Case Report

The role of plasma transglutaminase (F XIII) in wound healing of complicated pressure sores after spinal cord injury

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Study design: A case report.

Objectives: To demonstrate stimulating action of F XIII in wound healing of complicated pressure sores.

Setting: A Spinal Cord Injury Center in Germany.

Methods: Clinical exam, clinical and photographic wound control, biochemical serum monitoring.

Results: Recurrent pressure sores in plegic patients are common complications requiring long-standing conservative or operative therapy. Additional risk factors such as diabetes increase the complication rate for surgery. Surgery itself may be difficult in recurrent pressure sores due to limited remaining soft tissues. We report the case and treatment of a 47-year-old patient with long-standing and recurrent ulcers and complications after flap surgery. As a final option we added plasma transglutaminase (factor XIII) to our treatment scheme which changed the course of the disease dramatically and we achieved complete and rapid healing.

Conclusion: Our experience suggests that F XIII has a positive role in treating pressure sores as shown already in several other surgical fields. Its use is giving the surgeon an additional tool in complicated cases.

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Introduction

Impaired wound-healing is still a major problem in surgery. Several factors such as diabetes, overweight, immune deficiency, arteriosclerosis or protein deficiency directly affect wound healing. There is a whole variety of local dressings and applications available on the market reflecting this problem.

However patients with spinal cord injuries have to be considered as different from the rest of the population, since different neurovascular and sensory properties of the tissue are additional risk factors in developing pressure sores. In the case of neglect, those sores easily erode the underlying tissue and develop into large soft tissue or even bone defects which need a long-standing conservative or operative treatment. Conservative treatment of pressure sores often results in scar formation which is less resistant to local pressure and eventually repeats the vicious circle. Operations however have the disadvantage of being

restricted to local myocutaneous or fasciocutaneous flaps which are often not available after revision surgery in recurrent pressure sores.¹ In both methods of treatment the patient has to accept a long term hospital stay. Regarding the patient's situation and the general costs it is necessary to use additional treatment options to speed recovery.

Case report

We report the case of a 47 year-old male Caucasian patient with complete paraplegia below Th4 after Th4 fracture in 1982. During the following years the patient gained weight up to 127 kg (body height 1.80 m) and eventually developed diabetes type IIb. He was treated for the first time in our centre in March 1998 for a pressure sore over his right ischial tuberosity (1.5 cm, grade 3c after Daniel/Seiler) and another one over his right greater trochanter (6 cm, grade 2c after Daniel/Seiler). Conservative treatment for 36 days with local enzymatic medication (Fibrolan[®]) and disinfectant (Betaisodona[®]) resulted in complete healing of the trochanteric and a reduction

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of 50% of the ischial defect. Monthly outpatient follow-ups however showed a slow healing of the ischial sore which healed completely 9 months later. An insect bite in the summer of 1998 resulted in an infected abscess over the 11th/12th right rib, which had to be excised (November 1998) after having developed into a 12×4 cm large defect (grade 3b after Daniel/Seiler). Four weeks after discharge the patient showed a local infection on the operative site which developed rapidly into a 25×15 cm large defect. During the following weeks a debridement was necessary twice with additional fibrinolytic and disinfectant conservative treatment. As this defect was located on the right side of the patient and he therefore laid on the left side, a pressure sore developed on his left greater trochanter which rapidly progressed into a defect grade 5b after Daniel/Seiler despite all conservative and pressure relieving techniques. The defect was cleaned with several operative debridements, and additional local therapy as described above, and closed temporarily with VAS (Vacuum Assisted Surgery) in April 1999. This procedure was repeated twice in 10 days. Finally the wound showed good granulation tissue (see Figure 1) and therefore was covered with tensor fasciae latae

flap after resection of the greater trochanter (see Figure 2). A seroma and flap infection developed postoperatively despite perioperative antibiotic treatment with cefuroxime. Three consecutive revisions were necessary leading finally to flap survival but open infected defect under the flap (see Figure 3). In this situation we started the treatment with F XIII prior to secondary flap closure in July 1999. The therapy with factor XIII was performed via intravenous administration starting 1 day before until day 11 after surgery. Before and during therapy the serum levels of F XIII were monitored closely. We raised the serum level from 78% pre- to 142% postoperatively (normal range 70–120%) as shown in Table 1. After the operation we performed a daily change of dressing without adding other topical substances. The drains could be removed on the 5th day (secretion 1st post-op day 120 mls, 4th post-op day 25 mls). The flap firmly adhered to its bed after 14 days and fully healed after 5 weeks (see Figure 4). No further complications occurred. Surprisingly, the pressure sore on the right greater trochanter, persistent since more than 8 months also healed completely within 2 weeks.

