Diplomarbeit

Major Complication after Breast-Reconstruction

eingereicht von

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Doktor der gesamten Heilkunde

(Dr. med. univ.)

an der

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ausgeführt an der

Klinische Abteilung für plastische, rekonstruktive und ästhetische Chirurgie

unter der Anleitung von

Prof. Dr. Michael Schintler

und

Prof. Dr. Stephan Spendel

Eidesstattliche Erklärung

Ich erkläre ehrenwörtlich, dass ich die vorliegende Arbeit selbstständig und ohne fremde Hilfe verfasst habe, andere als die angegebenen Quellen nicht verwende habe und die den benutzten Quellen wörtlich oder inhaltlich entnommenen Stellen als solche kenntlich gemacht habe.

Graz, am 18.05.2010 Unterschrift

Martin Grohmann

Danksagung

Mein besonderer Dank gilt meinen beiden Betreuern Prof. Dr. Michael Schintler und Prof. Dr. Stephan Spendel, die stets bei Problemen und Fragen jeglicher Art verfügbar waren und mich von Beginn an hervorragend unterstützt haben.

Des Weiteren möchte ich an dieser Stelle meinen Eltern Evelin und Günter Grohmann danken, ohne deren großzügige Unterstützung meine Ausbildung auf diese Art kaum möglich gewesen wäre.

Weiters gebührt mein Dank natürlich all meinen Freunden, die maßgeblich daran beteiligt sind, dass mir meine Studienzeit für immer in schöner Erinnerung bleiben wird.

Ebenso möchte ich der in diesem „Case Report“ dargestellten Patientin meine Anteilnahme und mein Mitgefühl ausdrücken. Ohne Sie und ihren bewundernswerten Kampf gegen die Kombination aus schwerwiegenden Ereignissen und einer heimtückischen Erkrankung wäre diese Arbeit in dieser Form nicht möglich gewesen.

Content

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Abbrevations

A	Acinetobacter
Ab	Acinetobacter baumannii
DOB	Date of birth
FLN	Fluorescence-Lactose-Denitrification medium
MAb	Multi resistant Acinetobacter baumannii
MDR	Multi drug resistant
PG	Pyodrma gangrenosum
PSPG	Post Surgical Pyoderma gangrenosum
TX	Texas
V.A.C.	V.A.C.® System by KCI San Antonio/Texas
V.A.C.-Instill	V.A.C.-Instill® System by KCI
TRAM	Transversal Rectus Abdominis Muscle

1 Abstract

1.1 Abstract German

Das Postoperative Pyoderma Gangraenosum ist eine seltene, heimtückische Erkrankung. Besonders die oftmals verspätete Diagnose kann schnell zu einer lebensbedrohlichen Situation führen. Sobald jedoch die Diagnose gesichert wurde, kann mittels immunsuppressiver Therapie rasch ein Fortschreiten verhindert werden. Ein häufig mangels einer eindeutigen Diagnose vorangegangenes Debridement, der fehldiagnostizierten Hautläsionen, führte auch in diesem Fall zur Notwendigkeit einer plastisch chirurgischen Intervention. Das ausgedehnte Abtragen der zugrunde gegangenen Hautareale kann tiefe Weichteildefekte verursachen und führt dazu, dass Hauttransplantationen und sogar Lappenplastiken zum Einsatz kommen. Diese Läsionen, mit zum Teil freiliegender Knochenstruktur kombiniert mit einer immunsuppressiven Therapie und der Notwendigkeit von verlängerten Krankenhausaufenthalten unter systemischer Antibiose, können zu Komplikationen mit multiresistentem Acinetobacter baumanii führen. Dies ist ein Fallbericht einer unglücklichen Zusammenkunft lebensbedrohlicher Komplikationen, welche sich nach einer Brustrekonstruktion ereignet haben. Es trat ein Postoperatives Pyoderma Gangrenosum auf. Weiters führte eine Verkettung unglücklicher Umstände bis zu einem totalen Defekt der Thoraxwand, sowie einer Infektion mit multiresistentem Acinetobacter baumanii. Eine Interdisziplinäre Therapie unter Verwendung freier Lappen und moderner Wundverschließungs-Systeme, wie das V.A.C.- Instill®, ermöglichten das Überleben und den kompletten Wundverschluss. Auszüge aus dieser Diplomarbeit wurden bereits im „Journal

of Plastic, Reconstructive and Aesthetic Surgery“ Februar 2010 veröffentlicht.

1.2 Abstract English

Postoperative Pyoderma Gangrenosum is a rare, tricky and cruel, in case of late diagnosis life-threatening complication. Once diagnosed medical treatment using immunosuppressive agents can rapidly stop progression. Preceding repeated debridement often leads to skin defects requiring plastic surgical procedures. Extensive debridement performed in misbelieve may cause deep skin and soft tissue defects, requiring not only skin grafting but also flap surgery. Deep soft tissue defects with exposed bone interacting with essential immunosuppressive condition and preceding long-lasting hospital stay, especially in intensive care units and systemic antimicrobial therapy may be complicated by serious aquired multi drug-resistant Acinetobacter baumanii infection. This is the report of a case of an unhappy triad following breast reconstruction. - Postsurgical Pyoderma Gangrenosum - full thickness thoracic wall defect- and Multiresistant Acinetobacter baumannii infection. Interdisciplinary therapy using free flap surgery and the use of innovative wound treatement systems (V.A.C. Instill®) enabled survival and complete wound closure.

2 Introduction

2.1 The regular Pyoderma Gangrenosum

The Pyoderma Gangrenosum is a rare occurrence. It is an neutrophilic dermatosis which is non infectious. It begins with pustules and quickly evolves to ulcers that give the patients exorbitant pain. Since it has first been described by Brunsting LA in 1930 in patients with chronic ulcerative colitis [1] several variants have become known. The precise Aetiology though remains unknown and the Pathogenesis is also not well understood. Since there is also no valid test for it, the diagnosis remains critical and extremely difficult. The several variants of the PG are still a diagnosis of exclusion. An underlying systemic disease is in 50-70% associated with PG [2,3,4]. However, numerous reports support the role of a defective immune system and PG is potentially associated with diseases like inflammatory bowel disease, arthritis, or gammopathy [5,6] it has been reported in 1-10% of patients with ulcerative colitis and 0.520% of patients with Crohn's disease [7,8,9,10]. It also has been found in association with chronic active hepatitis [11], rheumatoid arthritis [12], acute myeloid leukemia [13], chronic myeloid leukemia, polycythemia Vera [14] and multiple myeloma [15]. Even if there is a typical clinical appearance a lot of other ulcers may look similar

2.1.1 Postsurgical Pyoderma Gangrenosum

PSPG (Postsurgical Pyoderma Gangrenosum) may at first sight be misdiagnosed as postoperative woundinfection [16] or necrotising fasciitis which makes a big difference in treatment. Necrotising fascitis for example is treated with extensive surgical debridement combined with appropriate systemic antibiotics [17]. Pyoderma Gangrenosum though must not be treated surgically! Systemic corticosteroids are necessary. Other agents, such as cyclosporine, azathioprine, tacrolimus, or one of the antimetabolites, should be used as steroid-sparing agents [18]. It is also necessary to be aware that Pyoderma Gangrenosum can reoccur in patients which had PG before. Aggressive treatment with steroids before any surgery is important to avoid recurrence [19] although any surgery should be avoided.

The Postoperative Pyoderma Gangrenosum is a rare and tricky complication after surgery. Once diagnosed it is relatively easy to treat but the often delayed diagnose due to it's rarity can lead to severe complications depending on the area of surgical intervention. There have been several reports of the PSPG after breast reduction [20, 21, 22, 23], breast surgery [24, 25, 26], breast reconstruction [27], but none with such severe complications nor with the combination of an Acinetobacter baumanii infection.

