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Case presentation

Extensive hidradenitis suppurativa (HS) Hurly stage III disease treated with intravenous (IV) linezolid and meropenem with rapid remission

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Abstract

A 57-year-old woman with Hurley Stage 3 hidradenitis suppurativa (HS) and multiple co-morbidities is presented. She had failed multiple antibiotic therapies and etanercept. She had end stage renal disease and was on dialysis. Her HS was put into remission with one month of daily IV treatment with 1.2 grams linezolid and 1 gram of meropenem, administered daily through her dialysis shunt. Unfortunately, her disease flared again two weeks after the cessation of the IV treatment. Nevertheless, more conventional therapy was then able to maintain her disease at a level that was significantly improved over baseline prior to the IV treatment. This case highlights above all a primary etiology of HS is stimulus of immune system's over-reaction in HS to the bacterial microbiome. If antibiotics are administered to a patient with stage 3 HS powerful enough to wipe out the bacterial biome, the immune system having no target retreats, permanent scarring in its wake and retreats to a certain but hardly permanent normalcy.

Case synopsis

A morbidly obese, 57-year-old woman with Hurley Stage Disease 3 hidradenitis suppurativa (HS) and end stage renal disease owing to polycystic kidney disease on dialysis trice weekly, had failed therapy with multiple antibiotic regimens and entanercept. Other medical problems included depression, hypothyroidism, irritable bowel syndrome, and osteoporosis. The HS began at age 12 on the thighs. The disease would come and go initially, but worsened over the years. At age 51, in 2007, the HS advanced in stage and became severe, first in her axillae and then her abdomen, flanks, buttocks, groin, and legs; she also developed pilonidal cysts. Upon physical examination in 2012, HS stage 3 was apparent at the abdomen, flanks, buttocks, groin and legs; pilonidal cysts were active and draining as well.

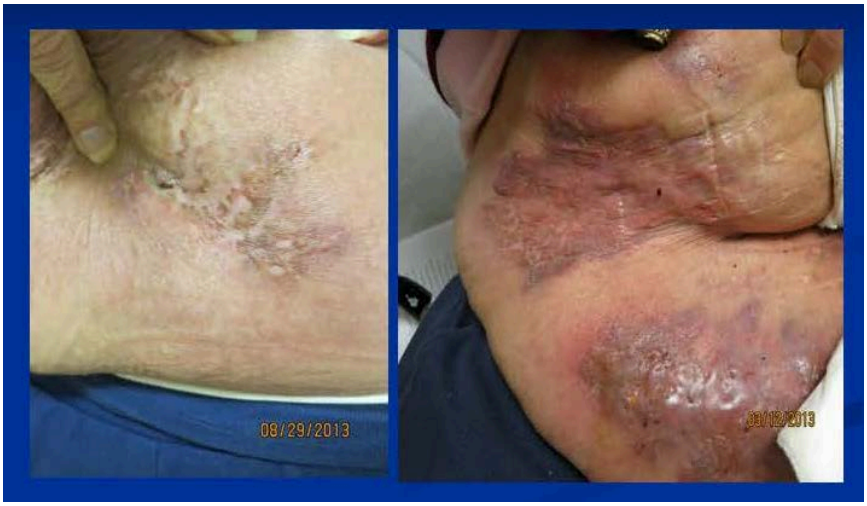

Figure 1 and 2. Abdomen After and before IV treatment

She was initially treated with clindamycin 300mg twice daily and rifampin 300 daily (dose for dialysis

patients), then changed to extended-release 115 mg minocycline with 300 mg oral rifampin. Every two weeks, un-roofing of lesions and injections with intralesional triamcinalone were performed. Open areas of the skin received silver nitrate application daily. The patient was also treated with duloxetine 60 mg daily and pregabalin 100 mg twice a day to optimize pain and depression control, with good effect. Topical dapsone gel was perceived as helpful to the patient. Oral dapsone 100mg BID and dutasteride 0.5 mg daily for 2 months did not have any effect. The patient continued to have copious oozing from many sterile

abscesses. Multiple cultures failed to reveal bacterial infection. The patient refused adalimumab and infliximab.

