A tricky trio of wounds

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Complex wounds can prove very challenging even for the most experienced clinician. Here we present a series of three cases where suboptimal outcomes from conventional treatments led to further investigation, resulting in unusual diagnoses that affect wound healing. These cases highlight the benefit of varied clinical input from a multidisciplinary team in the management of complex wounds.

Keywords: chronic wound, haemophilia, hemophilia, pemphigus, factor XI deficiency, Rosenthal syndrome, complex wound, haemophilia C

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Case 1

History and progress

Patient A, a 68-year-old male with a chronic scalp wound, was referred to the Cape Advanced Wound Care Centre (CAWCC) after having been treated with 5 fluorouracil eight weeks prior, with a working diagnosis of actinic keratosis. Although this cream typically causes an inflammatory reaction resulting in the skin peeling, this particular patient developed an unusually florid inflammatory reaction, resulting in most of his scalp becoming a large exudating wound. This was subsequently treated with desiccating powder by the dermatologist in an attempt to dry the wound. This resulted in crusts, which were painful and therefore very difficult to remove (Figure 1). He was referred to CAWCC for further dressings and advice.

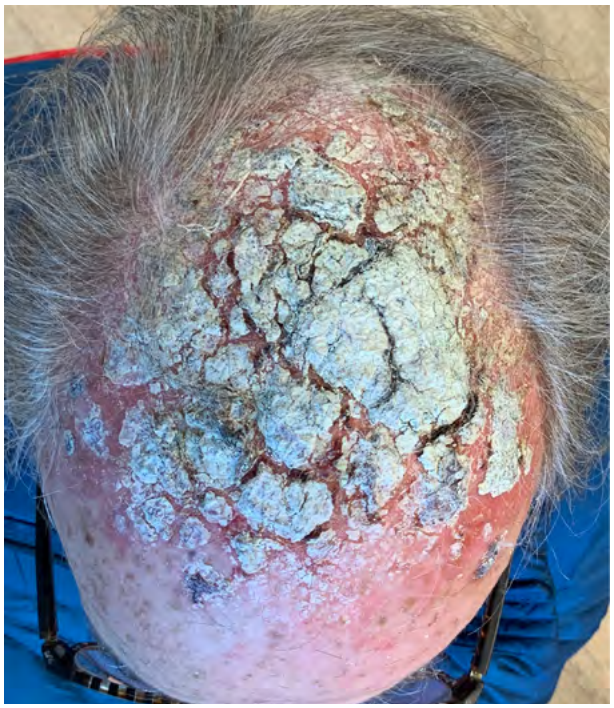

Figure 1: Painful crusts on chronic scalp wound

The plan was to autolytically debride the crusts with hydrocolloid gel dressings alone and success in removing them was achieved within the first week (Figure 2). However, epithelialisation was slow, dressing changes remained painful and any new epithelium was unfortunately easily removed with every dressing change, despite a non-adherent silicone interface dressing being used. This was unusual, as scalp wounds are generally not this painful and heal very quickly.

The patient coincidentally also developed painful mouth ulcers, for which an ear- nose and throat (ENT) surgeon's advice was sought. These were biopsied and a histological diagnosis of pemphigus of the oral cavity was made. This rare diagnosis prompted a subsequent scalp biopsy, which also confirmed the diagnosis of pemphigus vulgaris of the skin.

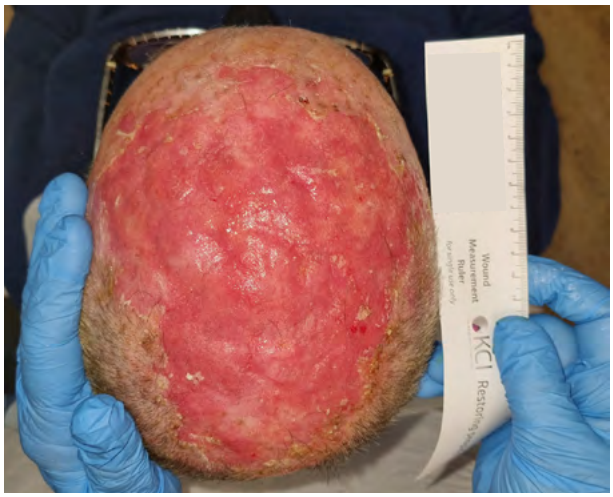

Figure 2: Wound (18 x 10 cm) after autolytically debriding crusts with hydrating hydrocolloid dressings. Moderately exudative, mixed partial thickness depth wound

