IBD Live Case Series: Case 12: Non-healing Gluteal Ulceration in a Patient with Crohn’s Disease

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Abbreviations: MRI = magnetic resonance imaging; MRSA = methicillin resistant staphylococcus aureus; IL-1 = interleukin 1; IL-6 = interleukin 6; TNF-α = tumor necrosis factor alpha

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PRESENTATION
By Dr. Corey A. Siegel: Gastroenterology, Dartmouth
Date of Presentation: June 29, 2017

This is a fairly complex patient and I would like to get some input from the group regarding how to proceed. The patient is a 23-year-old woman who has had ileocolonic Crohn's disease since the age of 15 with perianal involvement. She is from Saratoga, New York, where she is very active and works as a stage manager in a theater. Her perianal disease was limited earlier on, requiring just one seton until her recent problem. Her ileocolonic disease, however, has followed an aggressive course. Within a year of diagnosis, she went to an ileocecal resection and primary ileocolonic anastomosis. She did well for a short period of time off of all medication. Then she became more symptomatic and was started on infliximab. When she was given her first dose of infliximab, she reported feeling some tightness in her chest. She experienced chest tightness again when she was given the second dose. The infliximab was subsequently discontinued.

For a period of time, the patient remained off of all medications. Thereafter, she was started on certolizumab pegol and she experienced chest tightness after
receiving the first injection. After the second injection, she again experienced chest tightness and the medication was discontinued. She was then started on vedolizumab in April of 2016 but it didn’t appear to provide any benefit. Subsequently, her colonic disease became significantly more symptomatic. Over the past 18 to 24 months, this lesion developed starting at her anus then moving on to her sacrum forming a long, deep, fissured, region of ulceration that you can see in this photo (Figure 1). This second photo gives a closer view (Figure 2). The perianal lesion prompted her providers to recommend a diversion. A diverting loop ileostomy was completed in April of 2016 for persistent perianal disease. The patient had remained on vedolizumab after having her surgery because she thought that she might be having some improvement. In January of 2017, she was switched to ustekinumab. Since January, she reports that her lesion has progressively worsened. Currently, the lesion is her most salient complaint although she continues to have a lot of output from her rectum.

She passes tannish mucus six to eight times per day with some associated discomfort. She also has some left sided abdominal pain, which she attributes to her colon still being active. Within the past few months, she had a colonoscopy that showed significantly friable, pale mucosa. Upon air insufflation, there was some bleeding. The endoscopist’s note suggests that it was hard to tell between Crohn’s disease and diversion colitis but there was probably an element of both. She presented to clinic yesterday with this lesion.

To summarize, the patient has a diverting ileostomy, which was performed with the hope that this perianal lesion would get better. She has been on two anti-
TNFs that she has had trouble tolerating although I’m sure you’re all wondering whether she really had a reaction to them or whether something else was going on. She is on ustekinumab right now and things are getting worse. Question number one is, what is this? And the second question is, given what has been done already, what would you do next? She and I would greatly appreciate any input that you might have.

Dr. Miguel D. Regueiro (Gastroenterology, Cleveland Clinic)

Thank you, Corey. This is a complicated case, and it is obviously unfortunate for the patient. I know you just met her yesterday and you may have limited information at this time. I have a couple of questions before we open this up to others. Unfortunately we do see these types of lesions as well. I’m not sure there is ever an easy answer. My first question is, was this ever a site where they did an extensive fissurectomy, fistulotomy, or incision and drainage? I’m thinking about pathergy in pyoderma. Or was this lesion something that blossomed on its own?

Dr. Corey A. Siegel (Gastroenterology, Dartmouth)

This was something that I had wondered. Yesterday, I asked one of my colorectal surgeons to come in and look at the lesion and that was the first question that she asked as well. The answer is no. Other than having a seton placed a couple of years ago in the right perianal region, she has not had any manipulation in that area. It blossomed on its own, to use your words.
Dr. Miguel D. Regueiro (Gastroenterology, Cleveland Clinic)

How many doses of ustekinumab has she had?

