CASE REPORT

Dermatomyositis onset in the puerperium period

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SUMMARY

Dermatomyositis is rare during the reproductive period, but when it does occur, most cases have been reported from the viewpoint of the obstetric management of high-risk pregnancy. In return, there is little information concerning the contribution of pregnancy to the development and course of dermatomyositis. We describe a patient with dermatomyositis that presented after the delivery of a healthy infant. This case, with support from a literature review, suggests that pregnancy could be a trigger or contributor for the development of dermatomyositis.

BACKGROUND

Dermatomyositis (DM) is an autoimmune inflammatory disorder classified as an idiopathic inflammatory myopathy. It is a connective tissue disease characterised by proximal muscular weakness, muscle tissue inflammation and cutaneous lesions.

Its prevalence is roughly 5–22 cases/100 000 inhabitants,^{1 2} affecting all age groups; women are twice as affected as men.¹

DM pathogenesis is poorly understood, although autoantibodies, non-specific tissue inflammation, cellular death and vascular disease all play an important role. It is accepted that CD4 T lymphocytes probably stimulate T cells to synthesise antibodies capable of fixing in vascular beds, which, along with the complement (C5b-9), leads to local inflammation, ischaemia and, subsequently, necrosis.

DM may be associated with malignant tumours³ or with viral infections,⁴ suggesting a possible role of both tumour immunity and/or viral infections in the pathogenesis of this disease. In contrast, little is known about the relationship between DM and pregnancy.

Most cases of DM related to pregnancy have been reported from the viewpoint of the obstetric management of high-risk pregnancy, with only a few cases being reported by dermatologists.^{5 6} The reported relationship between DM and pregnancy is mostly related to the high risk for the woman and child when such diagnosis is already present before pregnancy.⁵

We report a case of a previously healthy woman who presented clinical manifestations of DM shortly after giving childbirth.

CASE PRESENTATION

A 26-year-old healthy black woman, born in Cape Verde, gave birth to a healthy child of 3100 kg, after an unremarkable pregnancy and vaginal delivery, with no complications affecting the mother or the child. The only relevant medical history was a first trimester miscarriage 18 months before this admission.

Figure 1 Multiple erythematous to violaceous, scaly papules are present over the extensor joints of the hand.

Six weeks after delivery, the patient developed muscle weakness and, shortly after, generalised muscle pain. A purplish rash was also noted, which was itchy but not scaly, distributed over her hands (**figure 1**), elbows (**figure 2**), knees (**figure 3**), eyelids, malar and frontal region (**figures 4–6**), with progressive worsening. Concomitantly, she noticed difficulties with some movements, such as flexion and extension of the fingers, as well as the appearance of eyelid oedema (**figure 4**). Three months later, movements were increasingly difficult, and she reported feeling ‘heavy legs’ and had extreme difficulty lifting her arms above her head. Finally, oropharyngeal dysphagia brought the patient to the hospital emergency department.

Physical examination showed decreased muscle strength, mainly proximal on the pelvic and shoulder girdles. The patient had a reddish-purple eruption on the upper eyelid (heliotrope eruption), accompanied by swelling of the eyelid (**figure 4**), violaceous facial erythema with mid-facial erythema that did not spare the nasolabial folds (**figures 5 and 6**), and small areas

Figure 2 Erythematous to violaceous patches with overlying scale are present on the extensor surfaces of both elbows.

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Figure 3 Erythematous to violaceous patches with overlying scale are present on the extensor surfaces of both knees.

of skin atrophy on her limbs and hands. Painless skin nodules in her legs and papules on the extensor surfaces of the metacarpophalangeal and proximal interphalangeal joints were recorded (figure 1). Erythematous to violaceous patches with overlying scale were present on the extensor surfaces of both elbows and knees (figures 2 and 3).

INVESTIGATIONS

Laboratory tests showed largely increased muscle proteins, creatine kinase (12 643 U/L) and myoglobin (2597 µg/L), compromised hepatic enzymology, lactate dehydrogenase (3129 U/L), aspartate transaminase (634 U/L) and alanine transaminase (310 U/L). C reactive protein (1.52 mg/dL) and erythrocyte sedimentation rate (14 mm/s) were also slightly increased. Also, complement component C3 (126 mg/dL) and C4 (23.4 mg/dL) as well as antinuclear antibody (>1/1280, mottled pattern) and double-stranded DNA antibody (4.3) were increased, and anti-Mi-2 antibody was positive while all other autoantibodies were negative (rheumatoid factor, antineutrophil cytoplasmic antibody, anti-Ku, anti-PM-Scl, anti-Jo1, anti-SRP, anti-PL-7, anti-PL-12, anti-Jo and anti-EJ).