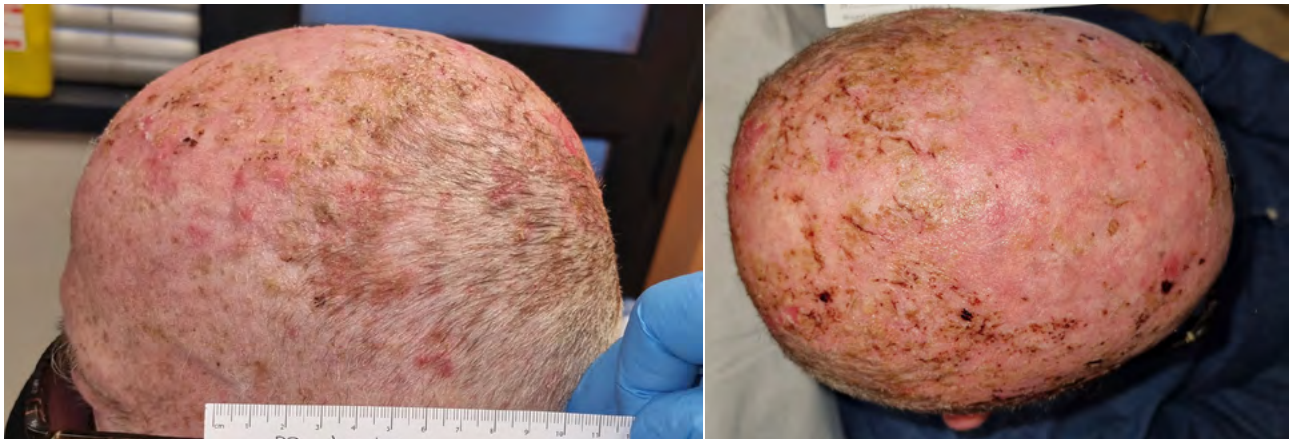

Figure 3: Scalp wound completely healed within a week of starting high dose oral steroids

After a month of little progress before this diagnosis, he was started on high dose steroids under the care of his dermatologist, following which his pain diminished very quickly and within a week the entire scalp wound was healed (Figure 3).

Discussion

Pemphigus is a group of autoimmune diseases that affect the skin and mucous membranes resulting in blistering lesions.[1] The two main subtypes being vulgaris and foliaceus. It is characterised by acantholysis, which is the loss of normal cell to cell adhesion, and by the presence of pathogenic autoantibodies (IgG) which attack the cell surface keratinocytes. The incidence is around 1–2 per 100 000/year and, although this patient was not Jewish, is more common in the Ashkenazi Jewish community.[2] Whilst it can affect the paediatric age group it commonly manifests in the 6th decade of life.

Diagnosis is usually made on history, clinical examination and typical histological findings.[1] On enquiry the patient may have oral lesions alone or accompanied (usually later) by skin lesions characterised by flaccid blistering on healthy skin or an erythematous skin base. These lesions tend to be painful but not usually pruritic. Typically the skin lesions should demonstrate a positive Nikosky's sign, which shows sloughing of the epidermis after gentle rubbing.[3] Histology shows an intraepidermal blister or vesicle resulting from the acantholysis. Both suprabasal and basal cells separate as well as basal cells from adjacent basal cells forming the characteristic Tombstone appearance.[3] Further definitive diagnosis can be made by direct immunofluorescence detection of anti-desmoglein autoantibodies, or even anti-desmoglein antibody detection in the blood serum sample.