Dr. Corey A. Siegel (Gastroenterology, Dartmouth)

She has been receiving regular doses after starting with an IV loading dose in January. I am not sure how many doses that works out to be, but she has received about 6 to 7 months of ustekinumab.

Dr. Miguel D. Regueiro (Gastroenterology, Cleveland Clinic)

We can go around our virtual room and, for those sites where there are surgeons present, we welcome your surgical input as well. Hans, have you seen this before? What do you think it is and what would you do?

Dr. Hans H. Herfarth (Gastroenterology, University of North Carolina)

Yes, I have seen this before. To me, this is pyoderma, which often develops independently of Crohn’s disease activity in many patients, but may resolve by treating the underlying IBD. In her case, the pyoderma could still reflect some remaining inflammatory activity in the colon. In a similar patient with Crohn’s ileocolitis and a diverting ileostomy as well as severe perianal pyoderma lesions, I performed a colectomy without success because I thought that perhaps the remaining colonic inflammatory activity was the trigger for the perianal pyoderma lesions. I tried a number of systemic drugs, including cyclosporine and cyclophosphamide without success. One can try a topical steroid spray, such as
fluticasone, four times a day. That at least often keeps the pyoderma at bay. One can also inject triamcinolone around the lesion, which I did in my patient. However, local triamcinolone injections have systemic steroid side effects that I only realized after my patient became Cushingoid. I injected about 20 mg of triamcinolone every four weeks. After failing all the above therapies, my patient improved on a combination of infliximab, which initially did not help, and thalidomide. Aside from blocking TNF activity, thalidomide, in contrast to infliximab, also has some anti-angiogenic activity. I assume that the neovascularization was blocked by thalidomide and that with the combination of both drugs her lesions completely closed.

Your patient has been on infliximab only, so given my experience, one could consider starting her on adalimumab as well as thalidomide. Or you could add the thalidomide to the ustekinumab. However, a thalidomide prescription is not straightforward and you have to have to obtain a specific certification before you can order it for your patient. She is a young woman, so you also would have to perform pregnancy tests every four weeks. I would try hyperbaric oxygen. Corey is absolutely set up to try that at Dartmouth. Unfortunately, there is no one size fits all kind of treatment for this issue. Kim Isaacs had two patients for whom medical honey worked. All the different medical approaches reflect the treatment dilemma for pyoderma lesions. It’s a trial and error process to find the right medication or combination of medications.
Dr. Miguel D. Regueiro (Gastroenterology, Cleveland Clinic)

Thank you, Hans. First of all, Hans feels that this is pyoderma or something like pyoderma and makes suggestions from cyclophosphamide to thalidomide to medical honey to injecting steroids. Unfortunately, as Corey already pointed out, I think our standard medication for this patient would have been infliximab. The question is, did she have a true reaction to infliximab, and would you go back and try it again? And as I was hoping somebody would say, and Hans started off, that you’re at the hyperbaric oxygen treatment facility of the world. The question is, do you proceed with wound care and hyperbaric oxygen? Hershey, what your thoughts? Have you seen this type of lesion? What is it? What would you do?

Dr. Kofi Clarke (Gastroenterology, Penn State Hershey)

Miguel, I’ve never seen anything exactly like what Corey’s patient has. I share all of Hans’ thoughts in trying any of the medications that he mentioned. I would not have thought of thalidomide, but I think that’s a fine idea as well. I also think that we should specify a certain spectrum of time where we leave the patient on this therapy. Would it be six weeks or three months? If the patient does not show resolution or some significant benefit then maybe against all of what we know, you do a biopsy and see what it shows. And clinically, I agree with what Hans is saying. I don’t know if Manny has any additional thoughts.
Dr. Emmanuelle (Manny) D. Williams (Gastroenterology, Penn State Hershey)

We have used intravenous immunoglobulin (IVIG) for very severe pyoderma here with great success except for the unsuccessful reimbursement of such a therapy, but it was very helpful. I usually find that injected or systemic therapies work for pyoderma. One of our colleagues here mentioned using topical metronidazole (Metrogel) or silver-impregnated alginate, if the patient could keep a dressing on that area.

