Title page

Title: Hypergranulation: options for management

Word count: 2.522 with abstract and reference list
1965 without

Abstract

Hypergranulation (or overgranulation) is an excess of granulation tissue beyond the amount required to replace the tissue deficit incurred as a result of skin injury or wounding. An infrequent but not rare consequence of wounding, the dearth of reliable evidence on the subject of hypergranulation has led to widely varying practices over time, including some which cause pain or discomfort and some which may further impair healing. However, despite a relatively poor evidence base, it is possible to ascertain that clinicians recognise different types of hypergranulation tissue in practice and that a variety of factors contribute to their development. Coupled with an understanding of normal healing processes, this differentiation of types and identification of contributory factors goes some way toward identifying effective treatment pathways and justifying treatment decisions, one of which includes adopting a wait and see approach.

Key words

wound healing, proliferation, hypergranulation types, contributory factors, treatment options

Key phrases

- Limited understanding of aetiology
- Unknown prevalence (size of the problem)
- Limited evidence base for best practice
- Some practices painful or harmful to patient
- Justifiable treatment options exist
- ‘Wait and see’ is a viable option

Introduction

Hypergranulation tissue is an excess of granulation tissue beyond the amount required to replace the tissue deficit incurred as a result of skin injury or wounding Most wound care practitioners will see it at some point in their practice, some more frequently than others, however, the absence of published best practice guidance for managing hypergranulation tissue may lead practitioners to use out-dated or harmful practices to resolve the problem. The purpose of this article is to identify what is currently known about hypergranulation and offer guidance on how to make the best use of this knowledge to support clinical practice.

Healing in the proliferative phase

Hypergranulation forms in the proliferative phase of healing; in wounds healing by secondary intention this phase is characterised by the formation of granulation tissue and epithelial tissue. Granulation tissue is the wound filler, used to restore the tissue deficit caused by wounding (Tortora and Grabowski, 2000). It grows from the base of the wound until it comes level to the surface of the surrounding skin. When it has, epithelial cells at the wound margins and from around the base of any remnant hair follicles in the wound, start to divide and multiply, moving across the surface of the wound to re-establish skin integrity (Flanagan, 2000; Waugh and Grant, 2001). This re-epithelialisation of the wound can only occur when the wound defect has been restored sufficiently to bring it level to the surrounding skin (Dowsett, 2002).

Tissue types

Healthy granulation tissue presents as a highly vascular, moist, pinkish/red tissue

with an undulating (granular) surface; it is characterised by a dense network of capillaries, high numbers of fibroblasts and macrophages and newly formed collagen fibres (Vuolo, 2009). Epithelial tissue is seen as a delicate pinkish/white skin tissue (Flanagan, 2000) which provides coverage over the newly formed granulation tissue. It is characterised by layers of closely packed cells (stratified epithelium) (Martin, 1997); although fragile in the early stages of healing these layers eventually mature to form a robust protective exterior to the skin.

Hypergranulation

In some wounds, production of granulation tissue continues beyond the height of the wound surface resulting in a raised mass (or peduncle) in excess of the wound itself. This tissue, known as hypergranulation tissue, can impede healing in several ways. It may prevent the migration of epithelial cells across the wound surface i.e. these cells do not travel vertically, and increase the risk of infection i.e. the longer the wound is open the higher the risk of infection (Nelsen, 1999), particularly if the exuberant tissue is moist and highly vascular, as is often the case. It has also been suggested that hypergranulation tissue may increase the risk of scar formation by forcing the wound edges further apart (Dunford, 1999).

Characteristics of hypergranulation

Hypergranulation is known by many terms including overgranulation, proud flesh, hypertrophic granulation and hyperplasia of granulation tissue (Harris and Rolstad, 1994; Young, 1995). It is an aberrant healing response, presenting as an overgrowth of fibroblasts and endothelial cells with a similar structure to healthy granulation tissue (Dunford, 1999, Semchyshyn, 2009) but in excess of the norm.