Treatment often involves immunosuppressant medications, many of which have been used including, steroids, azathioprine, cyclophosphamides, cyclosporines, and dapsone.[4] Other treatments such as plasma exchange and topical epidermal growth factor have also been used. There is currently no consensus on which treatment is superior to the others.[4]

Case 2

History and progress

Patient B, a 78-year-old male presented to CAWCC with five-year-old chronic wounds of his lower legs (Figure 4).

He gave a history of having had minor trauma (knocked his right leg against a steel bucket) and subsequently developed his first ulcer. Following another minor trauma to the other leg a few months later, he developed ulcers on that leg too. He had seen a vascular surgeon in the past and underwent multiple investigations and treatments over the years prior to presentation to the wound centre. Included in these treatments were both multiple debridements and split-thickness skin grafts which ultimately failed.

An angiogram showed reasonable inflow and a venous assessment also did not demonstrate any outflow issues, excluding a vascular pathology as a cause for poor wound healing. The patient was not diabetic and therefore there was very little that could be offered as an explanation for his wounds. A biopsy was performed to rule out other potential causes and a histological diagnosis of pyoderma gangrenosum was made. The patient was started on high dose steroid therapy by the dermatologist on the multidisciplinary team and his wound exudate dropped within a week and, at the time of writing this report, he was showing signs of epithelialisation (Figure 5).

Discussion

Pyoderma gangrenosum is a rare, non-infectious, inflammatory disease affecting the skin and causing painful growing ulcerative lesions.[5] It is characterised by pathergy, which is the appearance of new lesions after trauma. The exact pathophysiology of the condition is not completely understood but is likely a combination of genetic factors, neutrophil dysfunction and a pathological inflammatory process. Approximately 50% of those diagnosed with pyoderma gangrenosum have an associated systemic disease most commonly inflammatory bowel disease or inflammatory arthritis.[6]

Historically the diagnosis of pyoderma gangrenosum has been one of exclusion given its varied presentation and lack of unique features both macroscopically and histologically.[5] A useful diagnostic criterion for effective identification of likely pyoderma gangrenosum suggests major criteria of a biopsy-proven lesion that shows neutrophil infiltration of the ulcer edge. If this is accompanied by one of four minor criteria a high predictive likelihood of diagnosis can be made. The minor criteria include: 1) exclusion of infection; 2) a history of pathergy, inflammatory bowel disease or arthritis, or rapidly ulcerating papule; 3) a clinical description of an erythematous border, wrinkled or cribriform