Dr. Corey A. Siegel (Gastroenterology, Dartmouth)

I’m not sure if it is possible to keep a dressing in place there. It's a tough spot, as you can see.

Dr. Miguel D. Regueiro (Gastroenterology, Cleveland Clinic)

Okay, so more aggressive wound care, similar to what we would do with our wound patients, might be helpful. And then Manny has suggested using IVIG with topical metronidazole and silver alginate being additional suggestions. I will tell you that we have several of these patients that are just brutally difficult. Unfortunately, the wounds of a couple of these patients have gotten so deep that they have had coccygeal osteomyelitis and severe wound complications like we might see with some of our worst wound patients. Our colleagues at Maryland, what your thoughts? Have you seen this type of lesion and what would you do for it?
Dr. Raymond K. Cross (Gastroenterology, University of Maryland)

I have seen this once, and it looked exactly like the picture that Corey showed. In some of our previous IBD LIVE sessions, we have seen patients that we treated for manifestations of Crohn's disease and found that what they really had were infectious complications. So I think that when you see something weird, it’s good to step back and get your dermatologist involved if it is an area that’s accessible for biopsy and culture. I think that’s always a good place to start to make sure that we are not missing something unusual. With the patient that I had, we thought it was an unusual manifestation of perianal Crohn’s. We put her back on infliximab and treatment doses of azathioprine, and we used wound care, and she closed completely. I think looking for unusual infections like atypical mycobacterial infections, and getting your dermatologist involved, would be good ideas.

Dr. Miguel D. Regueiro (Gastroenterology, Cleveland Clinic)

All right, so get dermatology involved. Again, we hear the idea of using the combination of a thiopurine and anti-TNF if she can tolerate it, and aggressive wound care, which is probably easier said than done with the location of this lesion. So our colleagues at Rochester, what are your thoughts?

Dr. Arthur J. DeCross (Gastroenterology, Rochester)

Well, I have seen this type of lesion a couple of times. One case did not respond to the diverting ileostomy. Our ostomy nurses are certified in wound care and this patient received aggressive wound care and was started on adalimumab.
That patient did ultimately respond, but it was a long, slow course. The second patient had an ileostomy when she was referred to us and she did not respond to anti-TNFs and ultimately was lost to follow up. We were thinking about a completion proctectomy. I think that today I would probably be pushing such a patient toward hyperbaric oxygen therapy and aggressive wound care.

Dr. Lawrence J. Saubermann (Pediatric Gastroenterology, Rochester)

I have seen similar severe cases of pyoderma but they have responded to the infliximab. Getting the dermatologist involved and trying some intralesional steroids may help.

Dr. Arthur J. DeCross (Gastroenterology, Rochester)

I guess the case does beg the question whether it is worthwhile to try this patient on adalimumab just to see what would happen.

Dr. Miguel D. Regueiro (Gastroenterology, Cleveland Clinic)

I see that Corey is taking notes. Your patient has been on two anti-TNFs and I wonder if you could coax her into a third. We use thiopurines for some of these cutaneous lesions, so the question is whether she could tolerate something like that as well? Corey, when we end with you, I am curious to hear your thoughts on hyperbaric oxygen given your research there and with others that you are working with. Our colleagues at Yale, please share your thoughts?
Dr. Myron H. Brand (Gastroenterology, Yale)

We agree with what everybody else has said. I have seen one case that is similar and I thought of it as being a pyoderma-type lesion. Obviously, wound care is critical. We talked about hyperbaric oxygen. I wonder about topical tacrolimus. You have to culture this and maybe even biopsy it, if possible, just to make sure that it is what you think it is. We agree with the other recommendations and that is what we would be trying.

Dr. Miguel D. Regueiro (Gastroenterology, Cleveland Clinic)

Thank you, Myron. Let’s go to Boston. Boston, what do you think is the answer?