Hypergranulation occurs in a wide range of wounds including pressure ulcers, burns and venous ulcers and presents clinically in several forms. Commonly, it is seen as a spongy, friable, exuberant mass of tissue; sometimes beefy red, sometimes almost purple in colour (Harris and Rolstad, 1994; Johnson, 2007). Unhealthy in appearance, this kind of hypergranulation tissue is often associated with wound infection (Johnson, 2007) in which case there may be high exudate levels with associated maceration. It may also bleed readily. Alternatively, 'healthy' hypergranulation tissue is characterised by an overgrowth of red-pink , moist tissue, which may bleed but not readily; it is otherwise symptom-free (see Hypergranulation - clinical presentation Box 1). In any form, hypergranulation does not appear to cause the patient discomfort or pain.

Cause

Relatively little is known about the cause of hypergranulation. It is not a rare phenomenon; most wound care clinicians will have seen cases, some quite regularly. It may also be that some cases go undiagnosed due to clinical inexperience. The (apparently) low prevalence makes it difficult to investigate in sufficient numbers (Nelson, 1999) and, although it can delay healing, it is much further down the list of research priorities than many other wound-related problems.

Suggested causes include prolonged inflammation caused by infection or foreign body irritant (such as dressing fibres) (Wood, 1976; Zitelli, 1984; Stone, 1986; Harris and Rolstad, 1994; Nelsen, 1999) or by external friction (Hanlon and Heximer, 1994). This latter cause has been postulated in relation to gastrostomy tubes and supra-pubic catheter sites where the constant rubbing of the tube against

the skin may cause an inflammatory response. If this is the case, then any similar irritation to the wound bed for example through dressing contact or through repeated patient contact could have a similar effect. Inflammation may also be caused by an allergic reaction e.g. to the dressing or adhesive backing. The result of prolonged inflammation, whatever the cause, may be a stimulation of ground substance formation (Dunford, 1999) in excess of what is required for wound healing.

Links between the use of occlusive dressings (such as hydrocolloids) and hypergranulation have also been made (Falanga, 1988). The enhanced effect of growth factors under occlusive dressings (Bolton et al, 1991; Harris and Rolstad, 1994), the accumulation of fluid beneath the dressing resulting in tissue oedema (Vandeputte and Hoekstra, undated) and the possibility that occlusivity induces cytoxic effects (Van Luyn et al, 1992) have all been cited as possible connections.

There may also be a relationship between matrix metalloproteinases (MMPs) and the development of hypergranulation. MMPs are a group of proteolytic (protein degrading) enzymes which play an important role in the proliferative phase of healing (Stephens and Thomas, 2002). In particular, collagenese regulates the balance between collagen synthesis and lysis by facilitating the growth of new connective tissue and the re-absorption of the extra cellular matrix (ECM), the temporary filler which physically supports the newly formed blood vessels and granulation tissue characteristic of the proliferative phase (Edwards al., 1987; Stephens and Thomas, 2002). Sussman and Bates-Jensen (2007) suggest an

imbalance of collagen synthesis and lysis could result in the unchecked proliferation of collagen leading to hypergranulation formation.

Treatment

The various causes of hypergranulation may be grouped under three headings, those that are inflammatory in nature (Type I), those that are related to an occluded wound environment (Type II) and those that are caused by a cellular imbalance of some kind (Type III). These three groupings provide the basis for different treatment pathways (Figure 1), however, before proceeding, it is important to rule out the possibility of malignancy in any hypergranulating wound as these two conditions may present with similar characteristics (Harris and Rolstad, 1994).

This is done by:

- taking a comprehensive patient and wound history
- undertaking a clinical examination
- ordering appropriate investigations where necessary e.g. tissue biopsy
- referring for expert opinion e.g. dermatologist

<u>Treatment - Type 1</u>

Type 1 hypergranulation, which is inflammatory in nature, should be treated so as to resolve the inflammation through removal of the irritant or inflammatory factors.

