Wound detectives: can you solve the case?

Welcome to our new regular "Wound detectives" feature. In each issue, Joy Tickle will share a real-world case presentation and ask whether you can solve the case. What do you think is the cause of the wound, what tests would you order to confirm your diagnosis and what treatment would you provide?

JOY TICKLE
Tissue viability nurse consultant

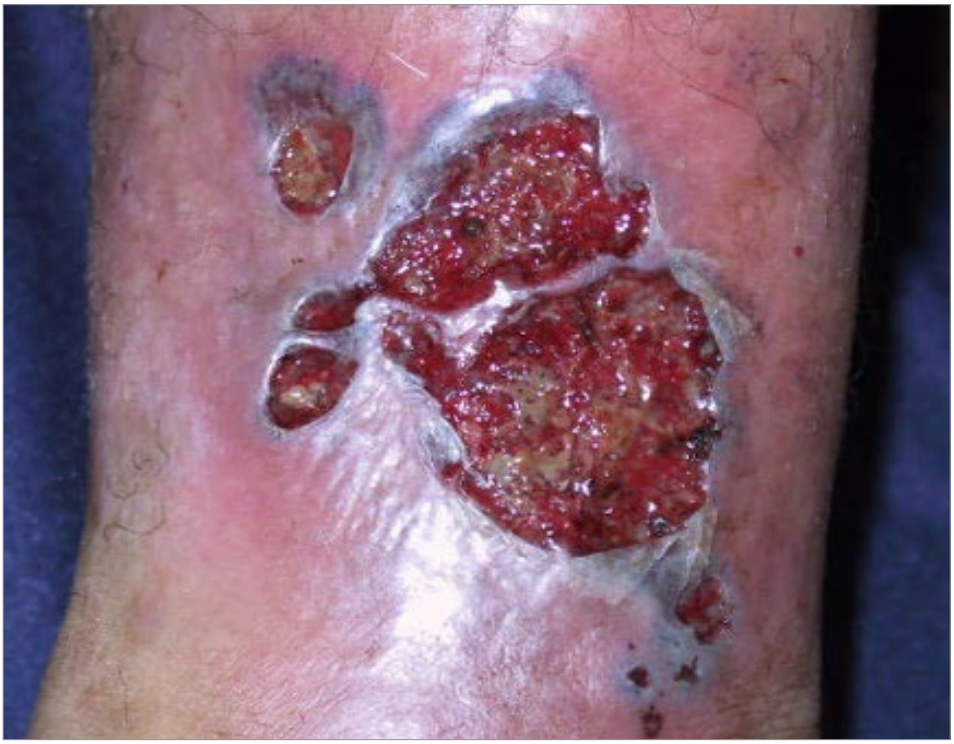

Figure 1. Image of the wound on presentation

A 60-year-old woman was referred to the tissue viability service by the GP practice with a late onset non-healing leg ulcer of three month duration. The patient had a medical history of irritable bowel disorder (IBD), hypertension as well as chronic limb oedema and venous disease.

Over the past three months there had been deterioration in her condition, the ulcer was increasing in size and not responding to various wound management plans, including antimicrobial dressings and numerous courses of antibiotic therapy.

On clinical examination in the tissue viability clinic a holistic patient assessment, wound assessment and vascular assessment were undertaken. On examination of her vascular supply her ABPI was 0.95 and her foot and limb were well perfused. Pedal pulses were triphasic and she had no clinical indicators of arterial disease. Despite this she could not tolerate compression therapy to her limb due to excruciating pain. The pain to her wound caused her significant stress, anxiety and sleep deprivation. This reduced her activity/mobility that further exacerbating the oedema to her limb. The wound was increasing in size and had a distinctive purple wound edge. Her fluid and dietary input was poor due to apathy and lethargy.

When asked how the ulcer developed, she reported that "it occurred out of the blue, it was a small dark coloured spot that grew quickly and began to weep blood stained fluid".

From the clinical examination the of wound the tissue had a granular appearance that was friable and bled easily in addition there was also a small percentage of necrotic tissue. There was surrounding erythema to wound edge only, but it was not warm to touch. The wound edge also had a distinct purple haemorrhagic boarder *(Figure 1)*.

Question 1

What may be the possible cause of the wound? Name 3

Question 2

From the information in the case study describe the wound appearance and symptoms which may lead you to suspect it was unusual?

Question 3

What investigations / tests could be undertaken in order to assist in ascertaining the wound aetiology?

From the initial assessment with the Tissue viability team it was concluded that the ulcer was not a result of venous insufficiency or arterial disease.