Dr. Francis A. Farraye (Gastroenterology, Boston Medical Center)

I agree with Ray. Before we all jump on the pyoderma bandwagon, we should consider alternative infectious diagnoses. Although it clearly looks like pyoderma and is ulcerated, it does not have the classically violaceous borders. I would want to be sure that we were not missing a second diagnosis. Again, she’s only on ustekinumab and this lesion predated the ustekinumab. She was on vedolizumab previously so she was not severely immunosuppressed to think about a Mycobacterium infection or something of that nature. We have seen several cases of metastatic Crohn’s disease respond to ustekinumab. It would be nice to know where it actually started. If this patient did not have Crohn’s disease, the lesion could be a pilonidal cyst that has spread in some way, shape, or form. Although our number
one diagnosis is pyoderma, we would get our dermatology colleagues involved
despite the caveats of pathergy. Unless they said it was classic, we would want to get
tissue to rule out other superimposed infectious complications, especially if we will
end up giving her thalidomide, tacrolimus, or another agent that will further
immunosuppress her.

Dr. Miguel D. Regueiro (Gastroenterology, Cleveland Clinic)

So, Frank is saying what many others have said. He feels that you should take
a step back, make sure this is not an infection or opportunistic infection, before
pursuing other immunosuppression, and he agrees with the same theme of
aggressive wound care. Samir, what your thoughts?

Dr. Samir A. Shah (Gastroenterology, Rhode Island)

I agree with what has been said, especially when Ray and Frank said to make
sure we are not missing something. If it were not something infectious, I would
encourage aggressive wound care. From there, you can add on other strategies, such
as hyperbaric oxygen and your favorite biologic as well as getting dermatology
involved.

Dr. Miguel D. Regueiro (Gastroenterology, Cleveland Clinic)

David Keljo at Children’s Hospital in Pittsburgh, have you seen this type of
lesion? What are your thoughts?
Dr. David J. Keljo (Pediatric Gastroenterology, Children’s Hospital of Pittsburgh)

I can’t say that I have ever actually seen this. I did find some interesting thoughts in the discussion particularly regarding the biopsy, but also trying thalidomide and IVIG. If one were going to try an anti-TNF again, I might think about pre-medicating her with steroids to avoid having symptoms like she had experienced previously. That is really all that I have to offer.

Dr. Miguel D. Regueiro (Gastroenterology, Cleveland Clinic)

The thalidomide and IVIG come up again. Let’s return to our surgical and medical colleagues in Pittsburgh. At the very least, Corey, I think that you can tell her that ten sites in the United States have discussed her issue. I don’t know if that is better or worse, but you can say we care and we have discussed her case. So, Dave and Andrew and any others in the room, could you share your thoughts?

Dr. Andrew R. Watson (Colon & Rectal Surgery, University of Pittsburgh)

I’ll take the surgical approach here. First of all, it is a hard location for a wound due to the mechanics of sitting causing pain. Ambulation disrupts your dressings. It is also a hard area socially, and we see these challenges. I do agree with what Frank and Ray had said about wanting to make sure that there is nothing else underlying. I did not hear about imaging, so that may be something I am sure was done. You would want to make sure there is an MRI of the pelvis at the very least to look for a reaction to a deeper collection, which I think is unlikely, but you would not want to miss that. Also the extent of any fistulizing disease or ongoing proctitis
may affect your decision-making. There are two issues here. There is treating this lesion and there is also the sequelae of what happens if you cannot treat it. When you divert these patients, much of the time it is for symptomatic relief, but the diversion in and of itself is not a cure because you still have ongoing proctitis and also the excretion of mucus. Therefore, you could be on the edge of a slippery slope.