- Examine the wound bed carefully; it is sometimes possible to see and remove dressing fibres and other potential irritants.

- Secure external medical devices such as gastrostomy tubes and central lines red in such a way as to minimise friction around the wound site.

- Identify wound infection, a key cause of inflammation in wounds. Treat with topical antimicrobials e.g. Actisorb®, Inadine®, Biatain Ag®. Select secondary dressing, if required, on the basis of exudate levels. Avoid occlusion. Treat systemic infection with oral or intravenous antibiotics as indicated. For further guidance on the management of wound infection refer to the EWMA Position Document 'Management of Wound Infection' (EWMA, 2006).

- If hypergranulation fails to respond to the above consider topical steroids; these can effectively dampen the inflammatory response and reduce hypergranulation production (NICE, 2004). However, they may also impede healing and products are often contra-indicated for use on open wounds (Young, 1995). Licensed usage must therefore always be checked. One potentially useful product is Haelan® tape (Typharm) which contains fludroxycortide, a moderately potent steroid. Haelan® tape is indicated as 'an adjunctive therapy for chronic, localised, recalcitrant dermatoses that may respond to topical corticosteroids' (Mason, 2009). There is also an ointment version.

  Use on hypergranulation tissue is at the discretion of the clinician and application/duration should be according to the manufacturer's instructions.

Treatment - Type II

Type II hypergranulation, developing as a result of an occluded wound environment, usually responds well to a change of dressing type.

- Where the dressing in use is occlusive e.g. a hydrocolloid, a switch to a more permeable product is indicated (Dunford, 1999). A film dressing e.g. Tegaderm® or a polyurethane foam dressing with a high moisture vapour transmission rate (MVTR) e.g. Lyofoam®, will improve gaseous exchange at the wound interface and increase the rate of vapour loss through the back of the dressing. Small studies by Harris (1991, cited in Harris and Rolstad, 1994) and by Harris and Rolstad (1994) found polyurethane dressings to be of benefit when compared with treatments such as topical silver sulfadiazine and hydrocolloids.

- Where exudate levels are higher, a more absorbent dressing can be used e.g. Mepilex®, Biatain®. The exact choice of dressing is dependant on exudate levels however where these are high the possibility of infection should always be eliminated first.

- Secure dressings in such a way as to allow them to manage exudate and vapour loss properly i.e. do not occlude dressings by applying layers of adhesive film over them.
- Where possible, apply moderate pressure to the wound using dressing pads, crepe or tubular bandage over the area (taking care to avoid constricting the blood supply). This may inhibit the further growth of hypergranulation tissue.
- Where bandaging is inadvisable, local pressure may be applied by

alternative means such as re-positioning the patient to lie on the wound for short periods or by encouraging mobility to increase foot pressures (taking care at all times not to cause the patient any harm as a consequence of applying pressure).

Treatment - Type III

Type III hypergranulation, appears to develop as a result of a cellular imbalance of some kind. It may be that the imbalance occurs as a result of an external factor and for this reason inflammation and occlusion should both be excluded as causes; however, if the trigger is internally located there may be little that can be done to reverse the cause. Therefore, until the causative mechanisms are better understood, effective management must rely on control of signs and symptoms using the same strategies as identified for Type I and Type II.

The 'wait and see' option

If malignancy and infection have been excluded a final option for all three hypergranulation types is to do nothing. Although an aberrant response, hypergranulation is normally transient and will often resolve itself as the wound contracts (Dunford, 1999). Adopting a wait and see policy may therefore carry fewer implications for the patient than some of the other options discussed.

