Acute Generalised Pustular Psoriasis of Von Zumbusch: A Conflict in the Flare of Psoriatic Arthritis

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Abstract: Psoriasis is a chronic autoimmune disease with characteristic inflammation of the skin and joints. Immunosuppressant drugs, especially methotrexate has emerged since the past decade in psoriasis treatment, mainly for psoriatic arthritis. Withdrawal of immunosuppressant drugs may trigger a more severe condition; acute generalized pustular psoriasis, which is a rare form of psoriasis. We report a 46 years old Indian woman, who had chronic plaque psoriasis with psoriatic arthropathy for the past 3 years and was stable on oral methotrexate 10mg weekly and oral prednisolone 5mg daily. She presented with generalized pustular eruptions for 1 week associated with fever for 3 weeks and bilateral knee pain. There was widespread erythema and scaling, painful and studded with pustules appearing on all limbs, trunk and face with body surface area of more than 90% involved. She had swelling of both knees which was warm and tender. Further history revealed that she had stopped taking methotrexate for 2 weeks prior. Her condition was complicated with *Klebsiella pneumoniae* bacteremia and flare of psoriatic arthropathy. She was started on oral prednisolone 30mg daily, followed by tapering doses. She was monitored in the ward in view of high risk of worsening pustular psoriasis while tapering the dose of systemic corticosteroids. Her condition improved with a short course of oral acitretin 25mg daily. We discussed this case to highlight the dilemma faced by both dermatologist and rheumatologist when immunosuppressants are withdrawn in psoriatic patients and the difficulties of managing flares of psoriatic arthropathy in the same settings.

1 INTRODUCTION

Generalized pustular psoriasis (GPP) is a rare and severe variant of psoriasis characterized by generalized inflammatory plaques with multiple sterile pustules (Griffiths & Baker, 2007). The commonest precipitating factor include abrupt withdrawal of systemic or ultrapotent topical corticosteroids and infection (Kamarashev et al., 2002). Withdrawal of systemic immunosuppressant therapy is also associated with GPP and risks of rebound of the disease is of concern. The complication of GPP is multi-system organ failure and early recognition and treatment is necessary (Pomahac et al., 2008).

2 CASE

We report a case of a 46 years old Indian women who presented with generalized pustular eruptions for 1 week associated with fever for 3 weeks with body aches and bilateral knee pain for 1 week. The rash was described as worsening widespread erythema and scaling, painful and non-itchy, studded with pustules appearing on all limbs, trunk and face. She had swelling of both lower limbs and exfoliated skin areas over all limbs. She was diagnosed with plaque psoriasis 4 years prior to this, which progressed to psoriatic arthritis Her latest dosage oral methorexate 10mg weekly, however she stopped the medication herself for 2 months without advice from doctors. She continued taking oral prednisolone 5mg daily and was adherent with no change in dosage. On examination, 90% of body surface areas were involved. The rash was

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characterized as multiple pustules about 1–2 mm in size and located on the anterior chest (figure 1), both arms, abdomen and both lower limbs (figure 2). There were few pustular lesions over the chin and perioral. The pustules were studded on erythematous plaques with scales and desquamation. Multiple erythematous plaque with scales were seen. Her face and scalp had faint erythematous plaque with thick scales. There was onycholysis of both finger nails and toes. Bilateral knee was swollen and tender upon palpation, warm to touch and erythematous changes over the overlying skin area.

Blood investigations showed white cell count of 21.32 x 10^9 /L, with neutrophil predominance 82% , haemoglobin of 10.9 /dl and platelet 442 x 10^9 /L . Inflammatory markers were raised, erythrocyte sedimentary rate was 107mm/hr and C-reactive protein was 28.7 mg/L . She had liver impairment , with raised alanine aminotransferase (ALT) 96 IU/L and alkaline phosphate (ALP) was 211 IU/L . Her renal profile was normal and corrected calcium was 2.28 mmol/l. Anti streptolysin O titer was negative. Pus cultures from the pustules showed no growth. She was diagnoses with acute generalized pustular psoriasis. The identified triggering factor was the withdrawal of the immunosuppressant drug, methotrexate. She required skin nursing with potassium permanganate dressing and emollients. Topical corticosteroids applied included hydrocortisone 1% ointment and bethamethasone valearate 1:4 cream twice daily. Blood cultures taken grew *Klebsiella Pneumoniae* sensitive to ampicillin and she was on intravenous piperacillin tazobactam 4.5 g TDS for 1 week.

She was maintained on oral prednisolone 30mg od and dosage was tapered slowly. She was monitored in the ward in view of high risk of worsening pustular psoriasis during the period of withdrawing the systemic corticosteroids. Oral acitretin 25mg od was started, however it was given only for a short duration for as patient could not tolerate the medication. Side effects of actitretin was observed as she had dry lips, mouth and eyes and skin peeling. The pustular lesions cleared with the short course acitretin.