We have one patient that just broke 101 days in the hospital. The other one will probably die in the hospital in his mid-20s if I was going to guess. We are doing wound vacuum dressing changes two to three times a week on these patients. It is consuming a third of an O.R. block of quaternary colorectal surgery. It is extremely labor intensive and very hard because we need to flip a morbidly obese patient prone three times a week. So, when you get involved with these non-healing perineal wounds, quite frankly, I am not sure we have a good solution. This is a whole other discussion because we have burn-like patients on colorectal surgery. They are nutritionally compromised, socially compromised, and they have non-healing wounds.

With this patient in particular, I agree with taking a very aggressive medical approach, and making sure that there is nothing underlying from a surgical standpoint. Long term, I think you need to start setting expectations with these patients early. You need to forewarn them that socially, financially, and career-wise, if this does turn into one of those non-healing perineal wounds, they are entering a world that is very hard to manage. I do not know if we have an answer for this here at the University of Pittsburgh Medical Center and we can sincerely use some help at another tailored conference to present the long term sequelae of a non-healing
perineal wound because I am seeing one in clinic today that is a heavy smoker. We also have a second similar patient. If these come to fruition, this will consume almost one full colorectal block three times a week, which is non-viable for many reasons.

Dr. David G. Binion (Gastroenterology, University of Pittsburgh)

We have definitely seen this problem. I can probably name about 6 patients that we share here in Pittsburgh who have gone through similar issues. One thing that favors this patient doing well is that she is motivated. She has traveled from her home in New York to an expert site in New Hampshire. I think that bodes well and demonstrates that she will take an active role in her care. Many of the patients that Dr. Watson described who have struggled and failed to improve are challenged by complex social, psychological and chronic pain issues, which overwhelm their ability to effectively cope with the challenges of not only a chronic illness, but also a chronic non-healing perineal wound. Patients that have become despondent or unmotivated, or who exhibit this “passive death wish,” are on a pathway to failure.

The other point that can be considered revolves around the complex pathophysiology of this non-healing perineal wound. I do not think this is one problem, but instead is likely a superimposed series of problems. There is a perineal wound, which is located in an area of the body that has high bacterial and microbial colonization. The perineum is a warm and moist area of the body with skin folds and because of sitting and the necessity of clothing, this area traps moisture, further
increasing the risk for superinfection. The superinfection may often be polymicrobial with both bacterial and fungal organisms.

We have had patients with blistering skin disorders and pyoderma-like processes that get superinfected with organisms like MRSA. Superinfection with MRSA can become catastrophic, due to the aggressive and invasive nature of this microbe. One of the other issues emerging in the medical literature regards the biofilms that develop in chronic wounds. We are starting to recognize the role of the microbiome in the context of many disease processes, but chronic wounds will actually harbor a biofilm—a bacterial colonization that is exceptionally difficult to clear. It is very, very difficult to achieve bacterial eradication and biofilm sterilization using antibiotics. The location of a non-healing perineal wound essentially guarantees that polymicrobial contamination will rapidly reoccur.

One of the novel approaches employed by our colleagues at the University of North Carolina was the use of Medihoney® on the chronic wound. Medihoney® is actually a wound care product derived from honey that contains significant amounts of antimicrobial peptides, known as beta defensins, which are typically secreted by mucosal surfaces. Bees will use their saliva to create honey, and saliva is a rich source of defensins. Honey has been recognized to have medicinal properties for hundreds if not thousands of years. By applying a layer of antimicrobial proteins in the form of defensins onto the wound, there is a nonselective killing of bacteria in a biofilm. Some of the silver alginates that were also mentioned by some of our colleagues also have antimicrobial properties, which are non-selective and will potentially help control bacterial populations in a biofilm adherent to a wound bed.
The complexity of this clinical problem will be further intensified when immunosuppression is added to the clinical scenario. Immunosuppression is definitely going to be required, but it has a strong likelihood of exacerbating the local infection of the wound. Therefore, I would bring in the wound care experts to help gain control of the perineal wound as efficiently as possible. Hyperbaric oxygen may also have bactericidal effects as well, so I think that's an excellent consideration.