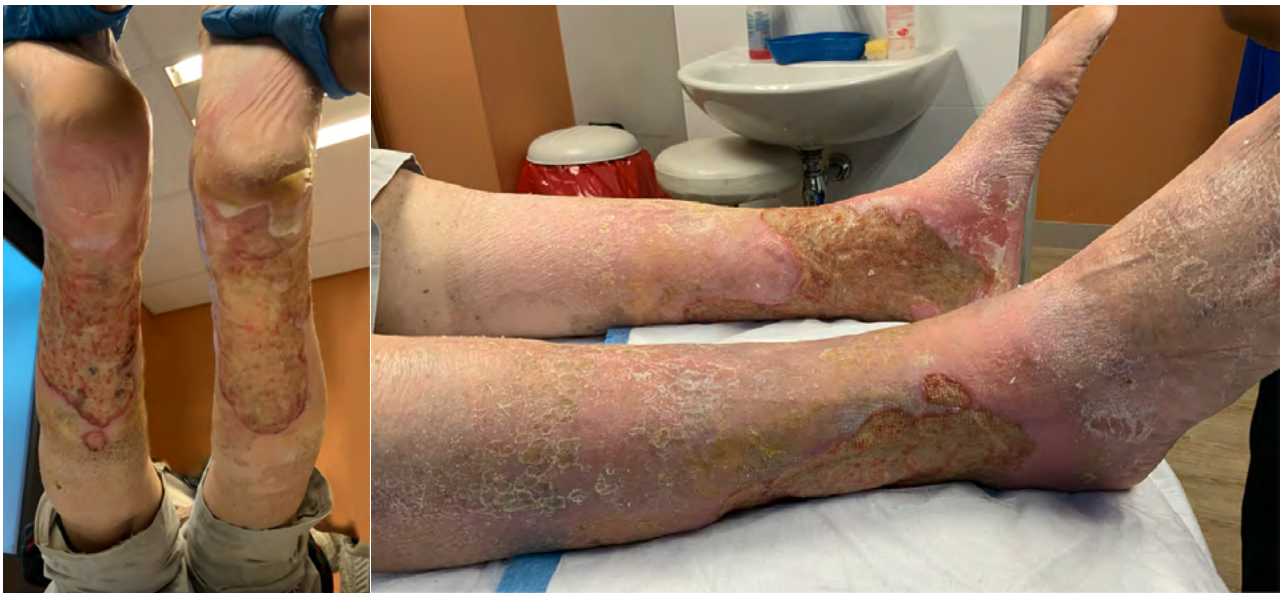

Figure 4: Multiple full-thickness leg wounds (over 20 cm in length in some areas), with dry slough on base

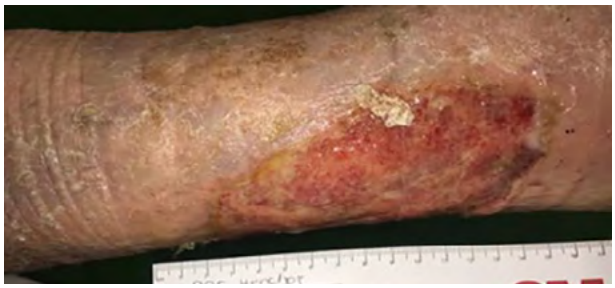

Figure 5: Early signs of epithelialisation from the wound edges of the lateral aspect of his right lower leg

appearance of healed ulcer or multiple ulcers and 4) treatment improvement with immunosuppressive medications.[7]

Management can be challenging and both systemic and local control measures are usually necessary. Typically, corticosteroids can be used systemically as first-line therapy although cyclosporines and tumour necrosis factor inhibitors have shown some success. Reduction of wound oedema, appropriate dressings and compression therapy (if arterial insufficiency has been excluded) form the foundation of local treatment. Topical or intralesional treatments can be of benefit as a singular modality of treatment for small lesions. Topical steroids, tacrolimus, dapsone and 5-aminosalicylic acid have been described in small studies.[8,9]

Case 3

History and progress

Patient C, a 37-year-old male with no known systemic comorbidities presented to CAWCC with a four-month-old chronic suprapubic wound. He gave a history of having had an infected haematoma of the abdominal wall after a laparoscopic sigmoidectomy for diverticulitis four months earlier. The evacuation of the haematoma necessitated a laparotomy. The skin wound was left open and was healed with conservative treatment. He also had a small suprapubic incision through which the resected colon was brought out (Figure 6). This wound did not heal.

He did not have any other obvious comorbidities and his panel of blood tests and wound swabs did not reveal any reason for poor wound healing. Therefore, the plastic surgeon on the CAWCC team elected to do a "woundectomy" (complete excision of the wound and all abnormal surrounding tissue) as described by the senior author,[10] undermining of the adipofascial flap edges and a layered closure a week later (Figure 7).

On postoperative day two, the wound became very painful and it was noted that there was bruising on the penis and scrotum. Almost a week later the wound had become even more painful, the patient spiked temperatures above 38 °C and his C-reactive protein markers elevated to 189 mg/L. The patient's symptoms progressed to worsening fevers and spreading erythema around the wound. New areas of bruising were also noted, despite no injections or trauma to the area (Figure 8).

A decision was then made to take him to theatre for exploration of the wound. Intra-operatively necrotic fat and early necrotising fasciitis was discovered, which was debrided and negative-pressure wound therapy (NPWT) was applied to the wound bed (Figure 9).