A muscle biopsy showed fragments of skeletal muscle tissue with perifascicular atrophic areas and intense focal perivascular lymphocytic inflammatory infiltrates, findings consistent with DM (figures 7 and 8).

DIFFERENTIAL DIAGNOSIS

The collection of clinical, serological and pathological data was negative for infectious or neoplastic diseases and excluded any pharmacological triggers.

Figure 4 A reddish-purple eruption on the upper eyelid (heliotrope eruption), accompanied by swelling of the eyelid.

Figure 5 Violaceous facial erythema.

TREATMENT

The patient was initially given prednisolone 80 mg/day (1 mg/kg/day). Muscle enzyme levels began to decrease and her muscle strength gradually recovered during the first weeks of treatment. Despite this clinical and laboratory improvement, the patient remained with symptoms. Therefore, it was decided to combine azathioprine 100 mg/day with an immediate decrease in the prednisolone dose to 40 mg/day and to 15 mg/day over 8 weeks. The patient became symptom free and blood tests remained normal with this treatment.

OUTCOME AND FOLLOW-UP

The patient was discharged home and no flares were recorded during the first year of follow-up.

DISCUSSION

DM is a systemic autoimmune disease characterised by a non-suppurative inflammation of skeletal muscle and by typical skin

Figure 6 Violaceous erythema on the upper lids and mid-facial erythema that does not spare the nasolabial folds.

Figure 7 H&E stain (original magnification $\times 100$ and $\times 400$) of skeletal muscle tissue biopsy with perifascicular atrophic areas and intense focal perivascular lymphocytic inflammatory infiltrate, perivascular detail.

lesions.⁷ Muscle weakness and inflammatory infiltrates of the skeletal muscles are its major clinical and histological findings.⁸

DM is more prevalent among women (age groups 10–15 and 45–60 years), but only 14% of the cases occur during reproductive age.⁹ Little is known about the relation between DM and pregnancy, namely the potential contribution of pregnancy to the development and course of the disease, with only a few cases of the association reported.

The physiological adaptation of the immune system to pregnancy (Th2-type response) potentially affects the course of the immune-mediated rheumatic conditions, while autoimmunity may compromise the fetal outcomes.^{10–12} Systemic autoimmune conditions may be induced as a result of maternal hormonal changes and aberrant function of the immune system during pregnancy (autoimmune rheumatic disorders associated with pregnancy) or as a consequence of maternofetal microchimerism, recognised as the long-term persistence of a small number of cells from a genetically distinct organism (autoimmune rheumatic disorders in the postpartum period).^{10 13 14}

Although the exact aetiology of DM is still controversial, there is now strong evidence that autoimmunity plays a central role in it, with perivascular B cells and TCD4+ cells involved.¹⁵

Pregnancy is characterised by a specific status of high levels of sex hormones and permanent crosstalk between mother and fetus, with two major processes being essentially involved in physiological adaptation to pregnancy: (1) the modification of

Figure 8 Masson's Trichrome staining method (original magnification $\times 100$) of skeletal muscle tissue with perifascicular atrophic areas.

maternal immune system with subsequent conversion of cytokine profile and (2) the changes of the hormonal milieu throughout the course of gestation.^{10 11 13} Crucial modification of the innate immune system generally occurs during normal pregnancy, aiming to attain immune tolerance towards paternal antigens expressed by fetal cells; and local (fetomaternal interface) as well as systemic changes are directly guided by increasing levels of sex steroids.^{16 17}

It is widely accepted that the maternal immune system modulates the cytokine pattern, promoting increased Th2-type cytokine production and decreased Th1-type response with subsequent Th2 polarisation, which is crucial for a positive pregnancy outcome.^{17 18} However, Th1-type cytokines are involved in cell-mediated immunity and inflammatory reactions and appear to have a primary role in early pregnancy, including embryo implantation and placental development.^{17 19}