Unsuitable options

Other treatment options cited in the literature include shave excision, curettage and surgery to mechanically debride the excess tissue and cautery, laser therapy, topical silver nitrate, phenols, copper sulphate and aluminium chloride to burn it

away (Harris and Rolstad, 1994; Dunford, 1999; Hawkins-Bradley and Walden, 2002; Semchyshyn, 2009; Stevens et al, 2009). Mechanical removal of hypergranulation is argued against on the basis of causing a return to the inflammatory stage of healing during the re-creation of what is essentially a new wound, whilst caustic agents may cause pain (Harris and Rolstad, 1994), provoke a further inflammatory response (Nelsen, 1999) and in the case of silver nitrate, cause conditions such as methaemoglobinaemia and hyponatraemia to develop (Rollins, 2000; Dealey, 2005).

Leaving the wound open is not advocated as wound bed exposure leads to cell death through tissue dessication and ultimately impacts on healing (Harris and Rolstad, 1994).

Conclusion

The literature indicates that a variety of factors contribute to the development of hypergranulation and that hypergranulation presents clinically in different ways. The recognition of contributory factors and clinical types facilitates decision making and, although the evidence based for treatment is limited, effective decisions can be made on the basis of identifying the likely cause of the problem. Finally, whilst several pathways for effective treatment exist it is important to remember that hypergranulation does not always impede healing and that sometimes adopting a ‘wait and see’ approach is the best option of all.

Hypergranulation – clinical presentation	
Unhealthy appearance	**Healthy appearance**
Exuberant tissue	Exuberant tissue
Dark red - purple in colour	Red – pink in colour
Wet / high exudate levels	Moist
Bleeds readily	May bleed
Friable (breaks down easily)	Not friable
Spongy / oedematous	

Box 1.

References

Bolton, LL., Johnson, CL. and Van Rijswijk, L. (1991) Occlusive dressings: therapeutic agents and effects of drug delivery. *Clinics in Dermatology*. **9**(4) 573-583

Dealey, C. (2005) The Care of Wounds: a guide for nurses. 3rd. Wiley Blackwell.

Dowsett, C. (2002) The management of surgical wounds in a community setting. *British Journal of Nursing* 7(6) 33-8 (supplement)

Dunford, C (1999) Hypergranulation tissue. *Journal of Wound Care* **8**(10) 506-7

Edwards, DR., Murphy, G., Reynolds, JJ., Whitham, SE., Docherty, AJ., Angel, P. Heath, JK. (1987) Transforming growth factor beta modulates the expression of collagenase and metalloproteinase inhibitor. *The EMBO Journal* 6(7) 1899- 1904

EWMA (2006) *Position Document: Management of Wound Infection*. London, MEP Ltd.

Falanga, V. (1988) Occlusive wound dressings – why, when, which. *Archives of Dermatology* **124**(6) 872-877

Flanagan, M. (2000) The physiology of wound healing. *Journal of Wound C*are 9(6) 299-300

Hanlon, M. and Heximer, B. (1994) Excess granulation tissue around a gastrostomy exit site with peritubular skin irritation. *Journal of Wound, Ostomy and Continence Nursing*. **21**(2) 76-77

Harris, A. and Rolstad, B.S. (1994) Hypergranulation tissue: a non-traumatic method of management. *Ostomy/Wound Management* **40**(5) 20-30

Hawkins-Bradley, B. and Walden, M. (2002) Treatment of a nonhealing wound with hypergranulation tissue and rolled edges. *Journal of Wound Ostomy and Continence Nursing*. **29**(6) 320-4

Johnson, S. (2007) Haelan Tape for the treatment of overgranulation tissue. *Wounds UK*. **3**(3) 70-74

Martin, P. (1997) Wound Healing: aiming for perfect skin regeneration. *Science* 276, (75-81) Available at www.sciencemag.org [on-line] [Accessed 9th November 2009]

Mason, R. (2009) Haelan Tape Clinical Indication. *Personal Communication*. 15th September.