No systemic complications due to intravenous factor XIII application occurred.

Figure 1 Ulcer left greater trochanter stad. 5c after Daniel/Seiler after surgical and enzymatic debridement prior to flap surgery

Figure 2 Covering the defect with tensor fasciae latae flap

Figure 3 Infected flap prior to F XIII administration and revision surgery

Figure 4 Serum level of F XIII prior, during and after F XIII administration

Figure 5 Wound condition 5 weeks after F XIII administration and revision surgery with complete healing of flap

Discussion

This is the first case report of the effect of factor XIII in paraplegic patients with pressure sores.

Paraplegic patients show peripheral vasoconstriction due to lack of central inhibition of the cerebrum and cerebellum and increased spinal activity.² Additionally, due to impaired sensibility the patients does not feel a wrong sitting position or increased local pressure which often results in recurrent sores. The rate of pressure sores actually lies between 9 and 22%^{3,4} and, therefore, is the most common complication in plegic patients. The most common cause for systemic infection in geriatric patients are pressure sores.⁵ Chronic sores furthermore cause loss of proteins, immunologic deficits and electrolyte disturbances.⁶ On top of these pathologies the treating surgeon has to consider other diseases which are endemic in the general population suffering from impaired wound healing such as diabetes or arteriosclerosis. Our patient suffered from severe obesity and diabetes as additional risk factors. Next to these additional risk factors we feel that the patient, who had received a gastric balloon in order to lose weight, may have caused a catabolic situation, so in addition to other therapies we decided to remove the gastric balloon.

The overall difficult situation with long-standing ulcers in the past and the described additional risk leads us to the treatment with factor XIII although until then there was no literature about the treatment in plegic patients. In the literature the effect of factor XIII is well documented in severe burns,⁷ abdominal surgery,^{8,9} fistula in general surgery⁹ and in ENT surgery.^{10,11} Those studies show a positive effect of factor XIII on wound healing with partially significant higher wound healing rates.¹² The often quoted depression of factor XIII in the postoperative phase which is widely accepted as being one of the factors in impaired wound healing^{13,14} could be demonstrated by

a reduction of factor XIII activity to 90% on the second postoperative day in our patient. However we were able to stabilise this depression rapidly (see Figure 4). Although until now the quantitative adaptation of the dose of factor XIII to the serum activity in patients could not be established, one should aim to raise serum levels well above normal. We therefore decided on a fixed regular dose of 1250 IU per day. Side effects and complications of this dosage have neither been shown in literature⁷⁻¹¹ nor in our patient.

The basic cell effect of factor XIII has been proven by multiple experimental and animal studies^{12,15-17} and is mainly due to fibroblast stimulation with increase of synthesis activity and adhesion potential. Furthermore a stabilising effect on the cell membrane was discussed.¹⁸ Those mechanisms lead to a rapid and uneventful healing of a previously infected tensor fasciae latae flap which had to be revised three times prior to factor XIII administration. In addition an ulcer on the right thoracic side which persisted since 9 months was completely healed within 2 weeks on factor XIII therapy.

We cannot prove statistically the value of factor XIII, but in our case there was a rapid and safe healing of a flap which finally led to the end of a 9 month treatment as an in-patient.

Conclusion

The positive effect of plasma transglutaminase on wound healing is demonstrated. In plegic patients we have to consider a disturbed neurovascular and sensory situation on top of other potential risk factors common in the general population. We used FXIII in a very difficult case and showed positive effects. Further studies are necessary in order to prove this effect statistically. Until then we recommend the use of FXIII in individual cases with difficult or long standing pressure sores.

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