Figure 3 and 4. Perianal and buttocks area before and after IV treatment.
Figure 5 and 6. Abdomen close up before and after IV treatment

In an attempt to treat the numerous painful and draining nodules and sinuses, intravenous (IV) linezolid 1.2 g and IV meropenem 1 g were each given daily (a renal insufficiency dosing) for one month during August of 2013 through her existing dialysis shunt. The effect was striking; on examination on August 29, 2013 with two days of IV therapy remaining, her pain level was 0 on a scale of 0-10 for the first time without pain medications, her lesions had stopped oozing, and white atropic scars were noted where active lesions had been. Unfortunately, the patient suffered diarrhea during her treatment.

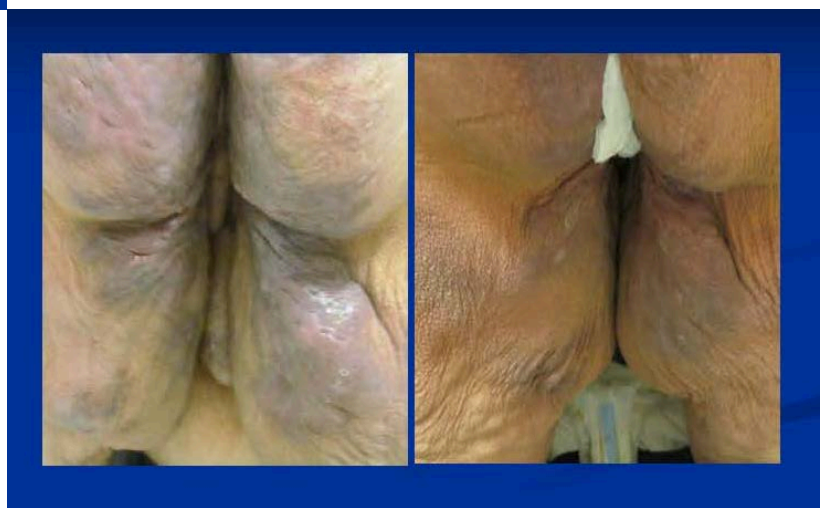

Figure 7 and 8. Buttocks and perianal area before and after IV treatment

Two weeks after termination of this treatment the patient's HS began to relapse. In mid September 2013, the patient noted some return of pain and oozing lesions on her buttocks and upper thighs and her pilonidal cysts returned. She was put on a combination of linezolid 600 mg daily, minocycline-ER 115 mg daily and rifampin 300mg daily with topical dapsone BID, a combination that she used for several months. The patient's HS was re-evaluated and although not as severe as before, the HS had returned. However, remission of disease of the abdomen and axillae was still notable. The oral regimen was combined with fortnightly intralesional triamcinolone acetonide injections and periodic un-roofing of abscesses and pilonidal cysts. Marked improvement over baseline was maintained. A list of her medications (April, 2014) is contained in Table 1.

Table 1. Medications patient took after intravenous therapy

Sevelamer carbonate) 800mg	4 Tabs with meals 2 tabs with snacks
Folbee Plus Tab (Vitamin B12 cyanocobalamin)	1 per diem
Esomeprazole 40mg	1 per diem
Synthroid 0.1mg	1 per diem
Fexofenadine 180mg	1 per diem
Fenofibrate 48mg	1 per diem
Celecoxib 200mg	1 per diem
Cinacalcet 90mg	1 per diem
Sodium Bicarbonate 325mg	2 per diem
Eszopiclone, 2mg	when needed
Acetaminophen and oxycodone 5-325mg	when needed-twice a month before patient visits
Fish Oil 1200 mg	2 per diem

Flaxseed Oil 1300mg 2 per diem
Glucosamine HCI with MSM 1500 mg 2 per diem
Calcium with Vitamin D 600mg 2 per diem
Duloxetine extended release 60mg BID 2 per diem
Pregabalin 100mg BID 2 per diem
Rifampin 300mg 1 per diem
Extended Release Minocycline 115mg 1 per diem
Clindamycin Phosphate Topical Gel 1% 60mg bid
Topical Dapsone gel 90g 1 per diem
Linezolid 600mg 1 per diem
Dicyclomine HCL 10mg 2 per diem