NICE (2004) *Frequency of application of topical corticosteroids for atopical eczema. Technology Appraisal 81*. London, NICE

Nelsen, L. (1999) Wound care: Points of friction. *Nursing Times*. **95**(34): 72, 75

Rollins, H. (2000) Hypergranulation tissue at gastrostomy sites. *Journal of Wound Care.* **9**(3) 127-9

Semchyshyn, NL. (2009) Surgical complications. E-medicine dermatology Available at http://emedicine.medscape.com/article/1128404-overview [on-line] [Accessed 25th September 2009)

Stephens, P. and Thomas, DW (2002) The cellular proliferative phase of the wound repair process 1. *Journal of Wound Care* 11(7) 253-261

Stevens, NM, Shultz, T., Ryan, LM and Gersh, M. (2009) Treatment in an out-patient setting for a patient with an infected, surgical wound with hypergranulation tissue*. International Journal of Lower Extremity Wounds*. **8**(37)37-44

Stone, O.J. (1986) Hyperinflammatory proliferative (blastomycosis-like) pyodermas: a review, mechanisms, and therapy. *Journal of Dermatologic Surgery and Oncolo*gy **12**(3) 271-273

Sussman, C. and Bates-Jensen, B. (2007) *Wound Care: A collaborative practice manual for health professionals*. 3rd ed. Philadelphia, Lippincott, Williams and Wilkins.

Tortora, GJ. and Grabowski, SR. (2000) *Principles of Anatomy and Physiology* (9th Ed.) New York, John Wiley and Sons.

van Lyun, M.J., van Wachem, PB., Nieuwenhuis, P. and Jonkman, MF. (1992) Cytotoxicity testing of wound dressing using methylcellulose cell culture. *Biomaterials.* **13**(5) 267-275

Vandeputte, J. and Hoekstra, H. (undated) *Observed granulation may be related to oedema of granulation tissue.* Medline. Available at http://tinyurl.com/m224l4 [on-line] [Accessed 11th September 2009]

Vuolo, J (ed.) (2009) *Wounds Care Made Incredibly Easy* (1st Ed.) London, Lippincott, Williams and Wilkins.

Waugh, A. and Grant, A. (2001) *Ross and Wilson: Anatomy and Physiology in Health and Illnes*s (9th Ed). Philadelphia, Churchill Livingstone

Wood, R.A. (1976) Disintegration of cellulose dressings. *British Journal of Medicine* **1**: 1444-1445

Young, T. (1995) Common problems in overgranulation. *Practice Nurse*. **6**(11) 14-16

Zitelli, JA. (1984) Secondary intention healing: am alternative to surgical repair. *Clinics in Dermatology* **2**(3) 92-106

Hypergranulation

Identify Cause

⇩

Eliminate malignancy

⇩

Inflammation (Type I)		Occlusion (Type II)	Cellular imbalance (Type III)
Infection?	**Irritation / allergy?**		
Topical antimicrobials plus systemic antibiotics if necessary Apply suitable secondary dressing.	Remove cause e.g. dressing, remnant fibre, wound debris, adhesive material, external device Apply high MVTR dressing* Apply local pressure** If no response after 7 days consider topical steroid e.g. Haelan®	Apply high MVTR dressing* Apply local pressure**	Manage symptoms e.g. ↑exudate Apply high MVTR dressing* Apply local pressure**

Consider 'wait and see' option for Type II and Type III when it is not possible to implement other management options or when hypergranulation is not impeding wound closure or patient rehabilitation.

*Choose dressings with a high MVTR e.g. film or polyurethane foam depending on exudate levels.

**Local pressure in the form of bandaging must only be applied where arterial blood supply is sufficiently robust and where there are no contra-indications for doing so; it should be applied initially in the form of a firm crepe bandage. It is preferable to try a high MVTR dressing first before applying bandages as they may compromise the MVTR of the dressing

Indicators of infection: High exudate levels, malodour, wound bed discolouration, cellulitus, bleeding, delayed healing

Figure 1