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I. Introduction

The occurrence of a painful, inflammatory swelling in a lower limb is consistent with several diagnoses, such as deep vein thrombosis, compartment syndrome, muscle rupture, soft tissue infection, hemorrhagic or neoplastic processes, myositis, pyomyositis, etc. In the diabetic patient, an unusual diagnosis should be added to this list, i.e. so-called diabetic muscle infarction (DMI). Skeletal muscle infarction is a rare condition occurring specifically in the diabetic patient. Accurate management of DMI depends mainly on the physician's awareness of this condition, which can avoid unnecessary or potentially hazardous investigations and delayed or inadequate treatment[1,2,3,4].

A delay in diagnosis may result in compartment syndrome, sepsis, and death. The long-term sequelae of pyomyositis include osteomyelitis of adjacent bones, muscle scarring, prolonged hospitalization, and significant functional impairment [5,6].

Diabetic wounds are unlike typical wounds in that they are slower to heal, making treatment with conventional topical medications an uphill process. Among several different alternative therapies, honey is an effective choice because it provides comparatively rapid wound healing. Although honey has been used as an alternative medicine for wound healing since ancient times, the application of honey to diabetic wounds has only recently been revived. Because honey has some unique natural features as a wound healer, it works even more effectively on diabetic wounds than on normal wounds. In addition, honey is known as an "all in one" remedy for diabetic wound healing because it can combat many microorganisms that are involved in the wound process and because it possesses antioxidant activity and controls inflammation. In this research the potential role of honey's antibacterial activity on diabetic wounds based on the most recent studies is described. Additionally, ways in which honey can be used as a safer, faster, and effective healing agent for diabetic wounds in comparison with other synthetic medications in terms of microbial resistance and treatment costs are also described to support its traditional claims[7,8,9,10].

Honey as an adjuvant for acceleration of wound healing is widely accepted in Falk medicine and the use of wound salves containing honey was mentioned in Egyptian papyrus dating from before 2000 BC. Honey was alleged to possess a wide variety of activities due to its physical properties, antibacterial power, epithelial regeneration, antioxidants it contains, and lastly the power to release cytokines and interleukins from their stores. Application of honey to severely infected cutaneous wounds is capable of clearing infection from the wound and improving tissue healing owing to physicochemical properties, stimulation of the immune response and antibacterial actions [11].

We make our study about the management of this kind of diabetic aggressive infectionin the deep muscular infections with the use of saturated honey packs as a local treatment in the deep diabetic infections pyomyositis. photo 1

2.1 Patients

II. Patients, Materials and Methods

The present study has been conducted on 20 diabetic patients presented with lower extremity purulent deep infections intermuscular problems in our department during the periodstarted from January 2014 to December 2019. All of our patients were mixed male and female their ages ranged between 40- 65 years. All patients having diabetes not less than 10 years. They were evaluated clinically. In the laboratory we choose C-

reactive protein (CRP) as an acute-phase protein that serves as an early marker for inflammation and infection and for follow up healing [12]. We use plain radiography for the initial screening. Also aCT scan provides better delineation of muscle than X-rays and can identify a muscle abscess(photo 2).But it may fail to demonstrate inflammatory changes in earlier stages(photo 3)[13]. The aim is to assess the present status and to plan for the future management aiming at decreasing morbidity and mortality with decreasing patient disability. The patients were onegroup.Our study of pyomyositis has been divided into three clinical stages: theinvasive stage, the purulent stage, and the late stage [14].

1-Invasive stage.

The invasive stage is noted by insidious onset of diffuse muscle pain or cramping and a "woody," indurated texture of the involved area. During the invasive stage 2 patients presented to us, the pathogen enters the muscle via local blood vessels or lymphatic vessels. Fever, leukocytosis, and other constitutional symptoms are variable, and no defined collection of pus in the muscle is present. Only 2 of patients initially present for medical care during this stage [15]. photo 4, photo5A 5B

2-Purulent stage.

The purulent stage occurs 10 to 21 days after the onset of symptoms and is characterized by localized abscess formation. Most patients are first seen during this stage because of the presence of fever, chills, progressive pain, and enlargement of the area over a 2- to 3-week period. The skin overlying the affected muscle is intact but erythematous. Leukocytosis of more than 10,000 cells/mm3 may be observed. 17 of patients initially present for medical care at this stage because of the increased severity of symptoms, photo 6 A,B,C

3- Late stage.

In our study one patient with pyomyositis initially present to us in the late stage with high fever and systemic toxicity. Involvement of the entire muscle group occurs and is marked by marked tenderness and fluctuance. manifestations of systemic infection, such as septic shock and even death[15-17].

