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HYPOTHESIS

JAK Inhibitors as Potential Therapeutic Strategy for the Dilemma of Psoriasis Concurrent with Dermatomyositis in the SARS-CoV-2 Era

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Abstract: Dermatomyositis is a rare inflammatory disease with potentially life-threatening systemic involvement that is treated with systemic corticosteroids. However, when psoriasis coexists with dermatomyositis, the administration of corticosteroids may exacerbate psoriasis after withdrawal, posing a treatment dilemma. Our search of the literature revealed 14 cases where various treatments were used, including methotrexate, corticosteroids, cyclosporin, ustekinumab, mycophenolate mofetil, and azathioprine. While methotrexate showed promise, it carries risks, and corticosteroids were used despite their potential to exacerbate psoriasis. Based on transcriptomic data analysis of psoriasis and dermatomyositis, the type II interferon-mediated signaling pathway was enriched in both diseases. Medication targeting this pathway, such as JAK inhibitors, could be a potential solution for the psoriasis concurrent with dermatomyositis dilemma, as JAK inhibitors have been proven effective in treating both dermatomyositis and psoriasis, with some being FDA-approved for treating COVID-19. Therefore, JAK inhibitors may be a potential therapeutic strategy for psoriasis concurrent with dermatomyositis in the SARS-CoV-2 era.

Keywords: psoriasis, dermatomyositis, treatment, JAK, SARS-CoV-2

Dermatomyositis is a rare inflammatory disease that presents distinct cutaneous manifestations and various degrees of potentially life-threatening systemic involvement,[1] such as pulmonary diseases or malignancies. The first-line therapy for managing dermatomyositis is systemic corticosteroids. However, in cases where psoriasis coexists with dermatomyositis, the administration of systemic corticosteroids may pose a dilemma due to concerns regarding the potential exacerbation of psoriasis after corticosteroid withdrawal.

In order to figure out the possible solution for this dilemma, we prepared a comprehensive full strategic electronic search of the PubMed, Scopus, Google Scholar and EBSCO databases, using the following keywords 'psoriasis', 'dermatomyositis' and covering the period 2003–2022. Over 200 articles were found. After reviewing these articles, fourteen cases[2–13] were concluded (Table 1). The treatment of these cases concluded methotrexate, corticosteroids, cyclosporin, ustekinumab, mycophenolate mofetil and azathioprine.

Among the available treatments for psoriasis concurrent with dermatomyositis, methotrexate has shown promise and was utilized in seven out of fourteen cases. However, the use of methotrexate to treat this condition carries certain risks, such as the potential for interstitial lung disease, which raises concerns that the treatment may trigger or exacerbate the interstitial lung disease associated with dermatomyositis. In some cases, corticosteroids were used in the treatment of psoriasis concurrent with dermatomyositis, despite their known potential to exacerbate psoriasis. Of the six cases in which corticosteroids were used, four were administered concomitantly with other immunosuppressants, including methotrexate, cyclosporin, mycophenolate mofetil, and azathioprine. However, the possibility of psoriasis exacerbation remained. Inkeles MS reported the effectiveness of cyclosporine monotherapy in the treatment of psoriasis concurrent with dermatomyositis, noting that its selection was based on its documented efficacy and safety in treating dermatomyositis, as well as its FDA-approved status for treating psoriasis. Nonetheless, limitations exist, such as the concern that

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Table 1 Cases of Psoriasis Concurrent with Dermatomyositis