Dr. Miguel D. Regueiro (Gastroenterology, Cleveland Clinic)

Corey, I'll give my two cents and then we will get back to what your thoughts are especially since hyperbaric oxygen has been raised. Andrew, David, and I have shared a number of these patients. I agree with possibly backing off of immunosuppression initially and taking more of a pure wound care approach. I think that your approach in using hyperbaric oxygen for something like this may actually be a very good option. However, we have fully immunosuppressed these patients and as you have heard from my colleagues here, sometimes these wounds become superinfected. Once that cascade occurs, it is very difficult to return to a baseline and get them healed. She has a lot going for her now as mentioned by David Binion and I agree with that and I think backing off the immunosuppression. The other thing you do not want to be too aggressive with is having enthusiastic surgeons trying to consistently debride this lesion because that can be also problematic. Let me go back to you. Was any of this new and novel to you and do you have any additional thoughts?
Dr. Corey A. Siegel (Gastroenterology, Dartmouth)

Thanks everybody. I really appreciate your help. It sounds like I am not the only who has struggled with how to take care of this type of lesion. I thought some of the same things. I heard a lot of new ideas, which I think are great, including tacrolimus, medical honey, and IVIG. I did send her to the dermatologist. They were very kind. They work right down the road from us and they saw her right after my appointment. They thought that this did not look particularly like pyoderma. They called this pathergy associated with IBD. They were hesitant to biopsy, which I think is probably a wise move although I would have liked to see some tissue to help guide us a little bit further. Unfortunately, they did not culture it. I wish they had because I think that is a good idea as well.

As she left clinic, I told her this is great timing because we have an excellent forum. I told her I would be presenting her case to all of you. She was really appreciative of this opportunity, but she did leave thinking that we were going to start hyperbaric oxygen. I think I convinced her to give adalimumab a try. After she had this reaction to infliximab, they kind of twisted her arm to try certolizumab pegol and then she had a very similar reaction. Needless to say, she is hesitant, but I think I have convinced her that adalimumab would be a good idea to try. After hearing this, I think I will go back and make sure we get this cultured. She is trying to get hooked up with wound care locally. Hyperbaric oxygen is easier said than done. First off, she lives just short of three hours from here and it is a daily treatment for a couple of weeks. Fortunately, I have another patient from that
practice getting outpatient hyperbaric oxygen locally for their treatment of ulcerative colitis, which seems to be helping. So, we may be able to pull it off.

Miguel, I think your comments are important about maybe holding immune suppression for a little while. She has said she has only gotten worse since she has started the ustekinumab. So, we could stagger things a little bit and try hyperbaric oxygen. I will think about tacrolimus as well as adalimumab. A question that did not come up is whether anyone thinks a colectomy should be considered. She is still pretty symptomatic from rectal discharge that, perhaps, is driving things. I heard Hans mention that they did a colectomy on one patient and it did not help. That’s my fear with her, too. I cannot ever see her having her ostomy taken down, and I think she is fairly understanding of that fact. I asked her to hold off on surgery until we see how things go over the next few months, so your thoughts are greatly appreciated.

To comment on the imaging, she did have a recent magnetic resonance (MR) enterography and I had also suggested getting an MR of her pelvis. The MR enterography that did go down to her pelvis did not show anything, but I think we need a more dedicated scan to make sure we are not missing anything. So again, thanks Miguel for letting me add this on. She in particular was incredibly appreciative of the opportunity, and I really appreciate your help.

Dr. Miguel D. Regueiro (Gastroenterology, Cleveland Clinic)

We are curious to see what happens with her. I will make one brief comment on your colectomy comment that I think Hans said initially. I am not a surgeon, but unfortunately some of these patients who we try to aggressively do a colectomy or
even a proctectomy do not heal. I think your dermatologist’s comment on pathergy is very important. I completely agree with holding off or, at the very least, minimizing surgery, whether it’s in the form of debridement or colectomy.