His septic markers improved postoperatively; however it was noted that he had unfortunately developed a hypersensitivity reaction to the

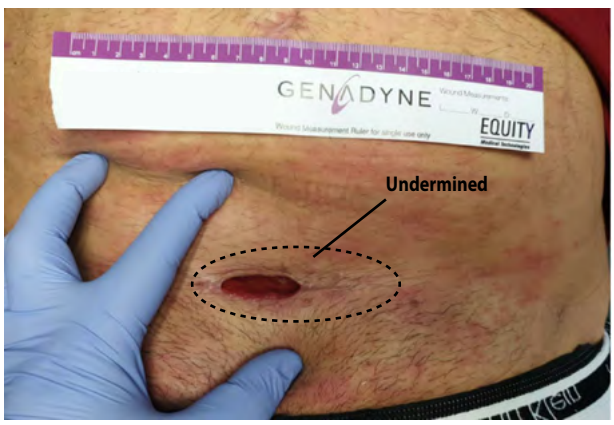

Figure 6: Chronic suprapubic wound, measuring 5 x 2 cm, with an area of undermining measuring 10 x 4 cm

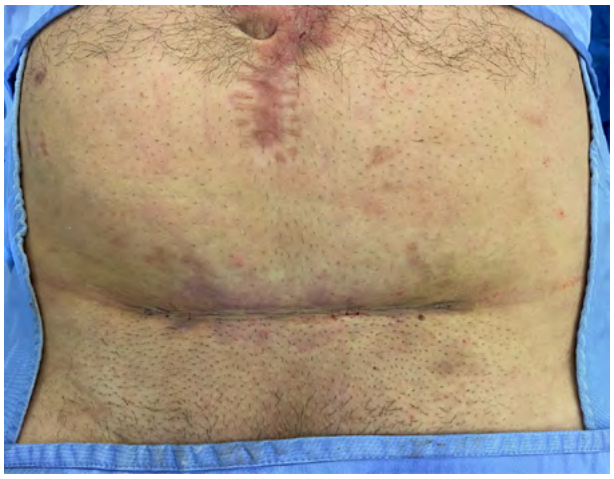

Figure 7: Tension-free closure which should typically have a low complication rate

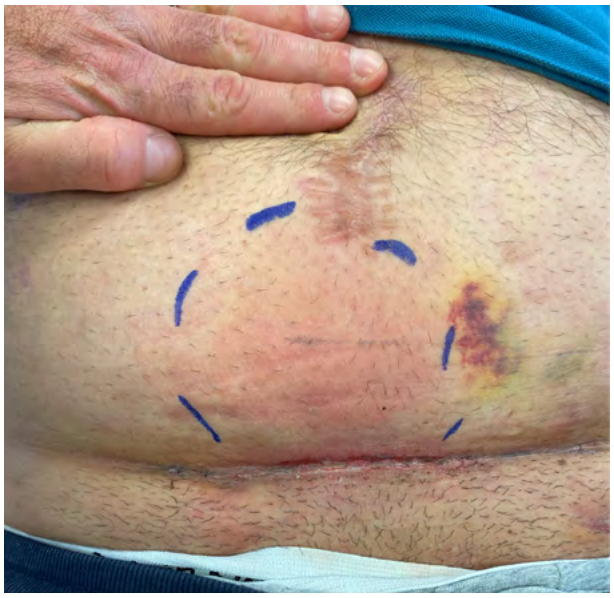

Figure 8: Increasing pain and erythema of peri-wound area with new areas of bruising

plastic drape used to seal the NPWT dressing. To alleviate this, a silicone interface dressing was used between the skin and an alternative drape to allow minimal contact between the drape and skin. Gauze instead of foam was also used to minimise pain during suction, because gauze has less of a compressive effect than foam because it is less collapsible (Figure 10).[11]

By the second week, the case was flagged as a complex case and discussed at the multidisciplinary wound team meeting. On further history, examination and blood testing the infectious disease specialist on the team made the diagnosis of a rare form of haemophilia, namely haemophilia type-C, which could affect surgical wounds. The patient was to be given fresh frozen plasma pre-operatively prior to the following debridement and closure, which was performed a week later. His postoperative course was satisfactory and at eight weeks post-operatively, his wound remained healed and pain-free (Figure 11).