2.2 Acinetobacter baumannii

The Acinetobacter is a source of infection in debilitated patients in the hospital it can occur in wounds, it can cause pneumonia and/or meningitis. It is a Gram-negative genus of bacteria which is non motile. All of the Acinetobacter species are oxidase-negative. The Acinetobacter species includes 17 officially named and 14 genomic unnamed species.

A routine Identification in a microbiological Laboratory is not easily possible and there is not a lot of knowledge about biology of acinetobacters at a species level. This might be because an identification of acinetobacters at species level is difficult. There are phenotypic species identification systems. A lot of genotypic methods have been explored and are now applied to find out more about the diversity in the species. For example high resolution fingerprinting with PCR [28]

They are divided and grouped into three main complexes:

- Acinetobacter calcoaceticus-baumannii complex: glucose-oxidising nonhemolytic
- Acinetobacter lwoffii: glucose-negative nonhemolytic
- Acinetobacter haemolyticus: hemolytic

The natural habitat of Acinetobacter is widely spread in nature. Acinetobacter is able to survive on moist and dry surfaces also in the hospital environment. A. baumannii for example can survive on the human skin or dry surfaces for weeks.

As mentioned before this is a critical factor and reason why it is a dangerous source of infection for debilitated and/or immunosuppressed patients.

To healthy individuals Acinetobacter genus can be seen as non-pathogenic. But several species can persist in hospital environments and cause sometimes life-threatening infections in debilitated patients. [29] The spectrum of antibiotic resistances of Acinetobacter and their survival capabilities make them a threat to hospitals as documented by recurring outbreaks. A horizontal gene transfer is possibly the reason for their pathogenic potential. This mechanism has so far only been proofed in Acinetobacter baylyi, a species that lives in the soil and has never been associated with infections. More information on this will possibly be available in the near future.

Most infections occur in immunocompromised individuals, and the strain A. baumannii is the second most commonly isolated nonfermenting bacteria in human specimens. A. baumannii can cause nosocomial pneumonia, it can cause especially late-onset ventilator associated pneumonia.

Since Acinetobacter is often seen in nosocomial infections it is especially common in intensive care units. It can cause various other infections as in our case including skin and wound infections, but also bacteremia, and meningitis are possible.

2.3 The V.A.C.-Instill® System

The V.A.C. Instill® combines the well known vacuum assisted closure system by K.C.I. with an irrigation technique which performs instillation followed by a period with no suction and then negative pressure time. V.A.C. Instill® Therapy™ System is used to manage infected wounds combined with the advantages of V.A.C.® Therapy. The infiltration lasts for an adjustable amount of time called the instillation time. Instillation times can be programmed (1 second to 2 minutes). The period of non suction is called the “Hold Time” and can be programmed as well.

Features:

- The Fluids can be instilled via the solution delivery tubing or a pad. Instillationtimes can be programmed (one second to two minutes)
- Uniform fluid distribution over the wound bed due to complete contact of the dressing with the infected area, fluid can perform its mode of action
- Desired hold time can be programmed to optimize dwell time (one second to one hour)
- During the vacuum phase, infectious materials and wound exudates can be removed
- Vacuum time can be programmed (five minutes to twelve hours)
- Cycle of Instillation, Hold and vacuum will repeat automatically

Solutions that can be used are:

- Topical cleansers / carriers
- Topical antibiotics
- Topical antifungals
- Topical antiseptics
- Topical anesthetics

The combination of the benefits of V.A.C.® Therapy with instillation therapy to help promote the healing process of the wound leads to new fields of application. Many acute, chronic and infected wounds can benefit from the automated delivery and drainage of solutions. As presented in this Case report The V.A.C.-Instill®-System has been one of many important factors to enable survival of the patient.

3 Case Report

This case presents a 45-year-old Caucasian female with post-surgical woundbreakdown (Figure 1) following breast reconstruction with a free transverse rectus abdominis myocutaneous (TRAM) flap. (Primary surgery performed externally.)

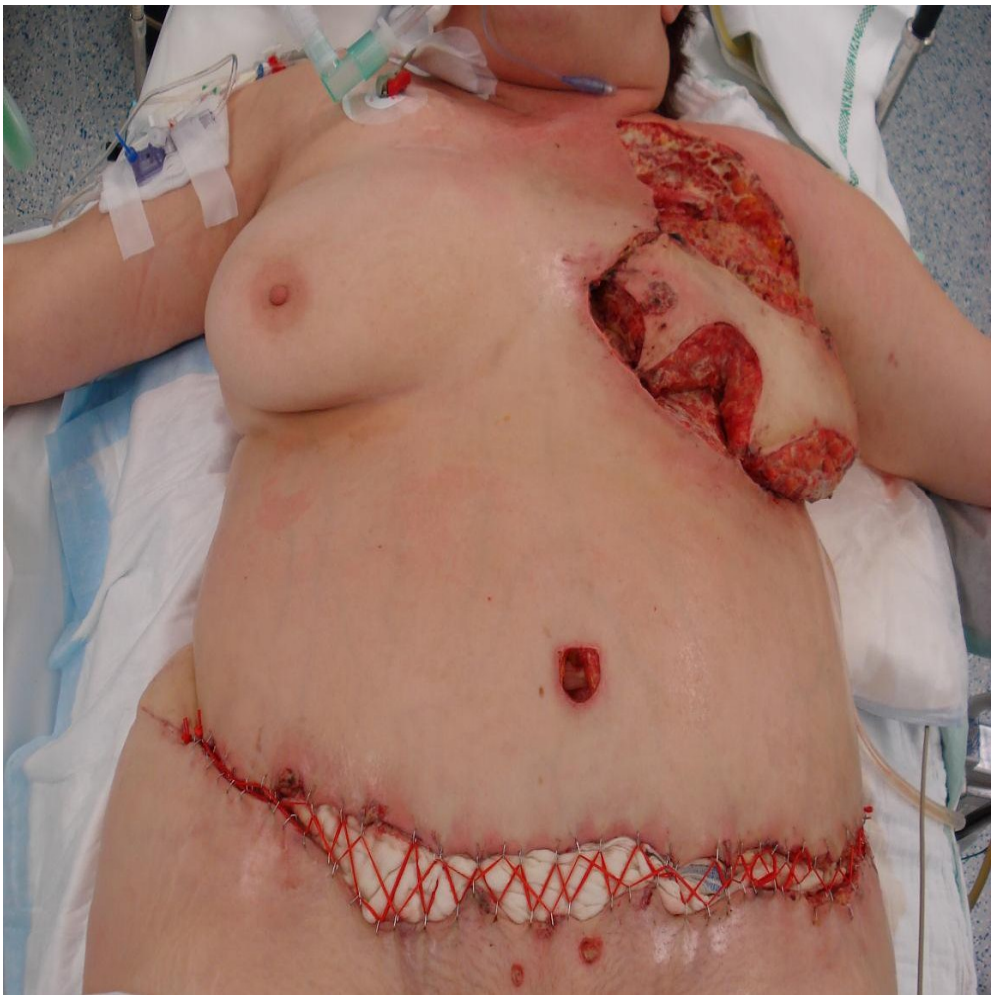

Figure 1

Repeated radical debridement led to dramatic wound deterioration, flap loss and a huge abdominal donor site defect (Figure 2, 3).