FOLLOW UP

Based on evaluation from her gastroenterology team and consulting dermatologist, it was felt that the patient’s lesion was most likely related to pathergy, with or without associated pyoderma gangrenosum. The provider team and the patient incorporated joint decision-making, discussing all of her treatment options. Together, they decided to start adalimumab and hyperbaric oxygen therapy in conjunction with Medihoney® and topical corticosteroid cream and to provide close follow-up with wound care nurse specialists. With this treatment, she has had slow but significant improvement in the healing of this lesion. In June of 2018, approximately one year after her initial consultation, the lesion was almost completely healed (Figure 3).

DISCUSSION

Today’s case describes a 23-year-old female with ileocolonic and perianal Crohn’s disease that rapidly progressed to ileocolonic resection within a year of diagnosis. The patient had adverse reactions associated with anti-TNFs, which were quickly discontinued. Over the course of the past two years, she developed a large ulcerated lesion in her gluteal cleft that showed no improvement despite a diverting loop ileostomy and the addition of ustekinumab (Figures 1 and 2). At the time of
evaluation, the differential diagnosis for this gluteal lesion included pyoderma gangrenosum, inflammatory bowel disease (IBD) associated pathergy, perianal Crohn’s disease, hidradenitis suppurativa, pilonidal cyst, or a secondary skin infection.

Crohn’s disease and ulcerative colitis are not restricted to the gastrointestinal tract, but rather, are considered to be systemic inflammatory diseases that present in a number of associated extraintestinal manifestations. These manifestations are seen from 12% to 35% in patients with ulcerative colitis and between 25% and 70% in those with Crohn’s disease. Perianal Crohn's was the first consideration in the differential for this patient but her providers did not feel that this was a typical presentation of the disease. Crohn's disease is commonly complicated by perianal manifestations ranging from skin tags to fissures, abscesses, and perianal fistulas (Table 1). The true rate of perianal complications that Crohn’s disease patients will experience during the course of their disease is difficult to determine due to disparities in how perianal disease is defined. The incidence of perianal disease amongst individuals with Crohn’s disease has been described with a prevalence as low as 3.8% and as high as 80%.

In severe perianal Crohn’s, placement of a temporary diverting ileostomy or colostomy is a method of surgical management. The rationale behind this procedure is to reduce fecal flow across the affected area, allowing the mucosa to heal and lesions, such as fistulae or fissures, to close. Fecal diversion is not typically employed as a primary therapy because research has shown that individuals who undergo a diverting ileostomy or colostomy for perianal Crohn's disease seldom
have restoration of intestinal continuity.\textsuperscript{9-13} For the young woman that was discussed in this conference, the fact that her gluteal lesion did not improve with fecal diversion seems to support the idea that she may not have been manifesting perianal Crohn’s disease.

Another manifestation of IBD is pyoderma gangrenosum, a neutrophilic dermatosis primarily affecting patients aged 25-54 years without a clear gender predilection.\textsuperscript{14} The incidence of pyoderma in ulcerative colitis or Crohn’s disease has been reported to range from 0.5-1.9\%.\textsuperscript{15, 16} Pyoderma can be severe and debilitating. Although it may initially appear as a painful single lesion or multiple erythematous papules or pustules, pyoderma gangrenosum can quickly develop into deep excavating ulcerations with purulent but sterile infiltrate and violaceous borders.\textsuperscript{15} The diagnosis is one of exclusion. Histological findings in pyoderma are nonspecific; a biopsy from the periphery of the lesion can help to exclude other skin disorders. The pathogenesis of pyoderma gangrenosum is not fully understood although it is theorized to be a consequence of neutrophil dysregulation, which is reinforced by its clinical response to anti-neutrophilic agents (i.e. colchicine and dapsone).\textsuperscript{14} Genetic factors and systemic inflammation have also been discussed as potential contributors to these lesions. Pyoderma often presents on the extremities, although the lesions can appear anywhere on the body, with $\frac{1}{4}$ to $\frac{1}{2}$ of cases involving areas of trauma.\textsuperscript{14}

Pathergy is exaggerated skin injury that is frequently related to the induction or exacerbation of pyoderma in sites of incidental or iatrogenic trauma. Not all patients with pyoderma demonstrate pathergy and the phenomenon can occur in
the absence of pyoderma.\textsuperscript{2,17} The nature of pathergy is a reason to withhold a biopsy of suspected pyoderma gangrenosum, as biopsy can lead to a more eruptive and significant lesion. There are limited data regarding the frequency of pathergy among patients with IBD.

