CASE REPORT

Acute febrile neutrophilic dermatosis associated with JAK-2 positive myeloproliferative disorder

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SUMMARY

We present a case of a 77-year-old man with a history of myeloproliferative disorder. He was admitted with a 2-week history of erythaema, swelling and significant pain of the right forearm following a mechanical fall at home, which had caused a skin laceration. During his admission, he developed ongoing intermittent fever and persistently elevated C reactive protein, and total white cell count. Initially, he was treated with antibiotics for suspected cellulitis. However, symptoms continued to progress, making a suitable management plan challenging. Wound swabs, blood cultures and viral PCR did not confirm infection. A punch biopsy of a skin lesion on the forearm was performed. The histology demonstrated a dense infiltrate of neutrophils and neutrophilic debris in keeping with acute febrile neutrophilic dermatosis (Sweet's syndrome). He was treated with oral steroids and after that he had a complete resolution of symptoms. However, he required a period of rehabilitation before returning home.

BACKGROUND

This case report highlights the importance of considering medical history of the patient and associated conditions in working towards a diagnosis. We initially struggled to reach a unifying diagnosis for this patient's condition. We believe that this case report acts as a reminder of the association of this condition with malignancy and, specifically, haematological malignancy.

CASE PRESENTATION

A 77-year-old man with a recent diagnosis of JAK-2 positive myeloproliferative disorder with no further intervention for the same, type II diabetes mellitus and hypercholesterolaemia, presented to our district general hospital, with a 2-week history of right arm pain and erythaema. He reported having had a mechanical fall at home, which caused a skin laceration to the forearm. This was particularly relevant as the history suggested a breakdown in the skin integrity and potential route of entry for skin and soft tissue infection. Initially, the patient had been treated by his general practitioner, with oral flucloxacillin for cellulitis. However, the lesions failed to improve with oral antibiotics and he became feverish and noted severe pain at his wrist, he was therefore referred to the hospital for assessment.

On examination, he was noted to have erythematous, vesicular and pustular lesions of varying sizes over the dorsum of the right hand and forearm (figure 1) after 1 week of initial presentation, with

some of the lesions being bullous and haemorrhagic in nature (figure 2) after 2 weeks of admission. He developed crusting black tissue over the right ulnar styloid. During his admission, these skin lesions progressed proximally to involve more of the right forearm, as well as the left forearm and the face. The patient noted significant arthralgia requiring regular opiate medication for control of pain. He developed recurrent intermittent fever and elevated inflammatory markers. C reactive protein was consistently elevated >100 mg/L.

He also had a marked neutrophilia (21.6×10^9) and monocytosis with an elevated total white cell count cell count (42.4×10^9) on the background of myeloproliferative disorder. On examination of the blood film, the neutrophils had a dysplastic appearance. A significant monocytosis was also noted.

The patient was reviewed by the dermatologist towards the start of his admission and it was felt that the most likely cause of the skin lesions was cellulitis or an infective process, and he was therefore initially treated with a range of antibiotics. The patient was also regularly taking nicorandil, and this was stopped soon after admission due to its potential threat of causing skin ulceration.

The patient was also reviewed by the haematology team while remaining under the care of the ageing and health consultant. The microbiology team also reviewed the patient but again a unifying diagnosis was not found.

Antibiotic therapy was escalated. However, the patient continued to deteriorate, with ongoing pain and progression of the skin lesions.

INVESTIGATIONS

Initial investigations of the skin lesions included wound swabs sent to bacteriology. These were reported as negative for pathogens that could have been contributing to cellulitis. Blood cultures were negative, methicillin-resistant *Staphylococcus aureus* (MRSA) screen was negative, and herpes simplex and varicella zoster PCR investigations were also negative.

An aspirate was obtained from a pustule on the dorsum of the right hand and sent to microbiology. This was reported as having no bacteria present and the presence only of white cells was noted.

In view of the recurrent intermittent fever, a CT of the chest/abdomen/pelvis was performed to exclude a deep-seated abscess. The CT demonstrated hepatosplenomegaly with abdominal lymphadenopathy but no collection and no abscess.

An echocardiogram obtained to exclude infective endocarditis showed no evidence of valvular vegetations in the heart.

