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Case Report

Methamphetamine abuse: The link between Immunosuppression, Fournier's gangrene and Candida

Abstract

Fournier's gangrene is a rapidly progressive and potentially fatal infective necrotizing fasciitis of the perineum, external genitalia and/or perianal regions. The most common etiology of the infection is bacterial; however, there have been published cases of Fournier's gangrene caused by yeast in patients with severe immunosuppression. Cutaneous fungal infections are often opportunistic and typically occur in immunocompromised patients with diabetes and additional chronic conditions. None of the fungal Fournier's gangrene case reports thus far present a patient with diabetes and methamphetamine abuse. This case study presents a methamphetamine abuser with uncontrolled diabetes, both of which contributing to immunosuppression, who presented to the emergency department with a rare case of Fournier's gangrene caused by unspecified yeast. Methamphetamine abuse has not yet been demonstrated to be a risk factor for FG, although it has been proven to be a causative agent of both immunosuppression and malnutrition. This case report highlights the additive effects methamphetamine abuse has on immunosuppression that eventually caused fungal Fournier's gangrene.

Introduction

Fournier's gangrene (FG) is a rapidly progressive and potentially fatal infective necrotizing fasciitis of the perineum, external genitalia and/or perianal regions. It most commonly affects men, but can affect women as well. Previous studies indicate that the risk factors for FG include diabetes mellitus (most common), alcohol abuse, malnutrition and other immunosuppressive medical conditions such as HIV and chronic steroid use. Methamphetamine abuse has not yet been demonstrated to be a risk factor for FG, although it has been proven to be a causative agent of both immunosuppression and malnutrition. This case report highlights the additive effects methamphetamine abuse has on immunosuppression that eventually caused fungal Fournier's gangrene. Mortality rates, despite aggressive antibiotics and debridement, has been shown to be higher in patients with diabetes mellitus, a delayed presentation to the hospital, and patients presenting with sepsis at first admission to the hospital [1]. Common causes of death due to FG are sepsis with multisystem organ failure, coagulopathy, and diabetic ketoacidosis [2]. Thus, a high degree of suspicion for FG should be employed during physical exam (palpating for crepitus) and computerized tomography (CT) lower extremity (examining for emphysematous changes). FG is typically treated with broad-spectrum antibiotics, as the organism is usually bacterial, and surgical debridement.

This case study presents a methamphetamine abuser with uncontrolled diabetes, both of which contributing to immunosuppression, who presented to the emergency department with a rare case of Fournier's gangrene caused by unspecified yeast.

Case Report

32 year old female with a history of type one diabetes, malnutrition, and methamphetamine abuse presented to the emergency room with severe left sided groin pain that began two days prior with associated edema and erythema. The patient also complained of fevers, chills and nausea that began with the onset of pain. She denied any injury to the area, including methamphetamine injections, as she typically smokes methamphetamine and her last drug use was six days prior.

On physical exam, patient was afebrile with tachypnea and tachycardia. The left inguinal region was significant for erythema and induration extending eight centimeters distally down anterior thigh and also medially and posteriorly involving the left labia and left gluteal fold. There was also a significant amount of vaginal white purulent discharge. The patient was exquisitely tender to touch on exam, thus crepitus was difficult to appreciate secondary to a lack of patient cooperation. On vaginal exam, left labium was indurated and erythematous

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with a large amount of white purulent discharge, secondary to vaginal candidiasis. Patient also had severe generalized periodontal disease with multiple mobile teeth, most likely secondary to chronic methamphetamine abuse.

Labs revealed an elevated hemoglobin A1c of 15.6, glucose of 400 mg/dL, beta-hydroxybutrate of 13.6 mg/dL (0.2-2.8), anion gap of 19 mmol/L (8-12) and pH of 7.31 (7.32-7.43), suggesting mild DKA. White blood cell count was elevated at 16 (4.5-11), procalcitonin 1.9 ng/mL (0-0.05), lactic acid 1.7 (<2), and blood culture was negative for infection. Patient met criteria for sepsis with three of four systemic inflammatory response syndrome (SIRS) criteria: pulse >90, respirations >20, and WBC > 12K and a likely source of infection. Urine analysis was negative for nitrites and leukocytes but did show a significant amount of proteinuria. Urine culture was negative. Initial CT left lower extremity with contrast revealed prominent subcutaneous edematous changes in the left pelvic subcutaneous soft tissues extending inferiorly into portions of the proximal left thigh. No evidence of abscess, and a mild reactive prominence of a few lymph nodes. Patient was then admitted and started on 3.375 g piperacillin-tazobactam and 1,000 mg vancomycin IV.