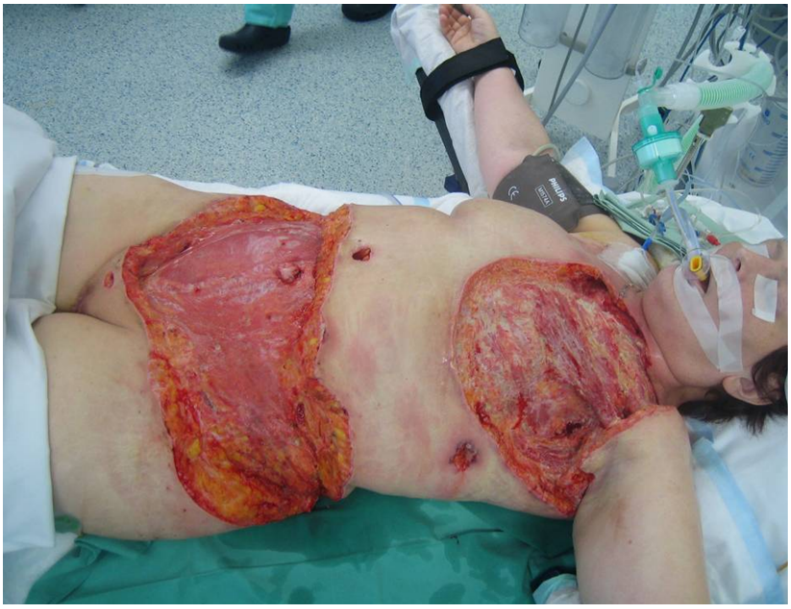

Figure 2

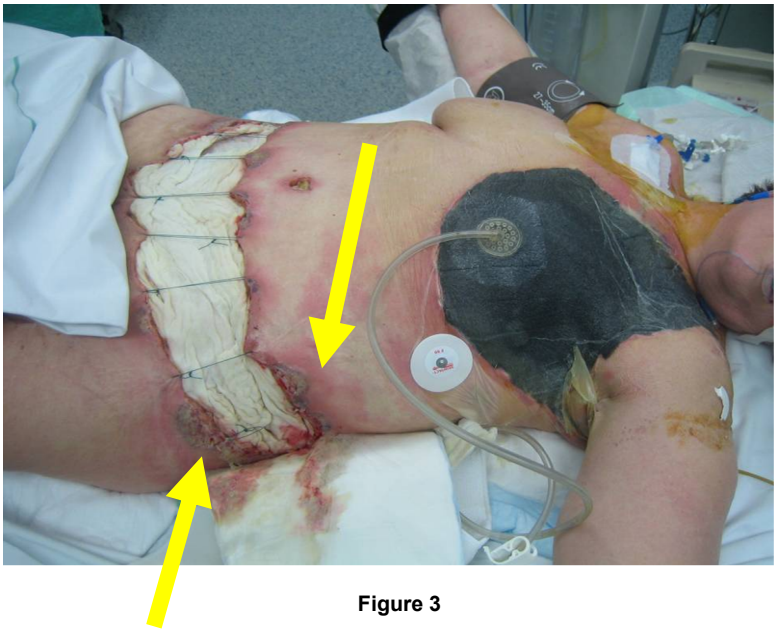

Figure 3

Wound margins showed purple discoloration (Figure 4, 5) and peripheral erythema suggesting pyoderma gangrenosum, which was confirmed histologically. Administration of systemic steroids, cyclosporin A and high dose immunoglobulins enabled disease control and successful skin grafting.

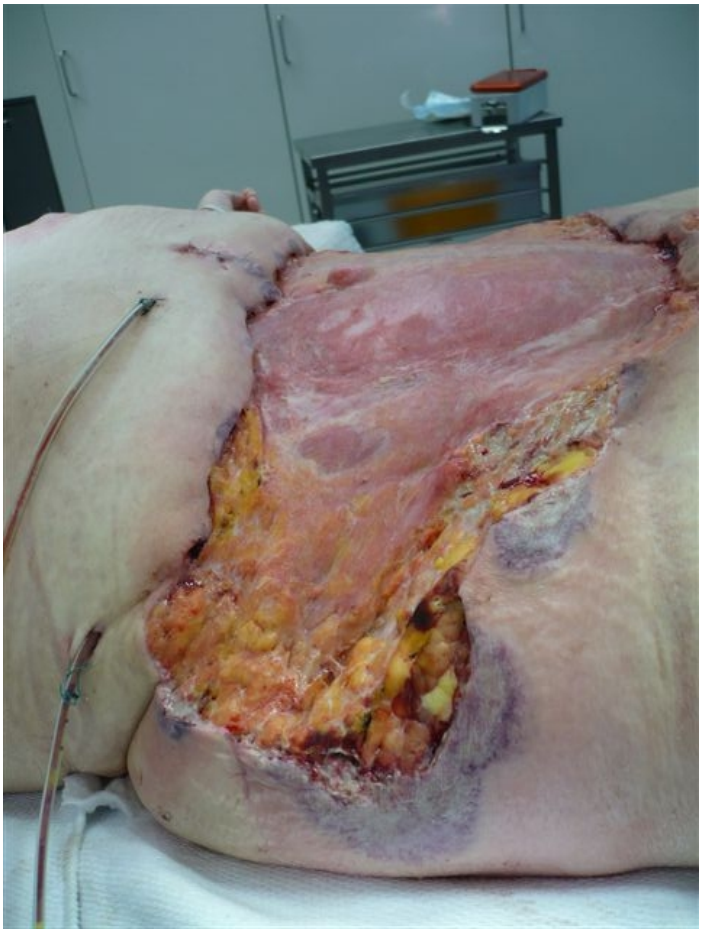

Figure 4

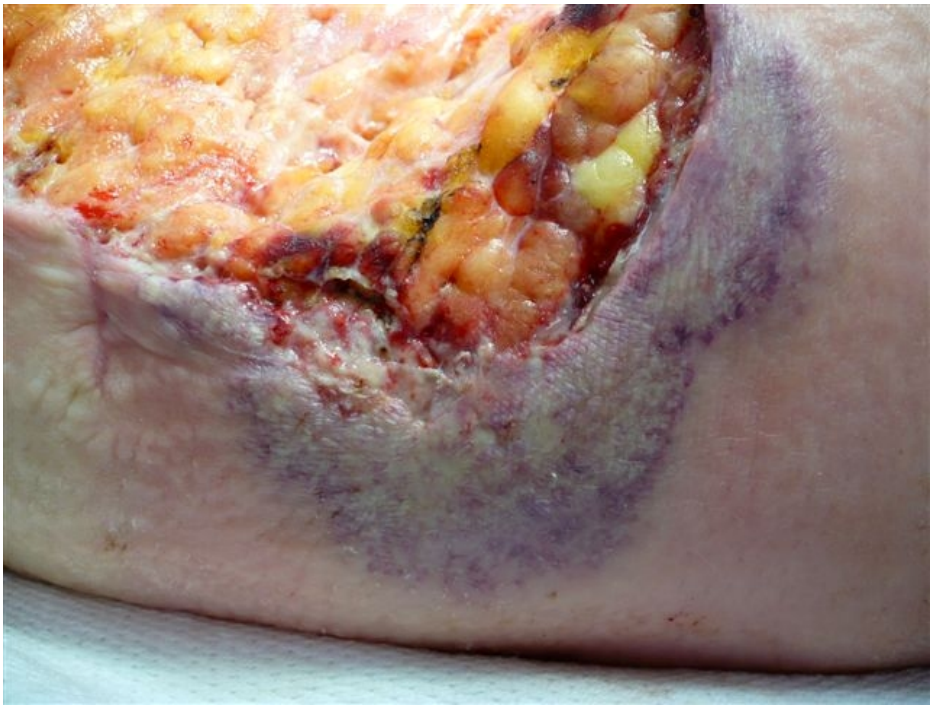

Figure 5

Two weeks later, the patient presented with partially exposed ribs and full-thickness chest wall infection. (Figure 6). This would lead to interdisciplinary cooperation with thoracic surgeons (Figure 7). A microbiologic analysis of the swab from the exposed ribs revealed an infection with Multi Drug Resistant Acinetobacter baumanii. Which complicated the patients situation even further.