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Figure 1 Severe pustular and vesicular lesions affecting the right wrist and elbow—1 week after presentation.

As the lesions progressed and the microbiology results were all negative, a review from dermatology was sought again. A punch biopsy was performed of a lesion on the dorsum of the right hand. The pathology of this specimen showed a dense infiltrate of neutrophils and neutrophilic debris. The neutrophilic infiltrate was noted to extend as far as the eccrine glands. These findings were reported to be in keeping with Sweet's syndrome.

DIFFERENTIAL DIAGNOSIS

In a patient with a background of haematological malignancy, a diagnosis of leukaemia cutis or bullous leukocytoclastic vasculitis may also be considered. However, a diagnosis of cellulitis would

Figure 2 Vesicles, pustules and bullous lesions affecting the dorsum of the right hand—two weeks after initial presentation.

also be a possibility, especially with a history of skin trauma. Given that the patient admitted was on various medications, a diagnosis of drug eruptions should also be suspected and investigated. Furthermore, dermatological conditions such as neutrophilic eccrine hidradenitis can mimic Sweet's syndrome.

TREATMENT

The patient was prescribed 60 mg oral prednisolone daily and we continued to withhold nicorandil medication. The response to treatment was assessed daily through examination of the skin lesions.

His mobility had declined significantly during admission, due to arthralgia, and he therefore required ongoing physiotherapy when pain control was inadequate.

OUTCOME AND FOLLOW-UP

With this treatment, the described skin lesions improved dramatically over the following days and the patient remained in hospital, following the resolution of the skin lesions, for physiotherapy and discharge planning. Follow-up was arranged with the haematologist, who confirmed persistent resolution of symptoms and almost normal skin after 2 months (figure 3).

DISCUSSION

Acute febrile neutrophilic dermatosis (Sweet's syndrome) was first described in 1964.¹ It is a syndrome associated classically with painful erythematous plaques or nodules, and fever. Indeed one of the main criteria for diagnosing it as Sweet's syndrome is a rapid onset of these skin changes; the other being the finding of a rich neutrophilic population in the affected tissue.²

However, the condition is also strongly associated with malignancy as well as inflammatory conditions. So the diagnosis of Sweet's syndrome should also be considered in patients presenting with this background, fever, elevated inflammatory markers or total neutrophil count.²

Figure 3 Resolution of signs following administration of oral steroids—after two months during clinic visit.

This case posed a diagnostic challenge, in that the extensive, bullous and haemorrhagic appearances shown in this case are not typical of Sweet's syndrome. In fact, these appearances have more commonly been described as a presentation of haematological malignancy, specifically in conditions such as acute myeloid leukaemia, in which bullous pyoderma gangrenosum is a recognised feature, and there are case reports in which these skin changes are identified as the presenting feature of acute myeloid leukaemia.^{3 4}

Apart from malignancy, the syndrome has also been associated with certain medications. There have been published case reports linking this condition to drugs such as granulocyte colony-stimulating factor (G-CSF),⁵ nitrofurantoin⁶ and trimethoprim,⁷ and also non-steroidal anti-inflammatory drugs such as diclofenac.⁸

There is no universally accepted pathophysiology for the development of Sweet's syndrome. The most supported theory is of cytokine dysregulation, a theory that suggests cytokines and chemokines mediate the development of the disease.^{9 10}

The current recommended first-line treatment is corticosteroids. The recommended dose is 1 mg/kg/day and recovery is usually prompt.¹¹ Potassium iodide has also demonstrated

therapeutic benefit in this condition but is not favoured due to potential side effects.¹² Colchicine has also shown a positive therapeutic effect in the management of the condition.¹³ If first-line therapy fails, indomethacin, clofazimine, cyclosporine and dapsone have shown benefit as second-line agents, either as monotherapy or combination therapy.^{14–16}

Learning points

- ▶ Acute febrile neutrophilic dermatosis is a condition that should be considered in a patient presenting with new skin lesions on a background of haematological malignancy or immunological disease.
- ▶ Punch biopsy of skin lesions should be performed and not delayed if a diagnosis of Sweet's syndrome is suspected.
- ▶ Oral corticosteroids, such as prednisolone are the mainstay of treatment for Sweet's syndrome and recovery is usually prompt.

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