Turn the page for part two

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Answers and part two

Question 1. What may be the possible cause of the wound? Name three

Answer. The possibilities are
- Wound infection
- Insect bite
- Drug reaction
- Skin Malignancy
- Inflammatory ulceration: Vasculitis/ pyoderma gangrenousum (PG)
- Systemic conditions: Rheumatoid arthritis, lupus erythematosus, sweets syndrome
- Factitious disorder.

Question 2. From the information in the case study describe the wound appearance and symptoms which may lead you to suspect it was unusual?

Answer
- Rapid onset: commenced as dark spot
- Granular appearance to the wound bed that that bled easily
- Erythema to the wound edge only
- Wedge also had had a distinct purple haemorrhagic boarder (inflammatory halo)
- Extremely painful
- Non responsive to treatment.

From the rapid onset of the painful ulceration, its unusual clinical presentation and the patients underlying comorbidities it was agreed that further investigations were necessary to ascertain its true aetiology in order to ensure effective management.

Question 3. What investigations/ tests could be undertaken in order to assist in ascertaining the wound aetiology?

Answer
- Patient history/physical examination
- Microbiology/culture and sensitivity
- Blood chemistry renal and hepatic function, Rh factor, full blood count (FBC), inflammatory markers in order to eliminate any underlying disorders / infection
- Screening of any possible underlying disorders
- Tissue histology
- Colonoscopy
- Radiography.

The patient underwent several investigations to ascertain the aetiology of the wound. This included a wound swab for MC&S, to ascertain if the cause of the ulcer was due to infection. Blood chemistry tests including inflammatory markers and full blood count in order to eliminate any underlying disorders. Her blood chemistry identified raised inflammatory markers; however, wound swab results indicated that only normal skin flora and *Staphylococcus aureus* were present suggesting that infection was not a significant factor, concluding the wound was not caused from infection. Based on the clinical picture and results of the investigation it was clear that the patient required referral on for further specialist input and it was agreed that due to the wound appearance and rapid deterioration urgent referral to the dermatologist was necessary.

The dermatology team undertook a tissue biopsy of the wound bed and wound edge for histology. The results identified acute inflammatory cell infiltration and also a lymphocytic vascular response. These results were consistent with a condition known as PG (Magro et al, 1997). The dermatologist also referred the patient to a colorectal consultant who carried out investigations of her IBD, as this can be a causative factor for the development of PG (Teagle et al, 2014) In this case, following colonoscopy, it was felt that this was not the case and despite further investigations the true cause of the PG could not be identified

PG is a rare inflammatory disease resulting in a chronic ulcerating skin condition, the exact cause is not fully known. It is a systemic auto-inflammatory disease and may be triggered by trauma, inflammatory or neoplastic processes (Ratnagobal and Sinha, 2013; Adışen et al, 2016).

Approximately 50% of cases of PG are related to an underlying systemic disease resulting in an immune mediated process. The patient with PG will present with a heightened and ongoing inflammatory response. (Young, 2018) This response may last weeks or even years (Ratnagobal and Sinha, 2013).

There are humoral and cell mediated abnormalities that have been associated with PG

Humoral: It can be an autoimmune disorder in which the body's own immune system will produce antibodies for attacking the skin/ bowel causing blisters and tissue necrosis (Ebringer, 1969)

Cell–mediated defects have been found to include altered production of macrophage inhibition by lymphocytes, decreased neutrophils chemotaxis and impaired monocyte phagocytosis (Nerella et al, 1985; Teagle and Hargest, 2014; Ratnaglobal and Sinah, 2013).

There are various thoughts of why PG occurs. It is seen typically in adults between 40–60 years of age and commonly the ulcers are found on the lower extremities/trunk.

However it is extremely rare in children and normally associated with inflammatory bowel disease, immunodeficiency, immunosuppression and HIV infection. In children if it occurs the ulcers are often seen on the buttocks, perineum, head and neck.

There are five subtypes of PG and unfortunately a patient may suffer from more than one subtype at any one time (Gameiro et al, 2015)

The subtypes are
- **Classic pyoderma gangrenosum**. This is often associated with arthritis, haematological malignancies and IBD

(Teagle and Hargest, 2014). This often starts as a small purple/black papule that breaks down rapidly to form a painful ulcer with a well-defined border (often referred to as a halo), accompanied by erythema of the surrounding skin

- **Peristomal pyoderma gangrenosum**. This type of PG presents close to abdominal stomas and is associated with IBD. Like classic PG the ulcers are painful, progress rapidly with a defined boarder (Afifi et al, 2018)
- **Pustular pyoderma gangrenosum.** This is associated also with IBD and presents as painful pustules that form lesions but do not ulcerate (Teagle and Hargest, 2014).
- **Bullous pyoderma gangrenosum**. This type of PG is often linked to haematological conditions and results in multiple haemorrhagic blisters forming mainly on the arms, face and hands.(Shavit et al, 2017)
- **Vegetative/superficial pyoderma gangrenous**. This is a rare superficial type of PG and presents as slow growing superficial lesions or plaques and often responds to topical treatment (Schotanus et al, 2014).