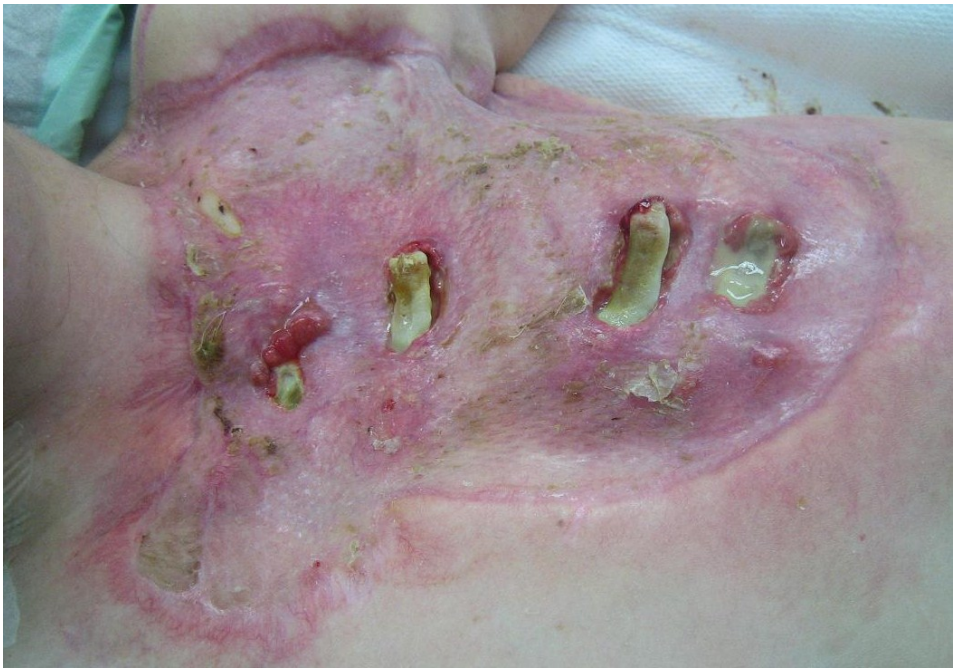

Figure 6

The diagnosed MDR *Acinetobacter baumannii* infection required chest wall resection and reconstruction with prolene polypropylene mesh and a free latissimus dorsi myocutaneous flap. (Figure 7,8,9) from the right side of the patient. This surgery was performed in cooperation with experts from the thoracic surgery department at the University Clinical Center Graz.