2.2 Materials and Methods

All patientsare evaluated on admission for the risk factors as age, smoking, onset and duration of diabetics, hypertension, coronary artery disease (CAD) and renal impairment. Patients presented with deep intermuscular infection. problems with acute or chronic peripheral ischemia were excluded from the study.

2.2.1 Management Program and Guidelines

All patients were subjected to a protocol of management for control of hyperglycemia and infection and local wound care and dressing.

2.2.2 Control of Infection

Materials used for microbiological evaluation of the infection were culture sensitivity swap and sent to the Microbiology Unit. All specimens were examined as gram-stained smears and cultured aerobically on blood agar and MacConkey agar plates and anaerobically on blood agar and incubator for 24 hours.

The isolated microorganisms were identified and the in vitro antimicrobial susceptibility of the bacteria isolated was determined by the disk diffusion. Empirical parenteral broad-spectrum antibiotics against gram-positive, gram-negative and anaerobic organisms were used initially (carbapenem antibiotic). Meropenem 1 gram intra venous every 8 hoursand metronidazole 500mg intra venous every 12hour andKanamycin Parenteral: 15 mg per kg per day IM or IV in divided doses every 8 hours.

Modification to a more specific antibiotic when initial culture and sensitivity results became available was mandatory. Infection was considered adequately controlled when cellulitis, lymphangitis and edema had resolved and wounds were free from purulence[18].

2.2.3 Debridement and Drainage

After Plain radiographic films of the area thigh or all lower limb or pelvic for gluteal infection were obtained to detect the presence of foreign bodies, soft tissue gas, bone changes suggestive of osteomyelitis. Patients with undrained pus or extensive necrosis underwent incision and drainage, debridement needed. All extensive debridement or procedures in sensate patients were performed in the operating room. Wide longitudinalincisions were placed in such a manner as to promote dependent drainage and debridement of the necrotic tissue and opening of the spaces and intermuscular edematous muscles according to the site of the infection. Deep packing of the wound with soaked packs of honey with plenty amount of honey was inserted intermuscular.Photo 7, photo 8

2.2.4 Dressing

Once infections had been adequately drained, attentive post-operative care was important in minimizing further tissue loss and achieving limb salvage. All wounds were examined daily 2-3 times and follow-up bedside sharp debridement was performed as needed to remove residual infected or necrotic tissue. Always start with clean hands, applicators and sterile gauze.

- Apply the honey to a dressing first, honey-impregnated dressings, in this type of deep wounds the honey should fill the wound bed before a dressing is applied.
- Place a clean, dry dressing over the honey. This can be sterile gauze pads or an adhesive bandage. An <u>occlusive dressing</u> is best over honey because it keeps the honey from seeping out.
- Replace the dressing when drainage from the wound saturates the dressing. As honey starts to heal the wound, the dressing changes will likely be less frequent.
- Wash your hands after dressing the wound.

Apply honey 2 to 3 times daily. Nevertheless, the required dosage of honey on the wound depends on the amount of exudates present; the beneficial effects of honey will be reduced if honey is diluted by a large amount of exudates. On the other hand, deep wounds require larger amounts of honey to exert antibacterial activity effectively. Honey dressing should be immediately applied on the wound for better outcome as well as to reduce the risk of microbial contamination in honey. The severity of the condition of the wound and the depth of the muscles affected determines the frequency of dressing i.e. in discharging wounds the dressing was done 2-3 times per day, while in clean or granulating wounds; it was done once/day or even every other day in order not to disturb the granulation tissue.photo 9

2.2.5 Follow-Up

Status of the deep infection on discharge from the hospital determines post-hospitalization care. In general, those patients discharged from the hospital with partially healed wounds were continued on oral antibiotic until healing was complete.

All patients discharged were monitored frequently (approximately once weekly) until full healing Occurred. Additional visits every month continued for 6 months. Wound siteexamination for the previous lesion or any new lesion was thoroughly searched for. Photo 10

2.2.6 End Points

The primary end point of the study was stop of infection discharge of pus and start of healthy granulation. The secondary end points were time of discharge from hospital.Charteris of discharge table

1	TEMP	37c
2	CBC	600-400
3	CRP	90-30
4	Wound	Signs of healing need dressing oncedaily

2.2.7 Statistical analysis

The statistical tests were run on a compatible personal computer using the Statistical Package for Social Scientists (SPSS) for windows [15]. Chi-square distribution was used for studying the frequencies of recurrence, pain, hospital stay and postoperative complications. The values were expressed as means \pm standard errors of deviation. The mean values of the groups were compared by one-way analysis of variance (ANOVA) and paired comparisons of the groups were done using the paired student *t* test. P < 0.05 was considered significant.

Pyomyositis usually involves the large muscle groups of the pelvic girdle and lower extremities, with the quadriceps muscles most commonly affected [5]. S. aureus is the usual pathogen, but rarer infectious agents include Streptococcus pyogenes, Streptococcuspneumoniae, Escherichia coli, Mycobacterium avium, and gramnegative bacteria [5].