3 DISCUSSION

Psoriasis is a chronic autoimmune disease with characteristic inflammation of the skin and joints. At present, guidelines have recommended that methotrexate is preferred in psoriatic arthritis with skin involvement (Gossec et al., 2015). Dermatologists usually avoids systemic corticosteroids when treating psoriasis because of the potential risk of pustular psoriasis when systemic corticosteroids are discontinued. In contrast, rheumatologists often use systemic corticosteroids, in smaller dosages of 5-10 mg/d for the treatment of psoriatic arthritis and combined with methotrexate.

Generalized pustular psoriasis (GPP) was described in in 1968 by Baker and Ryan and categorized into four clinical variants: acute GPP of von Zumbusch; subacute annular pustular psoriasis (APP); exanthematic; and localized GPP (Baker & Ryan, 1968). Systemic features are commonly involved, and patients appear ill, febrile, malaise with leukocytosis. Derangement in liver enzymes and elevation of acute phase reactants are associated with this disease. Complications reported are sepsis and renal, hepatic, respiratory, and cardiac failure.

Case reports have described in severe psoriasis with pronounced arthritis presenting with pustular exacerbation after withdrawal of an immunosuppressant drug (Kamarashev et al., 2002; Benner et al., 2009). In this present case, withdrawal of systemic immunosuppressants therapy triggered the pustular psoriasis. After restarted on systemic

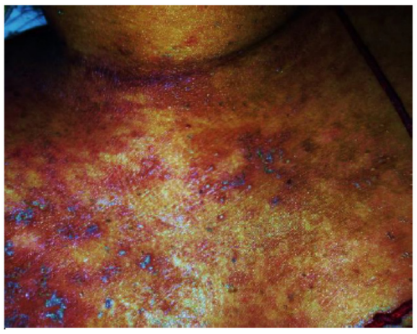

Figure 1: Multiple pustules seen on erythematous plaques on anterior chest.

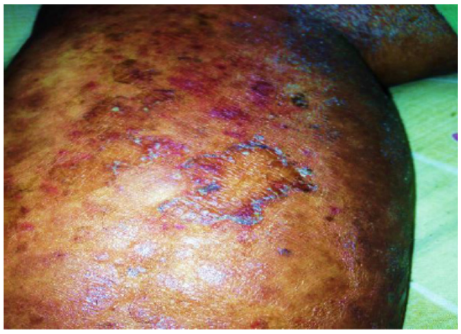

Figure 2: Multiple pustules on the scaly erythematous plaque seen on right leg.

corticosteroids, the patient was closely monitored for any rebound of her condition. A case review by Choon et al. described the commonest triggering factor was withdrawal of systemic therapy and was associated with higher risks of recurrent flares of GPP apart from other factors such as pregnancy and upper respiratory tract infection (Choon et al., 2014).

Despite early identification of the factors mentioned, GPP may still lead to unstable disease and frequently occurring pustular flares. Majority of corticosteroid induced GPP had mild psoriasis requiring systemic steroid indicated for both psoriatic lesions or arthritis (Choon et al., 2014). Corticosteroid has been well known as a trigger or aggravating factor for GPP ,and well reported in various case series , with strong association withdrawal of steroids (Brennet et al., 2009; Borges-Costa et al., 2011) . Patients are more commonly on these drugs when there is association with psoriatic arthritis.

Management GPP variant of psoriasis is still based on evidence from case reports and no universal guidelines are available at present. In this case, patient was given acitretin, however she developed side effects such as dry lips, mouth and eyes and skin peeling which are very common and not tolerable to some patients and was therefore withheld. Concerns on risk recurrence of pustular eruption and the need to maintain steroids for her arthritis arise in our case. The initial preference of methotrexate usage is due to its known therapeutic efficacy in improving both chronic plaque psoriasis and arthropathy.

Biologics alone or in combination with acitretin should be considered as have been describes in recent case reports in managing GPP. Evidence of rapid resolution of GPP with biologics especially with infliximab and also Etanercept was observed (Chandran & Chong, 2005). Combination therapy has also reported efficacy, acitretin combined with a biologic agent, adalimumab resulted in clearance of pustular lesions over 10 months (Gallo et al., 2013). However further studies are needed to address the efficacy of the biologics especially which agent would be more beneficial in both pustular psoriasis and psoriatic arthropathies.

4 CONCLUSION

Withdrawal of immunosuppressant drugs may trigger generalized pustular psoriasis and infection may worsened the pustular psoriasis flare. Acitretin has been shown to improve the pustular psoriasis in our case. The associated psoriatic arthropathy in patients with generalized pustular psoriasis need to be managed with caution when tapering the corticosteroid due to the risk of rebound of pustular psoriasis.

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