Also, profound changes of the hormonal state take place during pregnancy, with the Th1/Th2 shift being the result of a progressive increase in progesterone and oestrogen levels driven by the fetoplacental unit, with a peak level in the third trimester. At the high levels commonly encountered during gestation (3–8 times the baseline), oestrogen appears mainly to suppress Th1-cytokines, particularly tumour necrosis factor (TNF)- α , and to stimulate Th2-mediated immunological responses as well as antibody production.^{18 20 21} Progesterone, a potent immunomodulator hormone primarily secreted by placenta during the first 6–8 weeks of gestation, increases 4–6 times, while deoxycorticosterone, one of its metabolites, reaches 1000 times higher concentration than in the non-pregnant state. Progesterone inhibits Th1-type cytokine synthesis from T cells and induces Th2 cytokine, leading to a stimulation of humoral immunity.¹⁷ Temporary aberrant levels of free steroid hormones (glucocorticoids), gonadotrophin-releasing hormone (GnRH) and prolactin may also play a role in the pregnancy and postpartum period, inducing changes of the immunocompetent cells and inflammatory responses.^{16 17} It is now much better established that the particular hormonal, biochemical and immunological interference in pregnancy may shape the course of autoimmune rheumatic diseases, including DM.^{20 21}

Despite what is documented above, the onset of inflammatory myopathies is rare during pregnancy and even more so in the postpartum period, and cases of DM identified during pregnancy tended to improve after delivery. This suggests that the contribution of pregnancy in cases with postpartum onset may be different.

On the relationship between DM and pregnancy, three specific categories can be individualised: (1) flare-up/exacerbation of pre-existing disease during gestation, (2) onset of new polymyositis/DM throughout the course of pregnancy and (iii) postpartum flare or onset of myositis.²²

Nonetheless, the relationship between pregnancy and pathophysiological mechanisms of DM is unclear due to extremely limited data,²³ and the exact course of DM during pregnancy and in the puerperium is difficult to study since symptoms are non-specific (eg, slight fatigue and small skin lesions) and can easily be overlooked by patients and physicians.

Cytokines and chemokines are essential players in the initiation and progression of DM.^{15 24 25} It has been recently suggested that the onset of the disease may be triggered by the rise in serum oestrogen concentration with subsequent effects on TNF- α synthesis as described in early pregnancy.²⁶ Moreover, aberrant immunological response caused by the presence of fetal cells in the maternal circulation and/or certain viral infections (Coxsackie viruses, parvoviruses, enteroviruses and

retroviruses, in particular Human T-lymphotropic virus and HIV) with subsequent impairment of humoral immune responses have also been proposed for the pathogenesis of pregnancy-associated DM.²⁶

Bauer *et al*²⁷ suggested that the fetus and its foreign antigens might be involved in the development of DM during pregnancy. Production of antibodies to fetal (paternal) human leucocyte antigens has been confirmed. Such immunological changes in the mother may be potentially relevant to the development of an autoimmune disease.²⁸ More recently, it has been shown that fetal cells can persist even after delivery.²⁹

In our patient, due to the fact that postpartum onsets of disease have rarely been reported, we must consider the possibility of accidental onset after delivery, but it is possible that fetal microchimerism, suggested to be one of the causes of the increased susceptibility to the disease, caused a subclinical DM during the pregnancy, which was then triggered by another stress factor, such as the delivery, a dramatic fall in hormonal levels during the puerperium or a viral infection. Hormonal serum levels, measured at the time of the patient's admission, were all in the normal range and we did not find any serological evidence of a viral infection, but considering the timing of testing and presentation, a correlation could not be excluded.

In summary, pregnancy could be the trigger for our patient developing DM, but its relative contribution to the development and course of the disease is unknown. Of course, unmatched retrospective cohort studies cannot be taken as proof of high-level causality and further studies are needed to confirm this assumption.³⁰

This case report highlights this uncommon association and may help to improve knowledge of it. More studies are needed in order to conclude the follow-up of these patients and for further understanding of its aetiology, and for the best management of this disease association.

Learning points

- We describe the case of a 26-year-old woman who developed dermatomyositis after delivering a healthy infant.
- Owing to the fact that postpartum onsets of disease have rarely been reported, we must consider the possibility of accidental onset after delivery.
- However, we believe that the pregnancy, delivery or puerperium might have been a trigger in the development of the patients' dermatomyositis or that it exacerbated the disease in this patient.
- The usual management of the disease is effective and safe during the postpartum period.
- More case reports would be useful and further studies are needed to fully establish and better understand the association between dermatomyositis and pregnancy/puerperium changes.

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