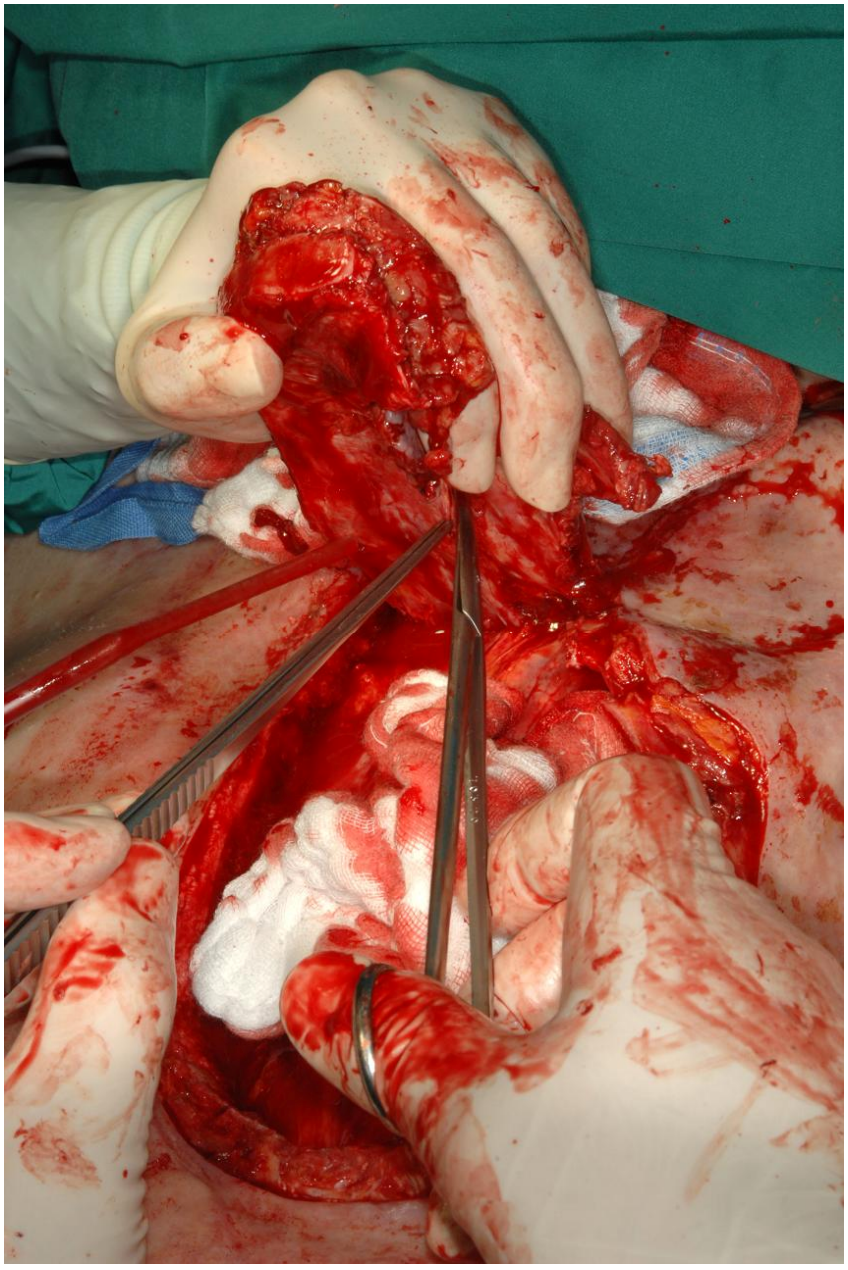

Figure 7

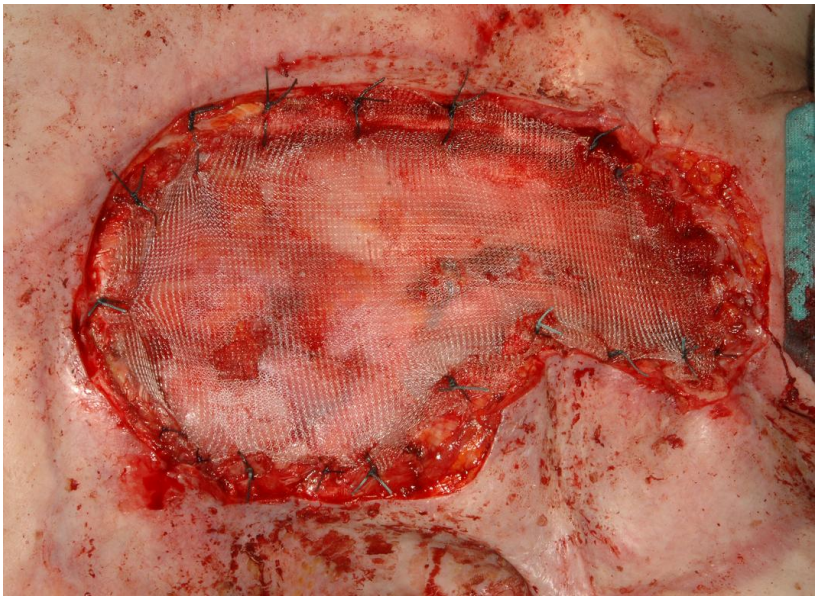

Figure 8

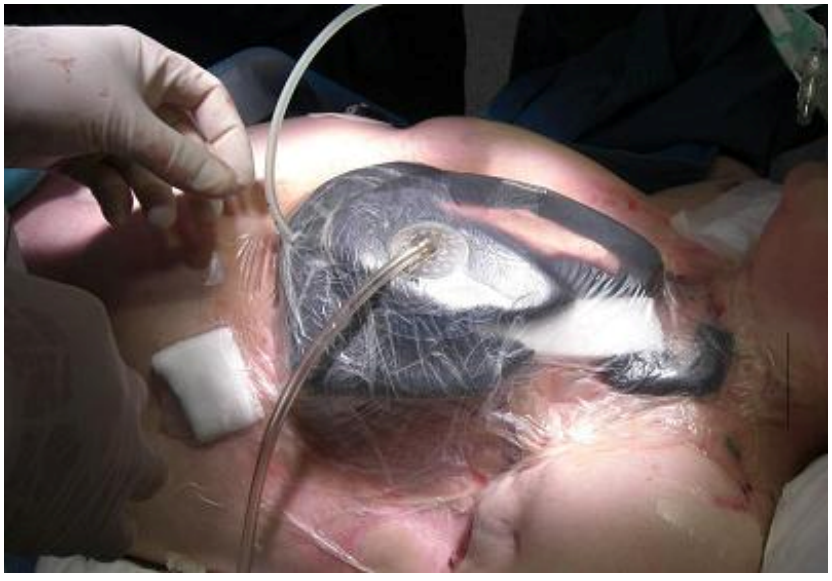

Figure 9

Distal muscle tip necrosis, with potential for recurrence of PG [4], required revision surgery, which revealed recurrent purulent epipleural and prolene mesh infection (Figure 10).

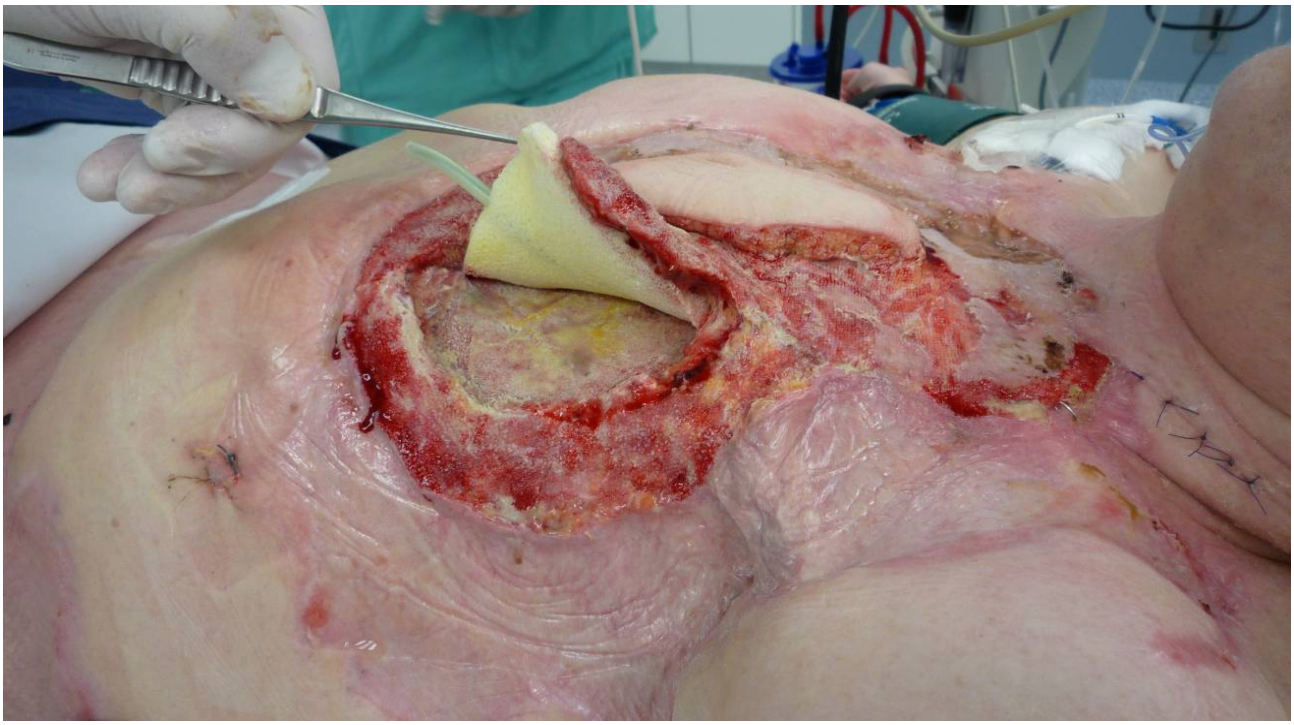

Figure 10

Serial debridements and a salvage procedure using the V.A.C. Instill® Therapy System (KCI Licensing Inc., San Antonio, TX,) for intermittent topical instillation of an antiseptic agent (polyhexanide) for three weeks provided infection control (Figure 11) and wound closure with a left abdominal wall visor flap.

