/L and from 307 to 420 U/L, respectively. More details of patients' clinical characters and index changes are in the online supplemental material. During our observation period, no increase in the infection rates with Epstein-Barr virus, cytomegalovirus, varicella-zoster virus and tuberculosis occurred as reported by another study.<sup>6</sup> No thromboembolic event was observed as well.

This is the first case series study summarising the JAKi treatment on patients with refractory JDM. In our observation, JAKi improved refractory rash and muscle involvement, helped to reduce or stop glucocorticoid and no obvious side effects were found. Therefore, our study suggested that JAKi might be an idea choice in children with refractory JDM.

Yuchuan Ding,<sup>1</sup> Baozhen Huang,<sup>2</sup> Yuan Wang,<sup>1</sup> Jun Hou,<sup>1</sup> Ying Chi,<sup>1</sup> Zhixuan Zhou,<sup>1</sup> Jianguo Li<sup>1</sup>

<sup>1</sup>Department of Rheumatology and Immunology, Capital Institute of Pediatrics, Beijing, China

<sup>2</sup>Department of Chemical Pathology, The Chinese University of Hong Kong Faculty of Medicine, Pokfulam, Hong Kong

**Correspondence to** Dr Jianguo Li, Rheumatology and Immunology, Capital Institute of Pediatrics, Beijing 100020, China; [jianguo\\_li6@hotmail.com](mailto:jianguo_li6@hotmail.com)

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**Patient consent for publication** Parental/guardian consent obtained.

**Ethics approval** According to the off-table principle, written informed consents of receiving JAKi treatment were obtained from the guardians of all patients before starting the treatment. The study was approved by the ethics committee of the Capital Institute of Pediatrics (SHERLL2019065).

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**ORCID iD**

Jianguo Li <http://orcid.org/0000-0001-9431-2950>

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