Throughout the following week, patient's clinical condition continued to deteriorate. She developed a fever >100.3 for three consecutive days, showed minimal change in WBC count, and clinically the inguinal infection was not improving despite antibiotic treatment. On day four, patient was started on 450 mg IV daptomycin, 600 mg IV clindamycin and 500 mg IV meropenem. Piperacillin-tazobactam and vancomycin were discontinued. Repeat CT left lower extremity without contrast revealed the findings as noted previously and an additional a small focus of superficial soft tissue emphysema that had developed in the lower anterior left abdominal wall.

Due to the high probability of a rapidly developing necrotizing fasciitis, the patient underwent an irrigation and debridement in the operating room the following day in which 150 mL of purulent fluid was evacuated from the wound and cultures were taken. Despite irrigation and debridement of the wound and maximum antibiotic therapy, the patient was still not improving. The culture was positive for yeast and negative for both anaerobic and aerobic bacteria. The patient was then promptly started on 400 mg IV fluconazole and clinical condition rapidly improved throughout the next few days.

Discussion

Fournier's gangrene (FG) is a rapidly progressive and potentially fatal infective necrotizing fasciitis of the perineum, external genitalia and/or perianal regions. This patient had the most common risk factor for FG, diabetes mellitus. She also suffered from malnutrition due to chronic methamphetamine abuse, both of these resulting in immunosuppression.

The most common isolates from wound culture are aerobic bacteria (E. coli, Klebsiella pneumonia, and Staphylococcus aureus) and anaerobic bacteria (Bacteriodes fragilis) [3]. Only in rare cases have yeast have been isolated as the single causative organism of FG, most of these being Candida [2,4,5]. Sources of infection for FG are typically from the urinary tract, lower gastrointestinal tract or overlying/surrounding skin [5]. This patient had vaginal candidiasis, which was most likely the source of her fungal FG, although the specific type of fungus was not cultured from her wound. Cutaneous fungal infections are often opportunistic and typically occur in immunocompromised patients, most commonly diabetes. Of course, not all patients with diabetes succumb to fungal Fournier's gangrene, but those who do typically have additional chronic conditions owing to their immunosuppression [5]. None of the fungal FG case reports thus far present a patient with diabetes and methamphetamine abuse.

Methamphetamine abuse has been shown to directly cause immunosuppression via biochemical alterations in both the central and peripheral immune system. Programmed cell death-1 (PD-1) receptor and its ligand PD-L1 are involved in a complex neuroimmune signaling pathway that induces T-cell apoptosis, energy exhaustion, and immune-mediated tissue damage. Blocking this pathway plays a large role in preventing neuroinflammation, thus it has been used to treat various neuropathological conditions. Methamphetime abuse has been shown to induce increased levels of PD-1 receptor and its ligand in cells such as microglia and macrophages that are critical for maintaining an adequate immune response in the brain [6]. Peripheral immune suppression has also been shown to occur which chronic abuse. Chronic abuse leads to an overall decrease in inflammatory cytokines (IL-6) and immune cells (granulocyte colony-forming units, NK cells, IgG, etc), leaving the patient defenseless against opportunistic pathogens [7,8]. Methamphetamine abuse can also decrease CD8+ T cells, which are responsible for fighting viruses and also fungi [9]. This may have contributed to the fungal infection our patient suffered from.

Abuse of methamphetamines also indirectly induces immunosuppression through its association with malnutrition. Methamphetamine abuse causes malnutrition through the intrinsic appetite suppressive effects of the drug and also socioeconomic influences; many abusers simply lack sufficient funds to purchase food [10]. The resulting malnutrition induces a state of immunosuppression through mechanisms that are currently being investigated. An interesting mechanism that induces immunosuppression is the deficiency of leptin that occurs with severe malnutrition. This hormone is present in adipose cells and induces a sensation of satiety when energy stores are sufficient [11]. The absence of this hormone, as seen in severe malnutrition, causes atrophy of the thymus, spleen, lymph nodes and their associated immune cells: T-lymphocytes, macrophages and pro-inflammatory cytokines [12].

Treatment for FG typically includes broad-spectrum antibiotics such as penicillin, metronidazole, and third-generation cephalosporin with gentamicin before surgical debridement, which should be repeated as the necrosis progresses [13]. Hyperbaric oxygen therapy has also been recognized as another treatment modality, as it enhances leukocyte activity and is directly antibacterial against

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anaerobes [13]. This case study shows that the addition of empiric fluconazole would be a prudent addition to cover fungal organisms as well in immunosuppressed patients, most specifically methamphetamine abusers with diabetes.

Conclusion

Due to the increasing number of FG caused by yeast, it has been suggested that immunosuppressed patients presenting with FG be treated with an empiric antifungal agent along with antibiotics and urgent surgical debridement [2]. Methamphetamine abuse, as well as malnutrition, are contributors to immunosuppression and require special consideration for opportunistic infections.

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