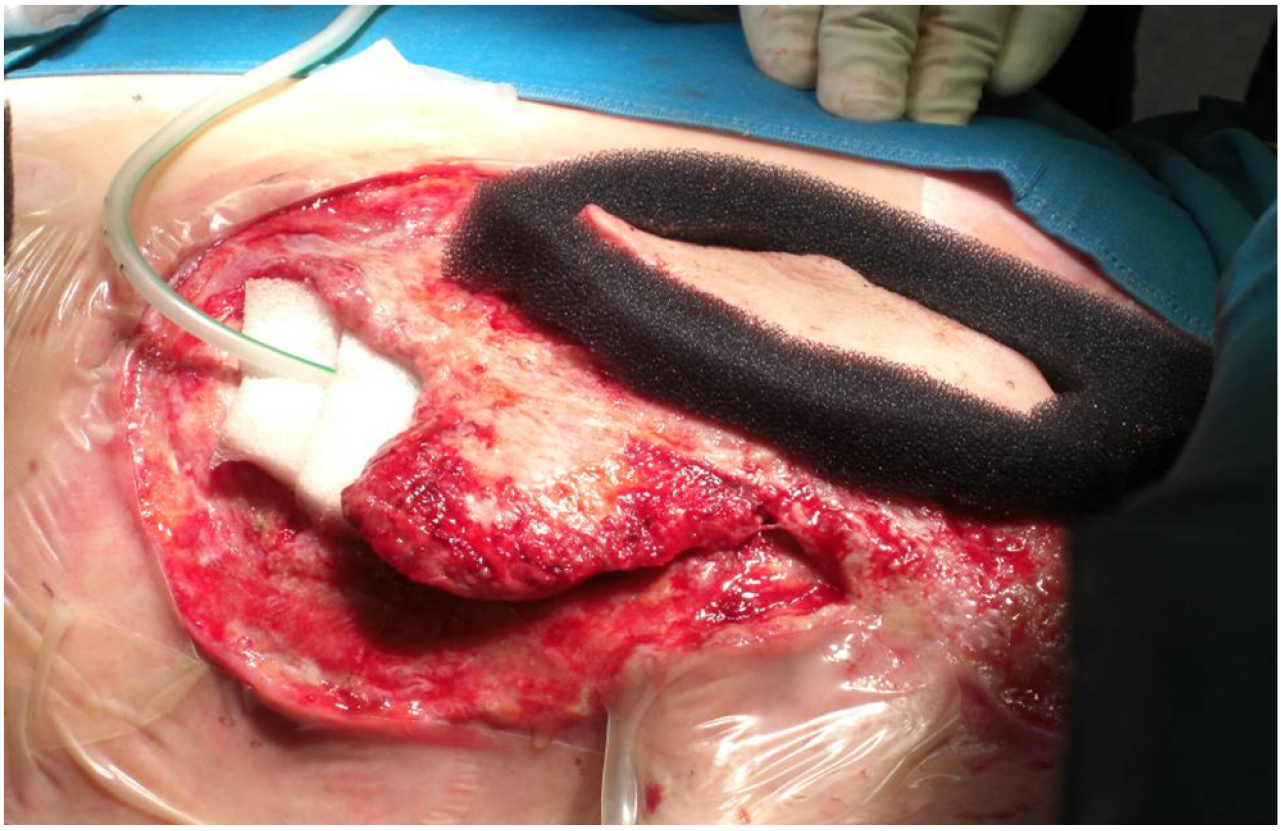

Figure 11

The flap donor site was closed by a split- thickness skin graft.