III. Results

There are no significant difference in the patients of the group as regard to their demographic data including age, sex, body mass index (BMI), duration of diabetes and smoking as seen in table 1.

Group	Age Mean ±SD	Sex		BMI Mean ±SD	Diabetes Mean ±SD	Smoking	
		Male	Female	DMI Mean ±5D	Diabetes Mean ±5D	Yes	No
А		16	4	26.8 ±2.68	12.3 ±5.74	16	4

The clinical presentations of our patients was shown in table 2.

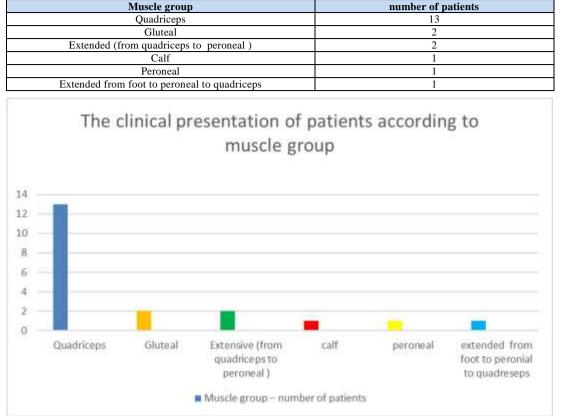


Table 2. showing the clinical presentation of patients according to the muscle group.

Table 3The causes of deep muscular diabetic infection

	The second se		
	Trauma	Injection site	Foot Brik
Patients	14	5	1
Percent	70 %	25%	5%

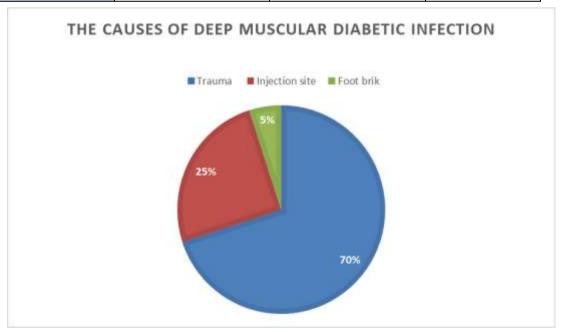
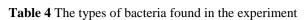


Table 4 The types of bacteria found in the experiment				
Bacteria type	Number of cases			
staphylococcus aureus,	10			
streptococcus pyogenes	2			
haemophilus influenza	1			
E-coli	1			
Klebsiella	1			
Acinetobacterbarmonni	1			
mixed growth	4			



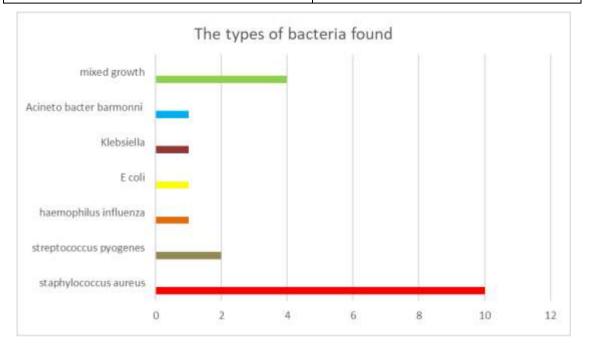
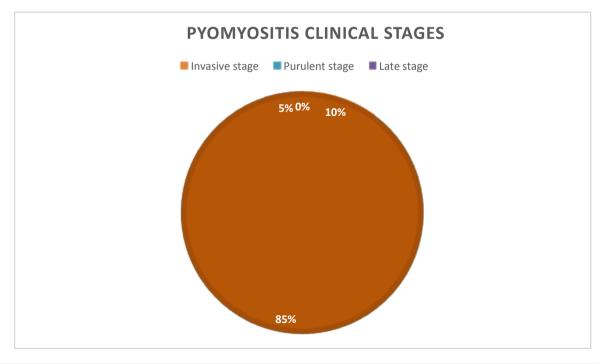


Table 5Pyomyositishas been divided into three clinical stages according to their presentation to us.

