News Release

Title; Increased JAK activation in cutaneous vasculitis

Key Points

・JAK inhibitors have been approved for a large spectrum of disorders.
・The relationship between the JAK-STAT pathway and the cutaneous symptoms of vasculitis has not been examined before.
・Our study indicate that both JAK1 and JAK2 play an important role in the development of cutaneous symptoms of small vessel vasculitis.
・We suggest that JAK inhibitors, especially pan-JAK or JAK1/2 inhibitors, have promising therapeutic potential.

Summary

In recent years, JAK inhibitors have been shown to be effective against various diseases and are known to be of particular use in treating atopic dermatitis. For vasculitis, studies have addressed their efficacy against large-vessel and ANCA-associated vasculitis, but no such reports exist for cutaneous vasculitis. In our study, we found that the expression of phosphorylated JAK1 and JAK2 (pJAK1 and pJAK2) in cells infiltrating the skin was increased in vasculitis compared to their expression in atopic dermatitis. These results suggest that JAK inhibitors could be effective against the skin manifestations of vasculitis.

Research Background

JAK inhibitors have been approved for a large spectrum of disorders, including atopic dermatitis (AD), in the last decade. Although recent studies have described the involvement of the JAK-STAT pathway in the pathogenesis of large vessel vasculitis and ANCA-associated vasculitis, the relationship between the JAK-STAT pathway and the cutaneous symptoms of vasculitis has not been examined before. To the best of our knowledge, this is the first report to elucidate this association, and discuss the efficacy of JAK inhibitors in the treatment of cutaneous vasculitis.

Research Results

We performed immunohistochemical analyses of paraffin-embedded tissue taken from patients who underwent skin biopsies and direct immunofluorescence analyses and were diagnosed as IgA vasculitis (IgAV) or cutaneous leukocytoclastic vasculitis (CLV) for the first time at our hospital from November 2016 to March 2022: 7 patients with IgAV and 6 with CLV were included. We also enrolled 5 patients with moderate to severe AD without any systemic treatment and 4 healthy controls (HC). pJAK1-positive cell counts were significantly increased in the IgAV group compared to those in the CLV group and HC ($p<.05$, $p<.001$), and were also significantly increased in the AD group compared to those in HC ($p<.05$). pJAK2-positive cell counts were significantly higher in the IgAV group than those in the AD group and HC ($p<.01$, $p<.001$). pJAK1- and pJAK2-positive cell counts in the CLV tended to be higher than those in HC.

Research Summary and Future Perspective

We suggest firstly that the dysregulation of the JAK-STAT pathway is associated with cutaneous symptoms of small vessel vasculitis, and secondly JAK inhibitors, especially pan-JAK or JAK1/2 inhibitors, have promising therapeutic potential.

Publication

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