Seven months after resuming linezolid, rifampin, and extend release minocycline, the patient presented with night sweats and extreme pain that began after a fall and leg injury the previous day. She was sent to the hospital and necrotizing fasciitis of her right leg was diagnosed. The patient underwent surgical excision of the involved areas of necrotizing fasciitis. The patient's HS remained stable in the hospital on vancomycin but flared when she was sent to a rehabilitation step down facility. During this time, treatment using clindamycin 300 gm twice a day, rifampin 300 mg once a day, and acitretin 10 mg daily was started. The HS was stabilized somewhat. The patient was discharged after two months and the antibiotics were continued; acitretin was increased to 10 mg BID. Lesion un-roofing, intralesional triamcinolone acetonide , and silver nitrate were continued. The patient improved on the regimen and the HS remained on her legs,buttocks, and isolated areas on her flanks. The acitretin was increased to 25 mg BID with added effect. The dose could not be increased further because the patient could not tolerate a higher dose of acitretin.

A list of her medications taken that she was currently taking as of December of 2014 is contained in Table 2.

Table 2. Medications as of December 1, 2014

Sevelamer carbonate) 800mg 4 Tabs with meals 2 tabs with snacks
Folbee Plus Tab (Vitamin B12 cyanocobalamin) 1 per diem
Esomeprazole 40mg 1 per diem
Synthroid 0.1mg 1 per diem
Fexofenadine 180mg 1 per diem
Fenofibrate 48mg 1 per diem
Celecoxib 200mg 1 per diem
Cinacalcet 90mg 1 per diem
Sodium Bicarbonate 325mg 2 per diem
Eszopiclone, 2mg when needed
Acetaminophen and oxycodone 5-325mg when needed-twice a month before patient visits
Fish Oil 1200 mg 2 per diem
Flaxseed Oil 1300mg 2 per diem
Glucosamine HCI with MSM 1500 mg 2 per diem
Calcium with Vitamin D 600mg 2 per diem
Duloxetine extended release 60mg BID 2 per diem
Pregabalin 100mg BID 2 per diem
Rifampin 300mg 1 per diem
Clindamycin 300mg BID 2 per diem
Clindamycin Phosphate Topical Gel 1% 60mg BID
Acitretin 25 mg 1 per diem BID
Dicyclomine HCL 10mg 2 per diem

No regimen was as effective as the intravenous antibiotics but this regimen could not be undertaken again owing to the (1) refusal the patient's nephrologist to use the shunt again for IV antibiotics, (2) the patient's unwillingness to go through the diarrhea she had experienced after the IV medication, and (3) the fact that the full remission had been temporary, in spite of only partial relapse.

Discussion

Antibiotic combinations are standard treatments for HS [1]. A few reports have noted the improvement of HS with a combination of powerful antibiotics. The bacterial microbiome plays an important role in the initiation, pathogenesis, and progression of HS [1]. Killing the bacteria and down regulating the reaction of the immune system in HS ameliorates the disease.

The use of powerful antibiotics is likely under-reported in the literature, but as the pictures contained herein attest, this modality can be strikingly effective against HS. Notably, a 4 patient case study **[**2**]** based on the compassionate usage of combination antimicrobial treatment found that powerful intravenous antibiotics in combination with oral antibiotics were highly effective for Stage 2 HS. Two patients with severe stage 2 HS took ertapenem (a carbapenem class drug), which has its antimicrobial effect through inhibiting cell wall synthesis, but does not treat MRSA. The patients had a complete remission; one of these patients also took oral metronidazole, rifampin, and linezolid 1200 mg, each daily for a month, then moxifloxacin, and amoxicillin **[**2**].** Two other severe stage 2 HS patients took intravenous ceftriaxone with excellent results; one of these patients also took rifampin, moxifloxacin, and metronidazole. All 4 patients achieved complete remission with the absence of any inflammatory lesions. This report was predated by a report in 2009. Gül [3] reported an HS patient who had acute bacterial meningitis treated with intravenous ceftriaxone (2 x 2 g/day) for 21 days and linezolid (2 x 600 mg/day) for 28 days. Besides successful treatment of the meningitis, significant improvement of the abscesses and fistulas of HS was also achieved. An assessment of the bacteriology of HS found that the highest effectiveness against isolates was observed for carbapenems. The usefulness of penicillins combined with β-lactamase inhibitors and fluoroquinolones trailed behind in effectiveness (8.5%, 11.9%, and 11.9% of resistant strains, respectively) [4].