Pyomyositis clinical stages	Number of patients
Invasive stage	2
Purulent stage,	17
Late stage	1



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		Umber of patient Day 1	Day 7	Day 10	Day 14	Day 21
Temperature	>38 C	20	1			
	37.5 C<		17	2	1	
	37 C		2	16	1	1
PatientsHospitalized		20	18	2	1	0
Patients Discharged		0	2	16	1	1

Table 6 Number of patients according temperature and time

Table 7Number of patients according the white blood count and time

		Day 1	Day 7	Day 10	Day 14	Day 21
WBC	>25000	4				
	1900-25000	16	18	2	1	
	6000-4000or less	0	2	16	1	1
Patients Hospitalized		20	18	2	1	0
Patients Discharged		0	2	16	1	1

Table 8Patient number according C reactive protein

Table of attent number according e reactive protein						
	Day 1	Day 7	Day 8-10	Day 14	Day 21	
Invasive stage C- Reactive Protein	190mg/l	30-90 mg/l		-	-	
Patients Hospitalized	2	0	0	0	0	
Patients Discharged	0	2	0	0	0	
	0	0	0		0	
Purulent stage	210-300 mg/l	100-150mg/l	90-30 mg/l	90-30 mg/l	-	
Patients Hospitalized	17	17	0	0	0	
Patients Discharged	0	0	16	1	0	
Late stage	350mg/l	280 mg/l	240 mg/l	180 mg/l	90-30 mg/l	
Patients Hospitalized	1	1	1	1	0	
Patients Discharged	0	0	0	0	1	

Table 10The primary endpoint according to the patient number

Tuble 10 The primary endpoint decording to the patient number					
	Day 0 - 7	Day 8 - 10	Day 11 - 14	Day 15 - 21	
Patients	16	1	2	1	

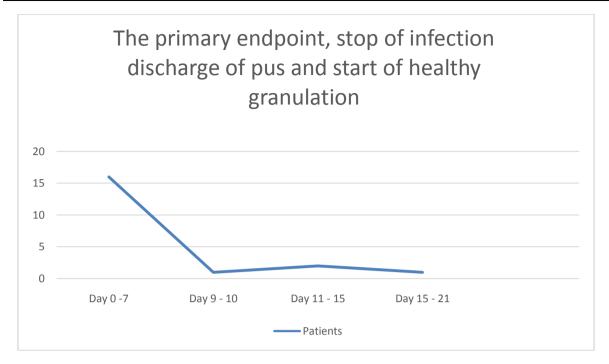


 Table 11
 The secondary end points were time of discharge from hospital when level of c reactive protein less

	Day 0-7	Day 8-10	Day 11-14	Day 15—21
Level of C-Reactive Protein	30-90 mg/l	30-90 mg/l	30-90 mg/l	30-90 mg/l
Patients	2	16	1	1

IV. Discussion

Pyomyositis (also known as tropical myositis, temperate myositis, pyogenic myositis, suppurative myositis, myositis, and epidemic abscess) is a primary infection of skeletal muscle and often associated with abscess formation. Intermuscular abscesses, abscesses extending into muscles from adjoining tissues such as bone or subcutaneous tissues, and those secondary to previous septicemia are not classified as pyomyositis Because of these differences, tropical and temperate pyomyositis were considered separate entities, but this distinction is more or less superficial, and therefore suggestions were made to rename this entity more appropriately as pyomyositis (which are used in this research), infectious myositis, or spontaneous bacterial myositis.

PROGNOSIS Heightened awareness, newer diagnostic modalities, and effective chemotherapeutic agents have considerably reduced the mortality associated with pyomyositis. The fatality rate still varies from as low as 0.5% to as high as 10%. Patients who recover even from severe disease have surprisingly little or no dysfunction in the affected part. Honey has been used as a debriding agent since ancient times. Its debriding properties have been rediscovered in more recent times, with various case reports published in the latter decades of the 20th century describing its effectiveness in cleaning up wounds. More recently its effectiveness has been compared with that of modern debriding agents, and honey has been found to work more rapidly than all except larval therapy [19]. A similar finding has been reported in an animal model, where adjacent experimental wounds were kept clean with honey-soaked gauze but formed thick dense scabs where treated with saline-soaked gauze. The mechanism of action of honey is as yet unknown, but appears to be by way of stimulating autolytic debridement.

Additional advantages using honey rather than other moist debridement are that its antibacterial action prevents bacterial growth from being encouraged, and its osmolarity prevents maceration of peri wound skin [20,21,23,24,25,26,27].

In our study I decided to use the honey as local fully soaked honey pack dressing as factor improving the outcome and fast the healing and reduce the mortality and economically low cost also any type of bur honey is used with no specification . our patient distribution male was 16 female4,BMI Mean 26.8+-2.68 diabetes Mean+- SD 12.3+-5.74

Where sixteensmoker'sANDnon-smoker is four.

pyomyositis usually involves the large muscle groups of the pelvic girdle and lower extremities, with the quadriceps muscles most commonly affected (28). In our study the most commonly affected group of muscles was the quadriceps in13 patient, the most extended infectionwas female 45 years old extended sever infection from the foot extensor aspect the leg and the thigh.PHOTO 10 A B C ,11,12

The causative usual pathogen organism in anther study's was S. aureus, but rarer infectious agents include Streptococcus pyogenes, Streptococcus pneumoniae, Escherichia coli, Mycobacterium avium, and gram-negative bacteria are reported (29), 30, In our studystaphylococcus aureus is the commonest bacteria found it was present in 10 out of 20 patients.

