



SYSTEMIC INFECTION WITH SINGLE OR MULTI-ORGAN DAMAGE CAUSED BY INADEQUATELY MANAGED CHRONIC WOUNDS: A CASE SERIES

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SUMMARY – Chronic wounds are often underestimated condition with increasingly growing inpatient and outpatient treatment costs. Since the patient population affected by chronic wounds is heterogeneous and includes diabetes, chronic venous insufficiency and peripheral artery disease patients, with additional differences in gender, age, previous medical history, treatment of chronic wounds is highly personalized and dependent on a variety of factors. This paper aims to highlight the problems that the chronic wound patient population is facing during the COVID-19 pandemic: from higher probability of an undesirable disease outcome to the fact that many of them have limited access to primary care providers and to the regular and continuous care that their condition demands.

This paper describe three patients with chronic wounds. Each of the patients had a significant worsening of their chronic wounds during the COVID-19 pandemic: either following an active SARS-CoV-2 infection or due to the limited access to primary care.

The cases described here highlight the necessity of providing proper and regular care for all patients during the COVID-19 pandemic, regardless of the current state of the healthcare system and the adversities and hurdles it currently faces, to prevent the pandemic from becoming a syndemic.

Keywords: chronic wounds, care, COVID-19 pandemic

Introduction

Chronic wounds are an often underestimated issue, even though there is data showing that they negatively impact the quality of life of 2.5% of the total US population and present a significant economic burden on the healthcare system.¹ With the advent of the novel coronavirus (SARS-CoV-2) pandemic, patients with chronic wounds are at an even greater risk, with the risk factors related to chronic wounds (hypertension, vascular disorders, diabetes) being some of the most important predictors of severe presentations and lethal outcomes of COVID-19. Having all the listed factors in mind, it is easy to see why proper, regular and time-

ly chronic wound care is a priority. Adding to that point is the fact that the lack of regular visits to a wound care clinic can increase hospitalization rates by up to 20 times.² In this case series, we present three patients unfortunately affected by a combination of the sequelae of a SARS-CoV-2 infection, lack of regular visits to a wound care clinic and an ineffective bureaucracy, the sum of which presents itself as serious infections with single or multi-organ damage.

Case 1

A 77-year-old female came to the Clinic for Chronic Wounds at KB Merkur, a tertiary care facility in Zagreb, Croatia. She had a history of arterial hypertension of more than 10 years, a past SARS-CoV-2 infection after being vaccinated and a cholecystectomy 10 years ago. At the time of the examination, she had chronic ulcers on both shins, which had been treated

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with various dressings for months. She was taking ciprofloxacin 500mg pills BID for a presumed infection at the site of the ulcers, prescribed for 10 days. In her therapy, the patient also had acetylsalicylic acid, bisoprolol, oxazepam, indapamide and lisinopril. The patient interview during the examination revealed that the patient had been demoted the dressings prescribed at the clinic, citing a guideline of the Croatian Bureau of Health Insurance (HZZO) to discontinue a dressing if it did not improve the status of the wound within 28 days. A physical examination revealed five ulcers (three on the right shin and two on the left) with a large volume of green secretion resembling pus. The patient's vital signs were stable, with a blood pressure of 110/70 mmHg, a pulse of 61 beats/min, 15 respirations/min. Her oxygen saturation was 95% on room air. A lavage with H₂O₂ and sterile saline solution was carried out, along with a dressing of 10% NaCl and 10% iodopovidone. The patient was prescribed tramadol 50mg hard capsules for pain from the ulcers and was sent to the emergency internal medicine clinic for further workup following complaints of dyspnea, a dry cough and diarrhea.

An electrocardiogram (ECG) and blood laboratory tests were made. The ECG showed a sinus rhythm with 61 beats per minute and a deviation of the electrical axis to the left, along with a left bundle branch block. The laboratory results showed a prominent leukocytosis of 39.90×10^9 leukocytes, microcytic anemia (Hb 73 g/L, MCV 69.0 fL), high neutrophile to lymphocyte ratio (NEU% 90, LYM% 4.9), hypocoagulable state (PT 0.35), hyperkalemia (6.5 mmol/L), hyponatremia (132 mmol/L), elevated urea (62.9 mmol/L) and creatinine (467 μ mol/L), elevated liver enzymes (AST 75 U/L, ALT 201 U/L, GGT 100 U/L), elevated CRP (123.3 mg/L) and high-sensitivity troponin I (26 ng/L). An arterial blood gas (ABG) test was also performed and showed an acidosis (pH 7.246) with hypocapnia (pCO₂ 2.65 kPa), hypobicarbonatemia (HCO₃ 8.6 mmol/L) and a base excess of -18.7 mmol/L. The patient was hospitalized with a diagnosed infection with multiorgan damage, acute kidney failure (AKF), hepatic damage, cardiac damage, coagulation breakdown, and administered a blood transfusion, antibiotics (piperacilin/tazobactam 4.5mg i.v.) and i.v. fluids (500mL of 5% glucose with 8 units of fast-acting insulin because of hyperkalemia with loop diuretics (due to hyperkalemia a dose of furose-