Question 4

From the description of the patients wound in the case study and the above description what type of PG do you think this patient had developed?

Question 5

What was the cause of this patients PG?

Question 6

In view of the various causes of PG who else may you refer to assist with the diagnosis and management of PG?

Question 7

How would you manage the wound signs/ symptoms?

Question 8

What are the possible systemic treatment options for this type of ulcer?

Question 9

How could you assist in improving the patient's quality of life?

Question 10

Who is most risk of PG?

Question 11

What are the 5 types of PG?

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Answers (questions 4-11)

Question 4 From the description of the patient's wound in the case study and the above description. What type of PG do you think this patient had developed?

Answer: Classic PG.

Around 50% of cases of PG are associated with a co-existing systemic disease such as

- Rheumatoid conditions (rheumatoid, arthritis, systemic lupus erythematosus
- Hepatic (chronic active hepatitis, primary biliary cirrhosis, sclerosing cholangitis
- Inflammatory bowel conditions
- Haematological disorders (lymphoid/ myeloid leukaemia, Myeloma, hepatitis C, HIV.

However other causes can be linked to:

- Drug reaction with Isotretinoin reported as a causative agent (Teagle and Hargest, 2014)
- Solid tumour development
- Pregnancy (Gameiro et al, 2015; Shavit et al, 2017)
- Following trauma including burns and surgery
- Idiopathic, having no known cause, approximately 50% (Teagle and Hargest, 2014).

Question 5 What was the cause of this patient's PG?

Answer: Idiopathic, no cause identified (colonoscopy results suggested that the patients IBD was not the cause).

Question 6 In view of the various causes of PG who else may you refer to assist with the diagnosis and management of PG?

Answer:

- Gastroenterologists
- GP
- Vascular team
- Dermatologists
- Plastic surgeons
- Tissue viability
- Dietician
- Immunologists
- Haematologists
- Rheumatologists.

As discussed the diagnosis of PG is largely on clinical appearance, from the patient's history and from the exclusion of other possible diagnoses for this reason, it is imperative that the patient undergoes investigation to establish any co existing conditions/factors that may have led to its development. It is also essential that the management of the patient's condition and wound is undertaken with an multidisiplinary team (MDT) approach and therefore, immediate referral(s) to appropriate clinicians/services and medical teams is essential. (Mehrtens and Crawley, 2015)

Now that the patient had a definite diagnosis, the MDT could tailor the treatment regimen to try to address the condition. In line with evidence, she was commenced on a high dose of oral corticosteroids in order to reduce the abnormal inflammatory response. In view of the recent wound swab, it was agreed that oral antibiotic therapy was not necessary. However the nursing team and the patient were advised to be vigilant for infection as high dose of corticosteroids can reduce the inflammatory response and so mask the signs of infection. (Young, 2018) The patient was also commenced on topical steroid therapy ointment to the wound bed.

In addition to this it was important the symptoms of the wound were also addressed these being

- Gentle but effective wound cleansing and debridement
- Reduction of microorganisms and prevention of biofilm formation
- Management of the haemopurulent exudate and protection of the peri wound edge and skin

Following discussion with the patient an appropriate treatment regimen was introduced. This involved

- Cleansing with a surfactant in order to remove devitalised tissue and to reduce the microorganisms and to prevent biofilm formation (Phillips et al, 2010)
- Application of a topical corticosteroid cream to the wound bed in order to reduce the inflammatory response
- Application of a low adherent contact primary wound dressing to ensure atraumatic dressing change
- Superabsorbent secondary dressings in order to absorb retain and lock the haemopurulent exudate and prevent possible damage to periwound skin

Most importantly the patient's pain was regularly assessed and her prescribed analgesia was monitored to ensure comfort and promote rest.

We discussed with her the importance of a well-balanced high protein diet and a good fluid intake in order to assist wound to heal. A quality-of-life assessment was undertaken to ascertain the impact for her living with the wound. One area that was affecting this was her ability to shower daily due to the wound therefore a waterproof shower protector device for her limb was prescribed.