Mixed growth were 4 patients, and 2 patients werestreptococcus.

The initial invasive stage begins with cramping and aches and progressive pain in the affected area associated with a low-grade fever. It may be 1-2 weeks before the correct diagnosis is made. By stage 2, muscle abscesses have formed and local and systemic manifestations are present. The affected area becomes fluctuant and tender, and the overlying skin is mildly erythematous. Needle aspiration yields purulent material. If pyomyositis is not treated in the second stage, it progresses to stage 3, which his characterized by signs of toxicity and septic shock.

In our studyHoney has been used in wound therapy for several decades. Recent studies have shown that honey has an inhibitory effect on approximately 60 bacteria species and acts against aerobes and anaerobes (15). In addition, it has antifungal action against Aspergillus species, yeast and dermatophytes (31,32,33,34). The advantages of honey include a high osmotic effect on wounds, which inhibits microbial growth, allowing creation of a perfect osmotic gradient that would mop up exudate from the wound, enabling faster healing. In addition, the sugar content including fructose (40%), glucose (30%) and 5% sucrose provides sufficient substrate for microorganisms and therefore prevents them from obtaining substrates directly from the wound site, effectively decreasing formation of bacterial biofilms (35). Honey contains an enzyme, Inhibin, that yields small quantities of hydrogen peroxide. The hydrogen peroxide concentration in honey is 1000 times less than in the 3% solution commonly used as an antiseptic (36). Honey's low pH inhibits the growth of bacteria, and its components provide an antioxidant effect (37, 38). Previous studies have associated honey with increased phagocytic and lymphocytic activity on a wound (39,40,41). The honey soaked gauzethat had been used use in our study was giving very high rate of cure and direct effect in decreasing the purulent discharge in the first 2 days and that give us clear evidence of the effective results of honey in deep pyomyositis. The honey we used had no specification type.It is just original flower honey from the bee.

The collective studies provide evidence that CRP is a valid marker of inflammation and could be used to determine inflammation status in patients with chronic wounds, two studies reported that in different types of wounds (i.e. burn wounds, diabetic foot ulcers) CRP levels were elevated in the wounds that were not healing properly (42).

Lower CRP levels have also been associated with more efficient healing wounds. One study found that lower baseline levels of CRP were associated with greater healing of diabetic foot ulcers[8, 9] and another study suggested that CRP could be used as a predictor of potential wound healing disorders [43,44].

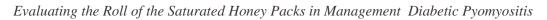
The CRP as a single marker had the highest sensitivity and specificity. It was interesting to note that the use of a high-sensitivity CRP assay brought no additional accuracy of diagnosis. Moreover, these blood test results and the follow-up of patients.45,46,47.

In our study I use the CRP as marker and singe of the cure it shows that it is effective monitor as base line and can be depended on as marker to follow the stages of pyomyositis until healing. As show in diagrams in the results .



PHOTO 1

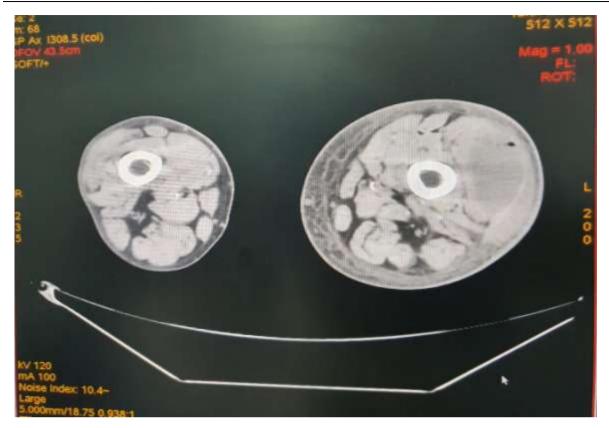
Honey dressing preparation







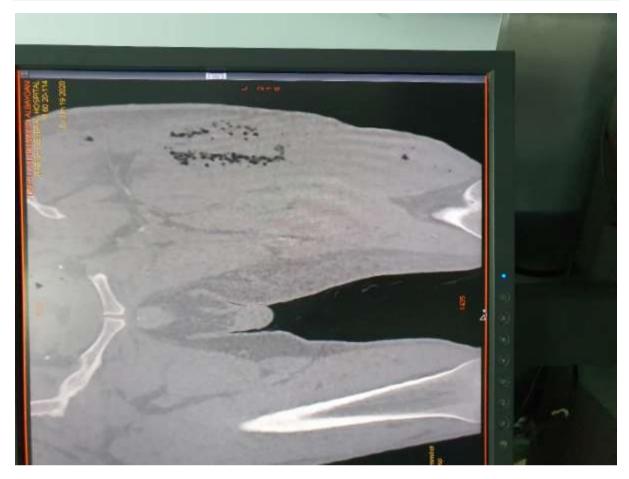
CT SCAN UPPER THIGH INTERMUSCULAR COLLECTION



