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Treatment of MDA5-positive dermatomyositis complicated by gangrenous cholecystitis with tofacitinib

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Abstract

Backgroud

Dermatomyositis is a diffuse skeletal myositis disease with a variety of causes.The onset is mainly related to humoral immune abnormalities.Some therapeutic drugs,such as hormones and immunosu - ppressants,have poor therapeutic effects.In recent years, tofacitinib has been reported to be effective in the treatment of dermatomyositis.But there are many reports about the treatment of autoimmune diseases and infectious diseases with tofacitinib.

Case presentation

We report a case of MDA5 antibody-positive dermatomyositis that was relieved after treatment with tofacitinib,during which gallbladder gangrene and suppurative cholecystitis occurred.After cholecystectomy,we continued to use tofacitinib and achieved good therapeutic effect.

Conclusions

Tofacitinib is effective in the treatment of MDA5 antibody-positive dermatomyositis,but the risk of infection is increased.It can still be used after infection control.A close follow-up should be performed during the use of tofacitinib.

Introduction

Dermatomyositis(DM) is an idiopathic inflammatory myopathy (IIM),and a variety of myositis antibodies can be detected.In particular, MDA5-positive dermatomyositis is characterized by interstitial lung disease,subcutaneous calcification,myalgia,skin involvement and vascular lesions[1, 2].Some forms of DM cannot be completely relieved with or even relapse on therapeutic drugs,including glucocorticoids and traditional immunosuppressants[3].In recent years,there have been many reports that the Janus kinase(JAK) inhibitor tofacitinib is effective in the treatment of DM but increases the risk of infection and thrombosis[4].We report a case of MDA5 antibody-positive dermatomyositis that was relieved after treatment with tofacitinib,during which gallbladder gangrene and suppurative cholecystitis occurred.There are no reports of similar cases at present.

Materials And Methods

Case presentation

More than 2 years ago,In a 56-year-old woman had a skin rash on the face(Fig.C),eyelids,neck,chest and fingers of both hands(Fig.G) and Raynaud's phenomenon in both hands,accompanied by finger ulcers (Fig.K),limb weakness,myalgia,dysphagia,joint pain,cough,airtightness, intermittent fever,and palpable nodules on the chest wall,hip and left thigh.A 6-minute walk test was 321 meters.CK,ALT and AST were normal;anti-MDA5 IgG was positive;Ro52 was 280.26 RU/mL,the ANA titer was 1:1000,the pattern was of

the nuclear granular type.Chest computed tomography showed chronic inflammation of lungs with multiple interstitial changes(Fig.AandE)and multiple subcutaneous calcifications(Fig.I).Pulmonary function indicated decreased diffusion function(22%).Electromyography showed that the time limit and amplitude of light muscle contraction were normal and the polyphase potential was increased.The diagnosis met the 2017 EULAR/ACR classification standard[5].Prednisone acetate combined with matimecophenol ester or cyclosporine and cyclophosphamide showed poor therapeutic effects.The patient had the skin rash,ulcers and dyspnea relieved after approximately one month of treatment with prednisone(15mg qd) and tofacitinib (5mg qd).However,chills and fever

with a maximum temperature of 40℃ occurred on February 25,2021,and the patient had epigastric pain and tenderness,with a positive Murphy test.Abdominal color Doppler ultrasound indicated cholecystitis.CT of the upper abdomen showed that the gallbladder was slightly enlarged,and the internal density was not uniform;the gallbladder wall was suspected of an uneven thickening and local nodular changes,and the surrounding of the gallbladder was blurred. After treatment with prednisone(15mg qd) and piperacillin tazobactam for 3 days,the patient still had fever, abdominal pain and a leukocyte count of 16.6×10^9/L.The treatment was adjusted to imipenem/cilastatin for anti-infection for 7 days,until the patient had no fever.Cholecystectomy was performed on March 12,2021, a frozen section of the gallbladder bottom was sent for examination.A few tissues had acute and chronic suppurative inflammation with necrosis (Fig.M).Postoperative examination indicated acute gangrenous cholecystitis of the gallbladder(Fig.N).The patient continued to take prednisone(15mg qd) and tofacitinib(5mg qd) starting on March 30, 2021.Five months later,the rash on both hands(Fig.H) and the face subside(Fig.D),the ulcers on both hands completely healed(Fig.L),and the range of HRCT interstitial changes in the lungs(Fig.B and F) significantly decreased.The 6-minute walk test was 506 meters,and the diffusion function(Table.1)improved from severely to mildly impaired. Subcutaneous calcification(Fig.J) was reduced.