mid was 80 mg iv). A chest X-ray and an abdominal ultrasound were also made. The X-ray showed an enlarged heart with a cranial redistribution of circulation. The abdominal ultrasound showing no abnormalities.

Case 2

This patient is a 42-year-old male who came to the emergency clinic with a primary complaint of erythema, pain and edema of the right foot. After taking a medical history, it has been established that the patient had been suffering from multiple conditions for more than 10 years, including arterial hypertension, hyperlipidemia, type II diabetes mellitus, and chronic ulcers on both feet. He had had no medication allergies in the past and reported taking bisoprolol, alogliptin, metformin, ramipril, amlodipine, hydrochlorothiazide, atorvastatin and glargine during his therapy. He had also had COVID-19 at one point in time, with a positive PCR test. Upon examination, the patient's right foot was edematous, red and painful, with pus secreted out of the wound. The foot was missing a second digit, which had been previously amputated. The sole of the foot was red, and the skin looked macerated. Arterial pulses were palpable femorally, but not distally. An emergency doppler ultrasound of the right leg vasculature showed no significant atherosclerotic changes and the flow through the large lower extremity arteries was satisfactory. The deep veins of the leg were compressible, anechoic, without signs of deep venous thrombosis (DVT). Blood samples were taken for laboratory analysis and the laboratory test results showed a prominent leukocytosis of 23.33×10^9 leukocytes/L, an elevated neutrophile to lymphocyte ratio (90.5%/3.9%) indicative of severe inflammation, hyponatremia with a sodium value of 127 mmol/L, hyperglycemia with a blood glucose level of 19.8 mmol/L, a high-sensitivity C-reactive protein (hs-CRP) level of 267.6 mg/L and kidney damage with a serum creatinine value of 273 μ mol/L. A swab of the wound was taken and sent for microbiological testing. The patient was admitted to the vascular surgery ward and given intravenous antibiotics. Following a 2-week hospitalization, the patient was discharged with instructions to come for control visits and redressing the wound every second day, either at the chronic wound clinic or his primary care provider (PCP). After several weeks of not showing up for control visits and wound redressing, the patient showed up at the emergency ward complaining of right foot erythema, edema and pain. The wound

had severely worsened, and a swab was again taken. It came back positive for *Klebsiella pneumoniae* and type B beta hemolytic streptococcus. The patient was once again admitted to the hospital and a reamputation of the second digit was deemed necessary.

Case 3

This patient is a 68-year-old male who came to the emergency ward complaining of pain and erythema on the left foot and erythema, pain, edema on the right shin. The patient had a medical history of type II diabetes mellitus for more than 20 years, glaucoma, diabetic retinopathy, arterial hypertension, hyperlipidemia and chronic ulcers of both feet. He stated a previous allergic reaction to penicillin and was taking rapid acting insulin, glargine, amlodipine, phenofibrate, atorvastatin, ramipril, hydrochlorothiazide, acetylsalicylic acid, dorzolamide and timolol in his chronic therapy. Upon physical examination, the right leg was erythematous and swollen and the left foot was erythematous with a large number of purulent and necrotic deposits inside the wound. A vascular murmur over the carotids was also noted. A wound swab was taken and sent for microbiological testing. The results came back positive for vancomycin sensitive *Enterococcus faecalis*. A doppler ultrasound of the leg arteries showed diffuse atherosclerotic changes without isolated significant stenotic changes – the finding was deemed overall satisfactory, with a control exam and regulation of risk factors recommended. Blood samples were drawn and sent for analysis. The laboratory test results showed pronounced inflammation with a hs-CRP of 121 mg/L, a hypokalemia with a serum potassium level of 3.3 mmol/L and significant acute kidney injury with a serum creatinine of 306 umol/L. The patient was admitted to the endocrinology ward.