РНОТО 3

CT SCAN OF EARLY PYOMYOSITES ANTERIOR COMPARTMENT OF THIGH LEFT SIDE





4 -Ct of case of early intramuscular infection with clear sub cutaneous edema



5a early sign in the anterior compartment of the thigh redness of the thigh



5b

CT OF THE THIGH SHOWING THE EARLY INFELTRATION OF THE ANTERIOR COMPARTMENT OF THIGH BY INFLAMETION



)6a (Deep pyomyositis in thigh with aggressive infection affecting the anterior and lateral compartment of the thigh with skin necrosis



6b

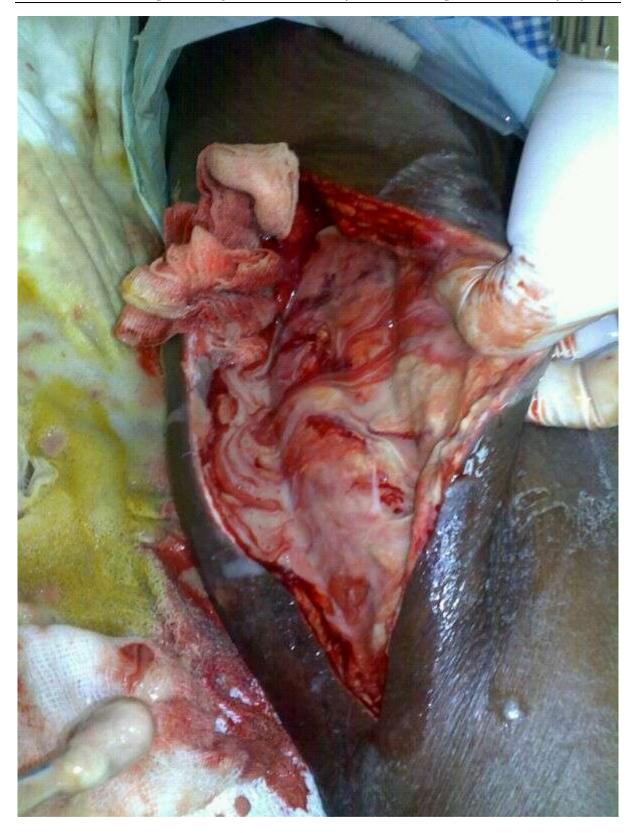
Deep pyomyositis in the thigh with skin gangrene



Photo 7

Case of deep pyomyositis in purulent stage showing the swelling of the muscles

And areas of deep facia necrosis



Evaluating the Roll of the Saturated Honey Packs in Management Diabetic Pyomyositis

Photo 8

Purulent stage after incision and drainage of the lateral compartment of the thigh with extensive infection



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photo 9

showing the last debridement pre discharge and the granulation of the thigh .



Photo 10

Extended deep pyomyositis taking the lateral and anterior compartment of the thigh with the knee lateral side and reach the lateral compartment of the leg the photo of the leg in healing stage follow up after 4 weeks