As discussed within this case study treatment regimens are dependent upon the severity of the symptoms and the presence or absence of underlying systemic disease. (Young, 2018). The mainstay of treatment is targeted at moderating the immune response and managing associated wound problems. Unfortunately there are no standardised treatment guidelines for PG due to its rarity. (Adisen et al, 2016; Wallace, 2017)

The use of topical steroid therapy may be implemented to assist in the management of the PG ulcer. (Petering, 2001) and may be

applied as an impregnated tape, as an ointment or intralesional injection.

However, if the condition is aggressive or more widespread a systematic approach is necessary. This may include IV or oral corticosteroid therapy (prednisolone) or immunosuppressant agents such cyclosporine, however they do have high associated risk. (Brooklyn et al, 2006b)

In some case antimicrobial treatments and sulfones have found to be useful in reducing the anti-inflammatory effect and additionally altering neutrophil function (Chow and Ho, 1996)

Newer biological therapies such as TNF inhibitors i.e. Infliximab do offer new options for PG management (Ratnaglobal et al, 2013).

What is crucial is that with any of these therapies they must be tapered off as soon as possible as this may decrease the potential life-threatening side effects of the drugs. (Teagle and Hargest, 2014). A stepwise approach to both topical and systemic therapies may also be beneficial along with the avoidance of switching from one drug on to another (Patel et al, 2015)

Overall wound treatment aims are to reduce the inflammation to the wound and surrounding tissue, prevent infection, promote healing, to assist in pain reduction and patient comfort. Wound dressings such as alginates, antimicrobials, and hydrocolloids have been reviewed for the treatment of the wounds. Other authors have suggested the use of negative pressure wound therapy, hyperbaric oxygen therapy and larvae therapy for the treatment of the wound symptoms (Laun et al, 2016; Pichler et al, 2016). With regards to wound cleansing and debridement surgical and sharp debridement are discouraged as they can potentially cause pathergy (Afifi et al, 2018).

Question 7 How would you manage the wound signs/symptoms?

Answer: Wound symptom management:

- Atraumatic dressing change to reduce pain and further trauma
- Effective gentle cleansing and debridement to reduce bioburden
- Primary dressing to meet wound symptoms
- Topical corticosteroid if indicated
- Antimicrobial for odour, critical colonisation, infection if necessary
- Early recognition infection
- Pain management.

Question 7 What are the possible systemic treatment options for this type of ulcer?

Answer:

- Oral or IV corticosteroids
- Antibiotics only if wound/skin infection is diagnosed
- Sulfones and other antimicrobial treatments
- Cyclophosphamide acts as a steroid sparring agent. Immunosuppressant's cyclosporine do have risks secondary infection/sepsis due to immuno-compromised patient
- Biological agent's TNF-inhibitors.

Question 9 How could you assist in improving the patient's quality of life?

Answer:

- Effectively managing the wound symptoms.
- Educate patients about risk factors and risk recurrence
- Given them advice regarding early indicators of the possible recurrence and how and where to seek advice immediately
- Offer the patient details of self-help groups for support.

The wound responded to the topical and systemic therapy and began to produce granulation tissue and reduce in size. The patient's quality of life improved as a result of this and also from the effective management of her pain. The wound completely closed after seven months and the patient advised about the early warning signs of the recurrence of PG and how and where to seek immediate help.

Question 10 Who is most risk of PG?

Answer:

- People with certain co existing conditions
- Following trauma/burn injury
- Typically, adults between 40–60 years of age
- Children with underlying comorbidities such as inflammatory bowel disease, immunodeficiency, immunosuppression and HIV infection.

Question 11 What are the five types of PG?

Answer:

There are five subtypes of PG and an individual can suffer from more than one type at any one time (Gameiro et al, 2015) (Box 3).

- Classic pyoderma gangrenosum
- Peristomal pyoderma gangrenosum
- Pustular pyoderma gangrenosum
- Bullous pyoderma gangrenosum
- Vegetative/superficial PG.

CONCLUSION

As discussed, PG is a rare condition that extremely debilitating and even life threatening. There is no equivocal diagnostic test and so PG is often undiagnosed or misdiagnosed. Diagnosis in the first instance relies on the presenting clinical picture of the wound/lesions and the patient history. Therefore, it is imperative that health professionals working within wound care are aware of this condition and have the skills to recognise it.

Thus, early MDT intervention can be implemented ensuring accurate diagnosis and the implementation of clinically effective management.

It is hoped that this case study has assisted you in understanding and recognising PG.

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