Discussion

The patients presented here were affected by either the reduced regularity of visits to the wound care clinic due to the COVID-19 pandemic or an ineffective and unforgiving bureaucracy that failed to recognize the need of chronic wound patients for regular reapplication of dressings specifically designed to prevent infection. It has been shown that regular visits to the wound care clinic play an extremely important role in preventing infection. One study determining the success of simple mechanical debridement in reducing

bacterial activity inside and peripheral to the wound using fluorescence imaging has shown that a single debridement reduces bacterial activity inside the wound by 99.4% and peripherally by 64.3% (before using antiseptic)³. Wound care clinics are also important because of the psychological effects that procedures such as changing dressings and interviewing the patient about their experience regularly allows for a more personalized approach to each patient, which has been shown to improve the psychological state of patients and the time needed to complete wound healing^{3,4}. In addition to the obvious benefits listed above, regular visits to the wound care clinic also allow for a timely diagnosis of wound infection. Several analyses have shown that there are reliable risk factors for the development of chronic wound infection, most of which can only be evaluated by regular physical examination of the wound: wound area >10 cm², new, increased or altered wound pain, malodor, increased wound area, erythema, increased wound temperature⁴ and heavy exudate from the wound⁵. It is also important for family physicians and bureaucratic entities providing health insurance to recognize and respect the expertise and importance of the wound care surgeon's opinion and findings in order to provide adequate multidisciplinary care to the patient, even outside the wound care clinic and ensure that the same level and quality of care is provided both in the inpatient and outpatient settings. Two of the three patients described in this case series had a history of COVID-19, after which their chronic wounds clinically increased in severity. It is therefore important to discuss the treatment of chronic wound patients infected with SARS-CoV-2, to ensure proper wound care during the acute infection phase, when patients are supposed to be in isolation for 1-2 weeks, and to provide adequate aftercare in the form of more frequent follow-up exams, as it has been shown that not only are chronic wound patients more susceptible to unfavorable COVID-19 outcomes, but that their chronic wounds (and other chronic conditions) can also rapidly progress into their later, more severe stages in the midst of an infection with SARS-CoV-2, which has been known to interact with important molecular mechanisms regulating blood vessel tone, integrity and other important properties, so some researches describe this situation as a "pandemic within a pandemic"^{6,7}.

In conclusion, in the wake of the COVID-19 pandemic, many healthcare topics have gone under the

radar, including chronic wound care. Since patients with chronic wounds are at risk of being exposed to a lack of regular care due to the increased load on the healthcare system and having significantly worse COVID-19 outcomes if infected, it is important to recognize the role of multidisciplinary care and proper communication between wound care specialists, family medicine specialists and insurance providers so that this sensitive group of patients will receive the best possible care, especially in these trying times of Covid syndemic.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

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Sažetak

SUSTAVNA INFEKCIJA S OŠTEĆENJEM JEDNOG ILI VIŠE ORGANA UZROKOVANIM NEADEKVATNO LIJEČENIM KRONIČNIM RANAMA: PRIKAZ SLUČAJEVA

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Kronične rane predstavljaju podcijenjeno stanje koje je povezano sa značajnim rastućim troškovima bolničkog i ambulantnog liječenja. Znajući da je populacija pacijenata s kroničnim ranama vrlo heterogena te obuhvaća populaciju dijabetičara, pacijente s kroničnom venskom insuficijencijom, perifernom arterijskom bolesti, te uvažavajući dodatne razlike vezane uz spol, dob te prethodnu medicinsku dokumentaciju, liječenje kroničnih rana je visoko personaliziran postupak i ovisan je o nizu različitih čimbenika. U ovome radu naglašen je problem populacije s kroničnim ranama tijekom pandemije COVID-19 u smislu veće vjerojatnosti neželjenog ishoda bolesti primarno zbog ograničenog pristupa liječnicima primarne zdravstvene zaštite, kao i regularne skrbi zbog drugih prilažećih kroničnih stanja. U radu su opisani prikazi slučajeva tri bolesnika s kroničnim ranama koji su imali značajno pogoršanje uslijed pandemije COVID-19. Isto se moglo prevenirati pravilnom i regularnom brigom, stoga smatramo da za sve pacijente tijekom pandemije COVID-19, bez obzira na trenutno stanje zdravstvenog sustava i postojeća ograničenja, prepreke nisu nesavladive, u cilju nadzora ovih pandemijskih problema koji postaju sindemija.

Ključne riječi: *kronične rane, njega rana, COVID-19 pandemija*