Linezolid is extremely expensive orally or intravenously. Linezolid has the advantage of having an IV and oral form allowing one to switch. Linezolid can be used in patients of all ages and in people with liver disease or poor kidney function. The potential adverse effects of short-term use include headache, diarrhea, and nausea. Long-term use, however, has been associated with serious adverse effects; linezolid can cause bone marrow suppression and low platelet counts, particularly when used for more than two weeks [6]. If used for longer periods still, linezolid may cause irreversible peripheral neuropathy, optic nerve damage [7], and lactic acidosis [8], all most likely owing to mitochondrial toxicity [9]. The patient herein suffered none of these side effects and her labs were monitored constantly at her thrice-weekly dialysis sessions.

Carbapenems are a class of β-Lactam antibiotics with a broad spectrum of antibacterial activity. They have a structure that renders them highly resistant to most β-lactamases. There are 4 types of carbapenems available in the United States doripenem, imipenem, meropenem, ertapenem. Of these, meropenam, and ertapenam appear to be the safest agents.

Meropenem was used in this case intravenously and dosed once a day in the setting of ESRD. The intramuscular formulation of meropenem may cause symptomatic local reactions at the injection site such as discomfort and occasionally pain or inflammation [10]. The spectrum of action of meropenem includes many gram-positive and gram-negative bacteria (including pseudomonas) and anaerobic bacteria. The overall spectrum is similar to that of imipenem, although meropenem is more active against enterobacteriaceae and less active against gram-positive bacteria. Meropenem is also very resistant to extended-spectrum β-lactamases, but may be more susceptible to metallo-β-lactamases. Meropenem is frequently given in the treatment of febrile neutropenia. This condition frequently occurs in patients with hematological malignancies and cancer patients receiving anticancer drugs that cause bone marrow suppression [10]. The FDA indications for meropenem are (1) complicated skin and skin structure infections, (3) complicated intra-abdominal infections, and (3) bacterial meningitis.

Ertapenem is an alternative carbapenem for treatment of HS. The FDA indications for ertapenem are (1) complicated skin and skin structure infections including diabetic foot infections without osteomyelitis, (2) complicated intra-abdominal infections, (3) community acquired pneumonia, (4) complicated urinary tract infections including pyelonephritis, acute pelvic infections, and postpartum endomyometritis, and (5) in adults for prophylaxis of surgical site infection following elective colorectal surgery. Interestingly, ertapenem, unlike meropenem, is highly protein-bound, which results in a longer half-life (4 hours). Ertapenem is not active against MRSA, ampicillin-resistant enterococci, *Pseudomonas aeruginosa*, or *Acinetobacter species*. Ertapenem also has clinically useful activity against anaerobic bacteria. Its optional use by intramuscular injection (IM) makes it the only IM carbapenem available in the United States. Local reactions of moderate-to-severe intensity at the infusion site occur but are infrequent and it also cause thrombocytopenia or bone marrow suppression infrequently [12].

Conclusion

This case highlights above all that a primary etiology of HS is stimulus of the immune system's over-reaction to the bacterial biome. If antibiotics are administered to a patient with stage 3 HS powerful enough to wipe out the bacterial biome, the immune system retreats, leaving permanent scarring in its wake.. The need for intravenous access and daily dosing along with the high cost complicates the use of powerful antibiotics that kill bacteria related to HS. The long-term burn-out of perhaps 20% of this patient’s lesions after IV antibiotics is interesting and parallels the effect that 10-12 weeks of clindamycin and rifampin or minocycline and rifampin can have on Stage I or early Stage II HS. The issue of resistance that will be generated with continuous

use of these powerful antibiotics must be considered as well. Knocking the bacteria down may give the immune system and the follicular unit the time to reset function, accounting for the limited but lasting effect of the IV treatment. Finally, the fact that the scars and strictures of HS remain even if there is no inflammation should make patients consider IV antibiotic treatment as a possible bridge to surgery. Effectiveness of this combination of antibiotics against HS suggests that neither *Pseudomonas aeruginosa* nor *Acinetobacter species* are important factors involved in HS; they are not covered by this effective IV combination for HS. It has yet to be defined whether these IV antibiotics should be given intermittently, used a bridge to surgery, or used in oral versions at lower doses. Nevertheless, an IV regimen may be considered in a patient with severe HS and this therapy could prove to be an effective bridge to other treatment modalities with longer-term results.

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