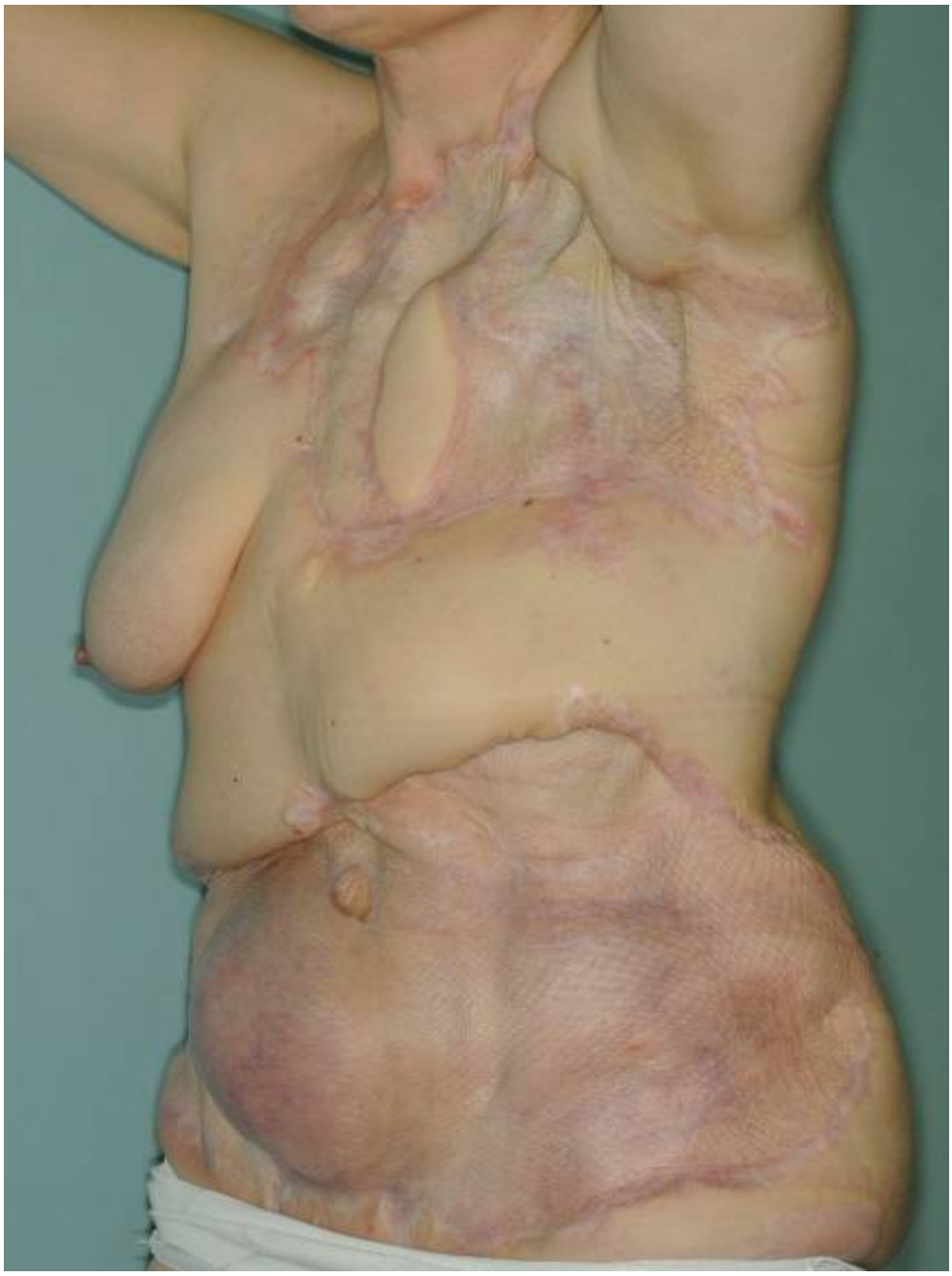

Figure 12

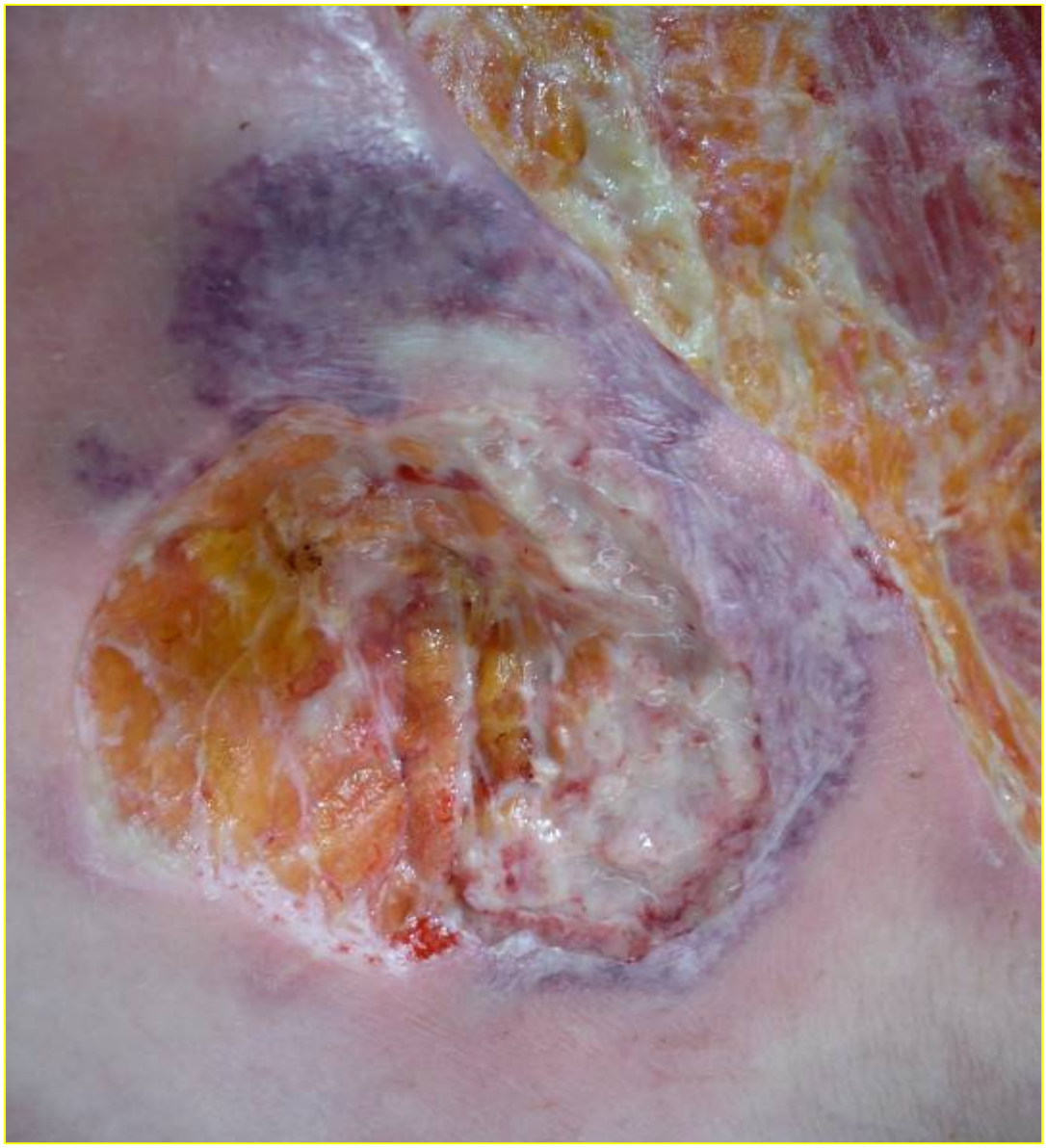

Figure 13

Figure 13 shows a close up of an ulcer in the abdominal area which presents the typical necrolytic ulceration with irregular borders. The wound margins show the already mentioned purple discoloration. There is also a halo of erythema and edema around the Wound.

4 Discussion

4.1 History and Discussion

After the first description by Brocq [30] in 1916, Brunsting [31] defined “pyoderma gangrenosum” as a new clinical entity in 1930. The exact etiology is still unknown. The association with systemic diseases, like inflammatory bowel disease, makes an immunological origin likely. Pathological features are inflammatory pustules and papules that rapidly enlarge to necrotic ulcers with purple, undermined edges. Quazzani described PSPG as a clinical entity after surgery [32]. A preceding surgical procedure as the initial triggering event for skin ulceration often goes unnoticed. Though major and minor criteria were proposed by W.P. Daniel Su in 2004 [18], most cases are misjudged as normal complications of wound healing. The surgeon’s reflex tendency to use the scalpel to treat wound breakdown, progressive infection and failure of antibiotics may result in further surgical procedures and dramatic deterioration.

Diagnostic criteria of classic, ulcerative pyoderma gangrenosum (PG):

Diagnosis requires both major criteria and at least two minor criteria.

Major criteria:

1. Rapid progression of a painful, b necrolytic cutaneous ulcer with an irregular, violaceous, and undermined border
2. Other causes of cutaneous ulceration have been excluded

Minor criteria:

1. History suggestive of pathergy or clinical finding of cribriform scarring
2. Systemic diseases associated with PG
3. Histopathologic findings (sterile dermal neutrophilia, ± mixed) inflammation, ± lymphocytic vasculitis)
4. Treatment response (rapid response to systemic steroid treatment) [18]

The diagnosis of PSPG is challenging and is almost never made in time. It remains a diagnosis of exclusion [18]. Primary sterile swabs can point toward PG if infection is suspected. Serial swabs may find different bacteria colonizing necrotic skin ulcers. Once diagnosed, immunosuppressive treatment can quickly arrest progression but thereafter can cause life threatening MDR infections.

Acinetobacter as mentioned above is a gram-negative bacterium and plays a significant role in nosocomial, mostly respiratory infections. Various mechanisms of antibiotic resistance have been recognized in these bacteria. Though skin grafting in a quiescent stage of disease was successful in our patient, small defects remained, leading to a secondary nosocomial chest wall infection. Sequestrating osteomyelitis of the ribs was achieved by a procedure requiring full-thickness thoracic wall, partial sternal and subtotal left clavicular resection and reconstruction with prolene mesh and free latissimus dorsi myocutaneous flap coverage. Except for a small distal portion, the flap survived. However, an additional surgical procedure revealed a major setback: an epipleural infection and recurrence under the viable flap involving the prolene mesh (Figure 10). Since it was not possible to create another free or pedicled flap (breast reconstruction had used up axillary donor vessels; the latissimus dorsi flap had exhausted the internal thoracic vessels, and both rectus flaps had already been used), our best option was debridement, partial mesh resection, antiseptic lavage with polyhexanide and the application of V.A.C.Instill® . (Figure 11). Multiple swabs from the thoracic wound produced positive cultures of MDR Acinetobacter baumannii. Colistin, the only effective antimicrobial agent, was given intravenously; serial dressing changes were performed every 2 days along with blunt and sharp debridements. Two weeks later, a “side-step” procedure in the form of a left lateral

thoracic visor flap adjacent and caudal to the defect was done following final debridement. The flap donor site was closed by a skin graft. Hematoma removal one week later was finally followed by complete healing. Infection markers decreased to normal in the following weeks. Administration of prednisolone 100mg, initially intravenously and later orally, cyclosporin A 200mg daily and one course of intravenous immunoglobulins 2g/kg stabilised the disease, allowing immunosuppressive drugs to be tapered off slowly over 6 months. There were no further complications. Normal wound healing followed with stable skin closure (Figure 12) and no severe functional impairment.

5 Conclusion

5.1 Conclusion

The PSPG can affect any surgical wound. If delayed wound healing is present, and/or dramatic deterioration is observed, especially following surgical debridement, diagnostic criteria should be considered. While PG is uncommon, surgeons must be aware of its existence.

Though dramatic resolution is usually observed after initiation of high-dose systemic steroid treatment, it may pose serious problems by interfering with wound healing, and especially by fostering MDR life-threatening nosocomial infection. As in this case The multi resistant Acinetobcter baumannii infection of the thoracic wall, leading to a life threatening complication.

The V.A.C.-Instil® -System promotes wound healing via a three-phase working cycle , including: automated topical solution delivery, hold period, followed by removal of infectious materials. It can be a useful tool to control infection and may be beneficial in creating a benefical wound healing environment in traumatic and chronic wounds. As mentioned above in this case it has been one of the main important factors to enable survival of the patient

6 Curriculum Vitae

Personal Data

DOB: 9/29/1979

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School

2001	External Graduation BG, BRG Wiku. RG for Employed Lichtenfellsgasse Graz
1990 – 1995	Highschool Lichtenfellsgasse Graz
1986 – 1990	Elementary School Nibelungengasse Graz

Studdies

10/2001 – 10/2003	Business at Karl Franzens University Graz
10/2003 – now	Medicine at Medical University Graz
9/2005	Finished 1. Section
2/2010	Finished 2. Section

Clerkship

Dermatology	University Clinical Center Graz (3 Weeks – 05)
Surgery Trauma	Hospital Schladming (5 Weeks – 07)
General Surgery	Hospital Schladming (2 Weeks – 08)
Plastic Surgery	University Clinical Center Graz (6 Weeks – 09)
Surgery Trauma	University Clinical Hospital Worms/Germany (5 weeks –10)
Urology	University Clinical Center Mainz / Germany (3 weeks –10)

Medical Association

2009	Angeborene und erworbene Deformitäten in der Kopf- und Hals-region im Kindes- und Jugendalter (Symposium)
2009	Diploma Woundmanagment