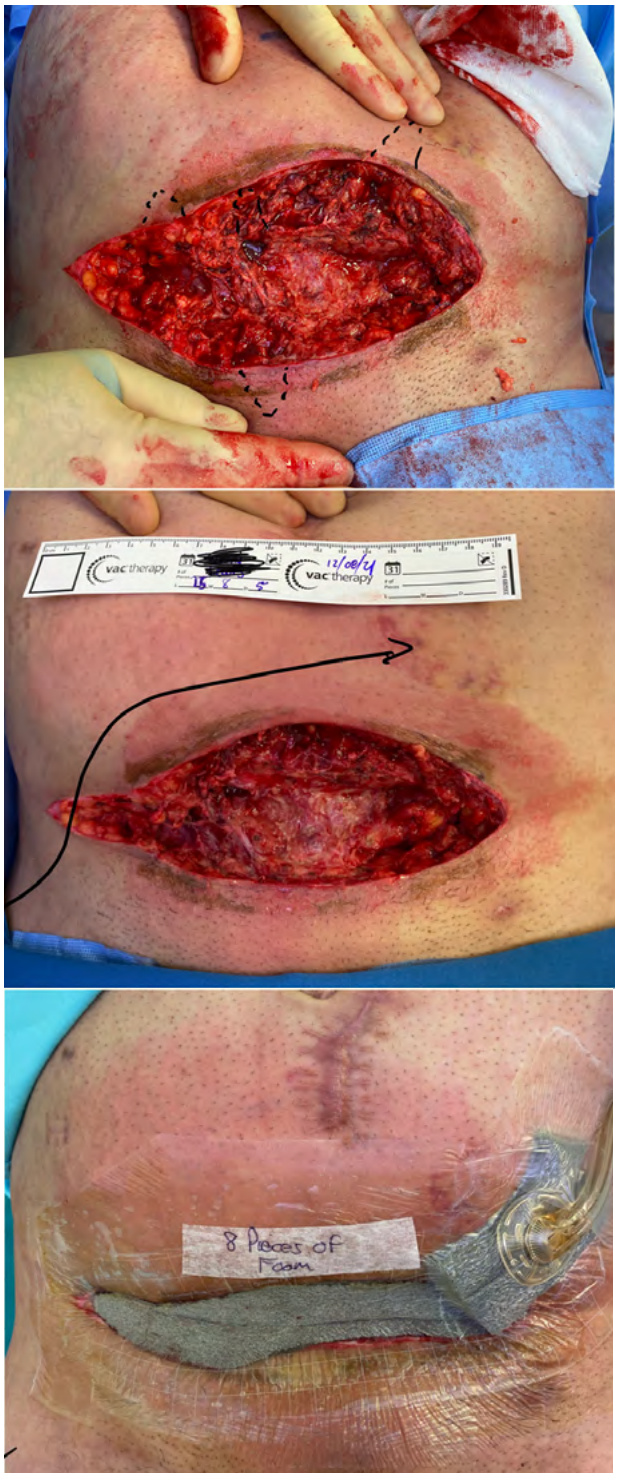

Figure 9: Sequence of pictures illustrating a) necrotic fat, with areas of tunnelling (marked by stippled lines), followed by b) a post-debridement photo (with the area of bruising, indicated by arrow) and c) a photo with NPWT in place. Note the surgeon's technique to ensure that the number of foam pieces in the wound are not forgotten.

Discussion

Haemophilia C, also known as Rosenthal syndrome, is an inherited disease resulting from a deficiency in Factor XI. It has a 1 per million frequency worldwide, however, is far more common amongst those of Ashkenazi Jew ancestry, affecting 1 in 450 in that particular population group. The patient in this series was of Jewish Ashkenazi descent. It