Year	First Author	Journal	Gender	Age, Years	Preceding Situation	Precipitating Factors	Treatment	Dose
2022	Danielle L Perna[2]	JAMA Dermatol.	F	In 20s	Psoriasis	Secukinumab	Methotrexate	N/A
2021	Schreiber C[3]	J Investig Med High Impact Case Rep.	F	45	Psoriasis	Long term psoriasis history	Methotrexate	20mg
2019	Xing Y[4]	J Cosmet Dermatol.	M	21	Dermatomyositis	N/A	Cyclosporine; methotrexate	2.5 mg/kg/d; 7.5 mg/kg
2017	Kato Y[5]	Int J Rheum Dis.	F	30	Dermatomyositis	Interstitial lung disease	Prednisolone	40 mg/day
2017	Montoya CL[6]	J Clin Rheumatol.	M	20	Dermatomyositis	N/A	Ustekinumab	45 mg at weeks 0 and 4 and every 12 weeks
2017	Inkeles MS[7]	Dermatol Online J.	F	45	Psoriasis	N/A	Cyclosporine	3mg/kg/d, increased after one week to 5mg/kg/d
2016	Akiyama M[8]	J Dermatol.	F	52	Dermatomyositis	Prednisolone halt	Prednisolone; methotrexate	20 mg; 6mg
2014	Dicaro D[9]	J Am Acad Dermatol.	F	37	Psoriasis	Adalimumab	Methotrexate	N/A
2011	Kim NN[10]	Arch Dermatol.	F	18	Dermatomyositis	N/A	Methotrexate	N/A
			F	4	Dermatomyositis	N/A	Topical corticosteroid	N/A
			F	8	Psoriasis	N/A	Methylprednisolone; methotrexate; mycophenolate mofetil	30 mg/kg; 25mg/m^2; 20 mg/kg, divided every 12 hours
2010	Machado NP[11]	Sao Paulo Med J.	M	51	N/A	N/A	Methylprednisolone; monthly intermittent intravenous cyclophosphamide	1 g/day for three days; 0.5 g/m^2
2009	Gran JT[12]	Tidsskr Nor Laegeforen.	M	In late 50s	Psoriasis	Hepatic tumor	Methylprednisolone	1000mg
2004	Pavlović MD[13]	Vojnosanit Pregl.	M	63	Dermatomyositis	N/A	Methylprednisolone; azathioprine	8mg every other day; 50mg/day

during the SARS-CoV-2 pandemic, immunosuppressants like cyclosporine may increase the risk of infection. Furthermore, biologics such as ustekinumab, which target Interleukin(IL)-12/23p40 and are effective in treating psoriasis, have shown promise in treating psoriasis concurrent with dermatomyositis. However, there have been reports of secukinumab, an interleukin 17 antagonist, acting as a precipitating factor for psoriasis concurrent with dermatomyositis, which has led to caution in using biologics that target the IL23-IL17 pathway in the treatment of this condition.

Then, what could be a solution for this treatment dilemma of psoriasis concurrent with dermatomyositis? We thought the same pathogenetic pathway might give us a hint. Thus, we download the skin transcriptomic data of psoriasis[14] (GSM5216154, GSM5216170, GSM5216195, GSM5216211, GSM5216226, GSM5216244, GSM5216272 as lesion samples and GSM5216067, GSM5216071, GSM5216086, GSM5216102, GSM5216106, GSM5216114, GSM5216118 as control samples) and dermatomyositis[15] (GSM3671281, GSM3671282, GSM3671285, GSM3671287 as lesion samples and GSM3671288, SM3671289, GSM3671290, GSM3671291, GSM3671292 as control samples). We used R studio in the analyses of the downloaded psoriasis (DESeq2 and clusterProfiler package) and dermatomyositis data (limma and clusterProfiler package). We found type II interferon-mediated signaling pathway (GO: 0060333) was enriched in both psoriasis (P = 0.003144649) and dermatomyositis (P = 1.37E-07).

Based on our data above, the medication targeting type II interferon-mediated signaling pathway could be a potential solution for the psoriasis concurrent with dermatomyositis dilemma. Type II interferon-mediated signaling pathway is controlled by Janus Kinase (JAK) 1 and JAK2 which several JAK inhibitors targeting this pathway including tofacitinib,[16] ruxolitinib,[17] baricitinib,[16] abrocitinib[18] and etc. There were several JAK inhibitors proved effective in the treatment of dermatomyositis. Meanwhile, these JAK inhibitors were also used in the treatment of psoriasis. These facts made JAK inhibitors eligible for the treatment of psoriasis concurrent with dermatomyositis. As mentioned above, in the SARS-CoV-2 era whether a treatment might aggravate SARS-CoV-2 should be taken into consideration. Baricitinib, one of the JAK inhibitors was approved by FDA for the treatment of adult patients hospitalized with COVID-19. While another JAK inhibitor, tofacitinib were also appeared to benefit attenuating SARS-CoV-2 infection. Thus, based on the psoriasis and dermatomyositis transcriptomic data as well as the lines above, we believe that JAK inhibitors could be the potential therapeutic strategy for the dilemma of psoriasis concurrent with dermatomyositis in the SARS-CoV-2 era.

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