University Clinical Center Graz /Johannes Gutenberg University Mainz/ Karl Franzens University Graz

2003	Business English (Karl Franzens University Graz)
2008	Urological Ultrasound elective (Johannes Gutenberg University Mainz)
2008	Hand surgery elective (Johannes Gutenberg University Mainz)
2008	Plastic surgery elective (Johannes Gutenberg University Mainz)
2004	Intubation (Medical University Graz)

International Expiriences

6/2010	„Emergency Medicine Ultrasound“ Rotation an der University of California/Irvine im Rahmen des Praktischen Studienjahres
10/2008 – 7/2009	1 Year exchange studies programe Erasmus Mainz/Germany

Scientific Expirience

2008 – now	Scientific research and clerkship at the department of plastic surgery Graz u Univ. Prof. Dr. Stephan Spendel, Univ. Prof. Dr Michael Schintler
2009	Supplement Woundmanagement

M.V. Schintler; E.-Ch. Prandl; G. Kreuzwirt; M.R. Grohmann; S. Spendel; E. Scharnagl. *The impact of V.A.C. Instill® in severe soft tissue infections and necrotizing fasciitis*. Infection 37 · 2009 · Supplement I © Urban & Vogel

Languages

English (fluent in word and speech)

French

German

Computer knowlege

Microsoft Office, Endnote, Macintosh und Microsoft

7 Literature

1. Brunsting LA, Goeckerman WH, OLeary PA.Pyoderma gangrenosum: clinical and experimental observations in five cases occuring in adults. *EArch Dermatol.* 1930; 22: 655-680.

2. Powell FC, Schroeter AL, Su WPD, Perry HO. Pyoderma gangrenosum: a review of 86 patients. *QJMed* 1985; 55 : 173–186.

3. Powell FC, Su WPD, Perry HO. Pyoderma Gangrenosum: Classification and Management. *J Am Acad Dermatol* 1996; 34: 395–409.

4. Crowson AN, Magro C, Mihm MC Jr. Pyoderma gangrenosum: a review. *Journal of Cutan Pathology.* 2003; 30: 97-107.

5. Powell FC, Schroeter AL, Su WPD et al. Pyoderma gangrenosum and monoclonal gammopathy. *Arch Dermatol.* 1983; 119: 468±72.

6. Stein Carsuzza F, Pierre C, Dubegny M. Pyoderma gangrenosum et gammapathie *B* JgA: association 3 une gastrite atrophique. *Ann Dermafol Venerol*. 1989; 116: 707.

7. Grimnstein AJ, Janowitz HD, Sachar DB. The extraintestinal complications of Crohn's disease and ulcerative colitis: a study of 700 patients. *Medicine* 1976; 55: 401.

8. Johnson ML, Wilson HTH. Skin lesions in ulcerative colitis. *Gut* 1969; 10: 255.

9. Moschella SL. Pyoderma gangrenosum. Arch Dermatol 1967;95:121.

10. McCallum DI, Kinmont PDC. Dermatological manifestations of Crohn's disease. *Br .I Dermatol* 1968; 80: 1

11. Byrne JP, Newitt M, Snmmerly R. Pyoderma gangrenosum associated with active chronic hepatitis. *Arch Dermatol* 1976;112: 1297.

12. Holt PJA, Davies MG, Saunders KC, et al. Pyoderma gangrenosum: clinical and laboratory findings in 15 patients with special reference to polyarthritis. *Medicine* 1980; 59: 114.

13. Maldonado N, Torrea VM, MCndez-Cashion D, et al. Pyoderma gangrenosum treated with 6-mercaptopurine and followed by acute leukemia. *J Pediatr* 1968; 72: 409-14.

14. Ho KK, Otridge BW, Vandenberg E, Powell FC. Pyoderma gangrenosum, polycythemia rubra vera, and the development of leukemia. *J Am Acud Dermatol* 1992; 27(5 PI 2): 804-8.

15. Horton JJ, Trounce JR, Mac Donald DM. Bullous pyoderma gangrenosum and multiple myeloma. *Br. J. Dematol* 1984; 111(2): 227-30.

16. A. Jain, J. Nanchahal and C. Bunker Pyoderma gangrenosum occurring in a lower limb fasciocutaneous flap – a lesson to learn *British Journal of Plastic Surgery* 2000; 53: 437-447.

17. A.L.Mahajan, N Ajmal Could your case of necrotising fascitis be Pyoderma gangrenosum? *British Journal of Plastic Surgery* 2005; 58: 409–412.

18. W. P. Daniel Su, MD, Mark D. P. Davis, MD, Roger H. Weenig, MD, Frank C. Powell, FRCPI , and Harold O. Perry, MD Pyoderma gangrenosum:

clinicopathologic correlation and proposed diagnostic criteria *Int. J. Dermatol*. 2004; 43: 790 –800.

19. Beryl De Souza, Richard Millard, Stewart Flemming Pyoderma gangrenosum: beware, it does recur

Br. J. PLast Surg. 2001 54:(1): 82

20. C Karoly Gulyas, M.D., and Frank W. Kimble, M. Med. (Chir), FRCS, FCS, (SA), FRACS Atypical Pyoderma Gangrenosum After Breast Reduction Aesth. Plast. Surg. 27: 328–331, 2003.

21. Ben Horner, Naguib El-Muttardi, Derek Mercer Pyoderma gangrenosum complicating bilateral breast reduction The British Association of Plastic Surgeons 2004; 57: 679–681.

22. Clugston PA, Thompson RP, Schlappner OLA. Pyoderma gangrenosum after reduction mammoplasty. Can J Surg 1991; 34:157–61.

23. Grau Salvat C, Miquel FJ, Pont V, Aliaga A. Pyoderma gangrenosum: unusual complication following mammoplasty reduction. *Int J Dermatol* 1998; 37: 794–796.

24. H Schöfer,* S Baur Successful treatment of postoperative pyoderma gangrenosum with cyclosporine *JEADV* 2002; 16: 148–151.

25. Davis MD, Alexander JL, Prawer SE Pyoderma gangrenosum of the breast precipitated by breast surgery *Journal of the American Academy of Dermatology* 2006 Aug; 55(2): 317-20.

26. V. S. Gudi, C. Julian and P. W. Bowers Pyoderma gangrenosum complicating bilateral mammaplasty *British Journal of Plastic Surgery* 2000; 53.

27. D. MacKenzie, N. Moiemen and J. D. Frame Pyoderma gangrenosum following breast reconstruction *British Journal of Plastic Surgery* 2000; 53.

28. Dijkshoorn L (2008). The Diversity of the Genus Acinetobacter. Acinetobacter Molecular Biology (Gerischer U, ed.). Caister Academic Press. ISBN 978-1-904455-20-2.

29. Gerischer U (editor). (2008). Acinetobacter Molecular Biology (1st ed.). Caister Academic Press. ISBN 978-1-904455-20-2.

30. Brocq L. A new contribution to the study of geometric phagedism. Ann Dermatol Syphil (Paris). 1916; 9: 1-39.

31. Brunsting LA, Goeckerman WH, O´Leary PA. Pyderma (echtyma) gangrenosum. Clinical and experimental observatons in fie cases occurring in adults. *Arch Derm Syph*. 1930; 22: 655-680.

32. Ouazzani A, Berthe JV, de Fontaine S. Post-surgical Pyoderma Gangrenosum: a Clinical Entity. *Acta chir. belg*. 2007; 107: 424-428

33. Weenig RH, Davis MD, Dal PR. Skin Ulcers misdiagnosed as pyoderma gangrenosum. *N Engl J Med* 2002; 347: 1412-1418