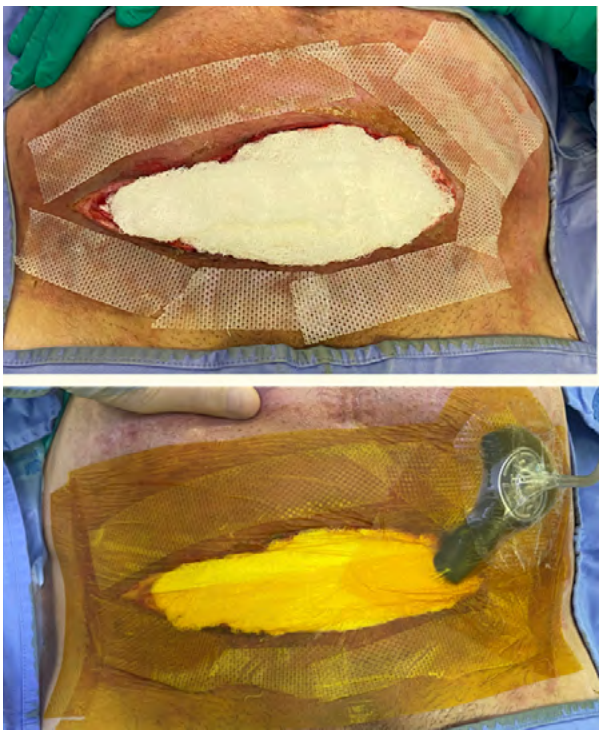

Figure 10: Silicone interface to minimise contact of skin and drape. Gauze used as alternative to foam to minimise pain.

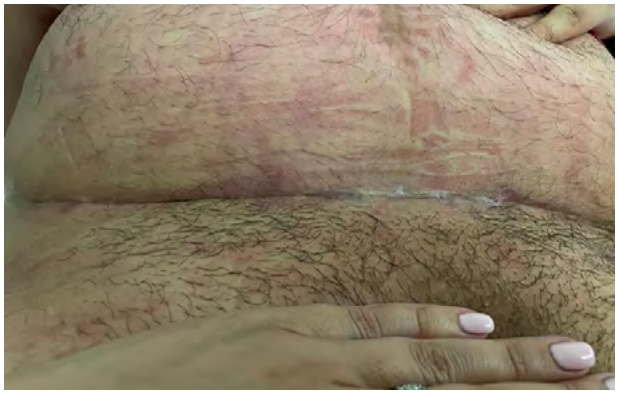

Figure 11: Wound healed and pain-free at eight weeks postoperatively

also has an increased incidence in other Mediterranean and middle eastern groups.[12] A distinguishing factor between this disorder and haemophilia A and B is that with haemophilia C spontaneous bleeding is uncommon and is usually seen after trauma. Haemophilia A and B have a X-linked recessive inheritance pattern, implying that only males are susceptible. Haemophilia C, on the other hand, is an autosomal recessive coagulopathy and not completely recessive, meaning heterozygous individuals can also display bleeding tendencies. Males and females are equally susceptible.

A typical history may include epistaxis, haematuria, menorrhagia or prolonged bleeding after trauma.[13] The symptoms are closely related to that of haemophilia A and B, however, there is no occurrence of haemarthrosis in Factor XI deficiency.

Diagnosis of haemophilia C is made due to a prolonged activated partial thromboplastin time (more than two standard deviations above the norm). However heterozygous individuals may have only a mild prolongation or even fall within normal range. Confirmation can be carried out with measurement of Factor XI via a specific assay.[14]

There is some evidence to suggest that cutaneous wound healing is impaired in haemophilia.[15] This may be caused by iron deposition and stimulation of angiogenesis which causes rebleeding and further tissue damage.[16] Thus, meticulous surgical technique and haemostasis coupled with the replacement of Factor XI (typically through fresh frozen plasma) should contribute to near-normal state for adequate wound healing, as was the case with our patient.

Conclusion

Dealing with complex wounds can be a challenge to surgeons, physicians and wound care specialists. The causes of poor wound healing are often multifactorial and can be influenced by both inherited and acquired pathologies. The problem may lie within the wound itself or be a systemic issue that is manifesting as a complex slow healing lesion. As highlighted by these cases, the role of a multidisciplinary team can be invaluable to facilitate the resolution of difficult to treat wounds. It is important to keep an open mind, especially with wounds that are not responding to conventional treatment methods and to look holistically at the patient for clues as to alternate diagnoses which could be contributing to poor wound healing. Having input from a variety of specialists and interested parties can shine light on a previously overlooked or even unthought of issue, which can lead to unusual diagnoses but effective treatment for the patient.

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