References

- Painful swelling of the thigh in a diabetic patient: diabetic muscle infarction.Lafforgue P¹, Janand-Delenne B, Lassman-Vague V, Daumen-Legré V, Pham T, Vague P. Diabetes Metab. 1999 Sep;25(3):255-60.
- [2]. [Painful syndromes in diabetic patients due to skeletal muscle injuries]. Arq Bras Endocrinol Metabol. 2006 Oct;50(5):957-62.Pereira FO¹, Medeiros YS.
- [3]. M. Bahrami, A. Ataie-Jafari, S. Hosseini, M. H. Foruzanfar, M. Rahmani, and M. Pajouhi, "Effects of natural honey consumption in diabetic patients: an 8-week randomized clinical trial," International Journal of Food Sciences and Nutrition, vol. 60, no. 7, pp. 618– 626, 2009.
- [4]. S. Wild, G. Roglic, A. Green, R. Sicree, and H. King, "Global prevalence of diabetes estimates for the year 2000 and projections for 2030," Diabetes Care, vol. 27, no. 5, pp. 1047–1053, 2004.
- [5]. Bickels J, Ben-Sira L, Kessler A, Wientroub S: Primary pyomyositis. J Bone Joint Surg Am 84:A2277–A2286, 2002
- [6]. Walling DM, Kaelin WG Jr: Pyomyositis in patients with diabetes mellitus. *Rev Infect Dis* 13:797–802, 1991
- [7]. E. W. Gregg, B. L. Cadwell, Y. J. Cheng et al., "Trends in the prevalence and ratio of diagnosed to undiagnosed diabetes according to obesity levels in the U.S.," Diabetes Care, vol. 27, no. 12, pp. 2806–2812, 2004.
- [8]. K.-H. Yoon, J.-H. Lee, J.-W. Kim et al., "Epidemic obesity and type 2 diabetes in Asia," The Lancet, vol. 368, no. 9548, pp. 1681– 1688, 2006.
- [9]. International Diabetes Federation, "World Diabetes Media Kit: every 10 seconds 1 person dies of diabetes," Brussels, Belgium, 2007, http://www.idf.org/webdata/docs/World Diabetes Day Media Kit.pdf.
- [10]. N. Singh, D. G. Armstrong, and B. A. Lipsky, "Preventing foot ulcers in patients with diabetes," The Journal of the American Medical Association, vol. 293, no. 2, pp. 217–228, 2005.
- [11]. Alexander Kosternoy, Emad K. Bayumi. Use of Honey in Management of Diabetic Foot Infection: Patient's Satisfaction and Outcome. Journal of Surgery. Special Issue: Postoperative Pain Syndrome. Vol. 3, No. 2-1, 2015, pp. 42-47. doi: 10.11648/j.js.s.2015030201.19(11)
- [12]. Front. Immunol., 13 April 2018 | https://doi.org/10.3389/fimmu.2018.00754Role of C-Reactive Protein at Sites of Inflammation and InfectionNicola R. Sproston and Jason J. Ashworth*(13)
- [13]. Bickels J, Ben-Sira L, Kessler A, Wientroub S. Primary pyomyositis. J Bone Joint Surg. 2002;84-A:2277-86.
- [14]. Clinical stage, age and treatment in tropical pyomyositis: a retrospective study including forty cases.Martínez-de Jesus FR, Mendiola-Segura I Archives of Medical Research [01 Jan 1996, 27(2):165-170]
- [15]. Pyomyositis is not only a tropical pathology: a case series, Laura Comegna, Paola Irma Guidone, +6 authors Nadia Rossi, Published 2016 in Journal of medical case reports
- [16]. Primary pyomyositis in North India: a clinical, microbiological, and outcome study Susheel Kumar, Ashish Bhalla, +5 authors Subhash K. Varma. Published 2018 in The Korean journal of internal medicine
- [17]. Diabetic pyomyositis: an uncommon cause of a painful leg. Michele Y YSeah, Sadanand N Anavekar, Judy Savige, Louise M Burrell. Published 2004 in Diabetes care.
- [18]. Clinical characteristics and predictors of mortality in 67 patients with primary pyomyositis: a study from North India. Aman Sharma, Susheel Kumar, + 6 authors Subhash K. VarmaPublished 2009 in Clinical Rheumatology
- [19]. JUDY A. SAVIGE, MB BS, FRCP, FRACP, FRCPA, PHD, MSC 2 LOUISE M. BURRELL, MBCHB, MRCP, MD, FRACP, FAHADIABETES CARE, VOLUME 27, NUMBER 7, JULY 2004
- [20]. National Bureau of Statistics. Kenya Population and Housing Statistics. 2009;
- [21]. Solis-Tellez H, Mondragon-Pinzon EE, Ramirez-Marino M, et al. Epidemiologic analysis: prophylaxis and multidrug resistance in surgery. Rev Gastroenterol Mex. 2017; 82(2):115–22.
- [22]. Boateng JS, Matthews KH, Stevens HN et al. Wound healing dressings and drug delivery systems: a review. J Pharm Sciences. 2008; 97(8):2892–923.
- [23]. Back DA, Scheuermann-Poley C, Willy C. Recommendations on negative pressure wound therapy with instillation and antimicrobial solutions—when, where and how to use: What does the evidence show? Int Wound J. 2013; 10Suppl 1:32–42.