Discussion

Dermatomyositis is a diffuse skeletal myositis disease with a variety

of causes.The main pathological features are skeletal muscle degeneration, necrosis and lymphocyte infiltration.The onset is mainly related to humoral immune abnormalities.It is speculated that DM may be a complement-mediated microvascular disease.Myositis-specific and myositis-related antibodies can be detected in the serum.Some therapeutic drugs,such as hormones and immunosuppressants,have poor therapeutic effects[6].In recent years,tofacitinib citrate has been reported to be effective in the treatment of dermatomyositis.Tofacitinib is a relatively nonspecific JAK-i that affects the phosphorylation of different STAT (including STAT1 and STAT3)targets and inhibits a variety of proinflammatory cytokines.Tofacitinib has a good therapeutic effect on MDA5-positive dermatomyositis.

We report a case of MDA5-positive dermatomyositis without remission after hormone and traditional immunosuppressive therapy. Therefore,we treated the patient with prednisoneat and tofacitinib.After one

month,the patient's all symptoms were relieved.however,severe cholecystitis and gangrene occurred.Burmester[7] and Fleischmann[8] reported that the risk of upper respiratory tract infection after tofacitinib treatment of dermatomyositis[9].Acute gangrenous cholecystitis occurred in our case.In addition to inflammation,gangrenous cholecystitis is mainly due to gallbladder circulation disorder,leading to bleeding and gallbladder tissue necrosis[10].Patients with dermatomyositis can have vasculitis, leading to tissue ischemia and necrosis.There are few reports of similar cases.There is an increased risk of infection during treatment of connective tissue diseases with tofacitinib.The infection in our case may have been caused by tofacitinib.Tofacitinib was used again two weeks after the operation.After 5 months,The patient's condition was controlled and no infection was occurring .

In recent years,there are many reports about the treatment of autoimmune diseases and infectious diseases with tofacitinib.Lee[11] reported systemic lupus erythematosus with cholecystitis as the first manifestations.Tofacitinib is effective in the treatment of rheumatoid arthritis,ankylosing spondylitis,psoriatic arthritis,Behcet's disease, systemic vasculitis and other diseases[12].Zhu[13] reported tofacitinib treatment of refractory cutaneous leukocytoclastic vasculitis.In infectious diseases,Tatiana[14] reported that tofacitinib was effective in 320 patients with COVID-19,this is a prospective observational series.Tong's findings that tofacitinib reduced death or respiratory failure at 28 day in patients hospitalized with COVID-19 pneumonia[15].

However,there is an increased risk of thrombosis and infection during treatment of connective tissue diseases with tofacitinib.such as herpesvirus infection and respiratory tract infection[4].

In conclusion,tofacitinib is effective in the treatment of MDA5-positive dermatomyositis.However,the risk of infection which leads to dysfunction of important organs is increased.Therefore,a close follow-up should be performed during the use of tofacitinib.

Declarations

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Authors' contributions

HF and LM were involved in concept and writing. CL was involved in literature searching and manuscript revision. HH was involved in data analysis. All authors read and approved the final manuscript.

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Availability of data and materials

Not applicable.

Ethics approval and consent to participate

The case report was approved and supervised by the ethics committee of the Suining Central Hospital.Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Consent for publication

Waiver of informed consent.

Competing interests

The authors declare that they have no competing interests.

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Figures

Figure 1

A-L Clinical course HRCT scans of the lung before(Fig. A and E) and after(Fig. B and F)6 months treatment from patient.The calcium deposits in the subcutaneous before(Fig.I) tofacitinib and its improvement after(Fig.J) 6 months of treatment in the patient. skin lesions on face before(Fig.C) and after (Fig. D)treatment for 6 months from patient. Palmar and opisthenar surface of hand with erythema(Fig.G) and ulcerations before(Fig.K) and after(Fig.H) (Fig.L)treatment for 6 months from patient.

Figure 2

M and N Gallbladder pathology Acute and chronic suppurative inflammation with necrosis(Fig.M) and acute gangrenous cholecystitis(Fig.N) occur after tofacitinib approximately one months treatment from patient.