- [24]. Isaac AMA-K, Salim ME, Ahmed IA-RM. An affordable custom-built negative pressure wound therapy. Ann Afri Surg. 2017; 14(1). 6. Barnea Y, Weiss J, Gur E. A review of the applications of the hydro fiber dressing with silver (Aquacel Ag®) in wound care. Therapeutics and Clin Risk Man. 2010;
- [25]. 21. 7. Johnston CS, Gaas CA. Vinegar: Medicinal uses and ant glycemic effect. Med Gen Med. 2006; 8(2):61.
- [26]. Borgquist O. Negative pressure wound therapy: Therapy settings and biological effects in peripheral wounds. Lund University; 2013.
- [27]. National Bureau of Statistics. Kenya Population and Housing Statistics. 2009;
- [28]. 29. Solis-Tellez H, Mondragon-Pinzon EE, Ramirez-Marino M, et al. Epidemiologic analysis: prophylaxis and multidrug resistance in surgery. Rev Gastroenterol Mex. 2017; 82(2):115–22.
- [29]. Boateng JS, Matthews KH, Stevens HN et al. Wound healing dressings and drug delivery systems: a review. J Pharm Sciences. 2008; 97(8):2892–923.
- [30]. References 31. Steinhoff G. Regenerative Medicine. Steinhoff G, editor: Springer Netherlands; 2011. XXIV, 1032 p
- [31]. Othman D. Negative pressure wound therapy. Literature review of efficacy, cost effectiveness, and impact on patients' quality of life in chronic wound management and its implementation in the United Kingdom. Plast Surg Int. 2012; 2012:6.
- [32]. Rhee SM, Valle MF, Wilson LM, et al. Negative pressure wound therapy technologies for chronic wound care in the home setting: A systematic review. Wound Repair Regen. 2015; 23(4):506–17.
- [33]. Kairinos N. The biomechanics of negative-pressure wound therapy. Doctoral dissertation, University of Cape Town. 2011
- [34]. Baranoski S, Ayello EA. Wound care essentials: Practice principles: Lippincott Williams & Wilkins; 2008.
- [35]. Bullough L. Negative pressure wound therapy treatment costs—a comparative evaluation. In press, 2015.
- [36]. Niaz K, Maqbool F, Bahadar H, et al. Health benefits of manuka honey as an essential constituent for tissue regeneration. Curr Drug Metab. 2017.
- [37]. Boukraâ L. Honey in traditional and modern medicine: CRC Press; 2013.
- [38]. Nwankwo C, Ezekoye CO, Igbokwe S. Phytochemical screening and antimicrobial activity of apiary honey produced by honey bee (Apis mellifera) on clinical strains of Staphylococcus Aureus, Escherichia coli and Candida albicans. 2014; 2367–72.
- [39]. Kotsirilos V, Vitetta L, Sali A. A guide to evidence-based integrative and complementary medicine. 1st ed. 2010 ed. Elsevier Australia: National Herbalists Association of Australia; 2011.
- [40]. Sussman C, Bates-Jensen BM. Wound care: A collaborative practice manual. Wolters Kluwer Health / Lippincott Williams & Wilkins; 2007. 20. Singer AJ, Hollander JE, Blumm RM. Skin and soft tissue injuries and infections: A practical evidence based guide. Shelton, CT: People's Medical Pub. House-USA; 2010.
- [41]. Tecilazich, F., Dinh, T., Pradhan-Nabzdyk, L., Leal, E., Tellechea, A., Kafanas, A., . . . Veves, A. (2013). Role of endothelial progenitor cells and inflammatory cytokines in healing of diabetic foot ulcers. PloS One, 8(12), e83314. doi:10.1371/journal.pone.0083314; 10.1371/journal.pone.0083314
- [42]. Blass, S. C., Goost, H., Burger, C., Tolba, R. H., Stoffel-Wagner, B., Stehle, P., & Ellinger, S. (2013). Extracellular micronutrient levels and pro-/antioxidant status in trauma patients with wound healing disorders: Results of a cross-sectional study. Nutrition Journal, 12(1), 157-2891-12-157. doi:10.1186/1475-2891-12-157 [doi]
- [43]. 44Koenig, W., Sund, M., Frohlich, M., Fischer, H. G., Lowel, H., Doring, A., . . . Pepys, M. B. (1999). C-reactive protein, a sensitive marker of inflammation, predicts future risk of coronary heart disease in initially healthy middle-aged men: Results from the MONICA (monitoring trends and determinants in cardiovascular disease) augsburg cohort study, 1984 to 1992. Circulation, 99(2), 237-242.
- [44]. Black, S., Kushner, I., &Samols, D. (2004). C-reactive protein. The Journal of Biological Chemistry, 279(47), 48487-48490. doi:10.1074/jbc.R400025200 [doi]
- [45]. Serum procalcitonin and C-reactive protein concentrations to distinguish mildly infected from non-infected diabetic foot ulcers: a pilot study A. Jeandrot& J.-L. Richard & C. Combescure& N. Jourdan & S. Finge& M. Rodier& P. Corbeau & A. Sotto & J.-P. Lavigne Received: 30 July 2007 /Accepted: 31 August 2007 / Published online: 13 October 2007
- [46]. Suzanne Av Van Asten, MoezMithani , Kathryn E Davis, international Wound Journal 14(1):n/a-n/a · March 2016 Erythrocyte sedimentation rate and C-reactive protein to monitor treatment outcomes in diabetic foot osteomyelitis