At present, there is no gold standard for the treatment of pyoderma. The goals of therapy include optimizing wound healing, controlling inflammation, and reducing pain and discomfort for the patient. According to the European evidence-based Consensus, pyoderma gangrenosum should initially be treated with systemic steroids, calcineurin inhibitors, or infliximab.\textsuperscript{18,19} A double blind, randomized controlled trial published in the \textit{British Medical Journal} in 2006 demonstrated that infliximab was superior to placebo in the treatment of pyoderma.\textsuperscript{20} This study remains the only randomized trial regarding the treatment of pyoderma.

Wound care is a critical supplement to systemic therapy for persistent pyoderma and chronic wounds. Wound healing can be optimized through the use of moisture-retentive occlusive dressings such as hydrogels for lesions with minimal exudates.\textsuperscript{21} When lesions are highly exudative, more absorptive dressings should be utilized including hydrocolloids, foams, and alginate fibrous dressings.\textsuperscript{14} Intralesional corticosteroids have been described as an adjunct to systemic therapies although they risk disrupting wound healing if they are injected too frequently. Triamcinolone acetonide diluted with 1% lidocaine to create a solution with a concentration of less than 10 mg/mL dosed every 4-6 weeks is thought to balance the risk of pathergy with the benefit of reducing inflammation.\textsuperscript{14,22}
Natural products, such as antioxidant therapies, are becoming increasingly popular for wound healing. These treatments are postulated to decrease wound oxidative stress, subsequently accelerating the rate of healing. Although many antioxidant therapies are available, Medihoney® is the only FDA approved antioxidant therapy for acute and chronic wound healing. Studies have shown that medical grade honey can decrease the time of wounds healing by secondary intention. A Cochrane evidence-based review concluded that there is high quality evidence that honey heals partial thickness burns 4-5 days more quickly than conventional dressings and moderate quality evidence that honey is more effective than antiseptic and gauze for wounds that have become infected after surgery. However, the authors of this review also concluded that it is unclear if honey is better or worse than other management options for acute or chronic wounds. The field of antioxidant therapy is growing and additional clinical trials will further elucidate the role of these treatments in wound healing.

Outside of antioxidant therapies and immunomodulators, hyperbaric oxygen therapy (HBOT) is a treatment modality that is relatively new to IBD management. HBOT has been pivotal in the management of arterial gas embolism, decompression sickness, and acute carbon monoxide poisoning. A large body of research has investigated HBOT as a treatment modality for chronic or problem wounds, such as diabetic foot ulcers, and the late effects of radiation injury. HBOT involves breathing 100% oxygen under increased atmospheric pressure in a controlled environment; it is generally safe and well tolerated. IBD is associated with a dysregulated tissue hypoxia response through the activation of pro-inflammatory...
cytokines and chemokines (e.g. IL-1, IL-6, TNF-α) as well as signaling pathways responsible for tissue response to hypoxia and wound healing, notably hypoxia inducible factor-1 (HIF-1) and heme-oxygenase pathways.\textsuperscript{32-34} Evidence suggests that HBOT is capable of upregulating these signaling pathways and suppressing the production of inflammatory cytokines by increasing plasma and tissue oxygen levels.\textsuperscript{34,35}

In a multi-center, double blind, randomized controlled trial, HBOT use as an adjunct to steroid therapy in hospitalized ulcerative colitis patients led to higher rates of response and remission as well as a reduction in colectomy rates.\textsuperscript{32} While recent research has been promising, further studies are needed to define the role of HBOT in ulcerative colitis. Some studies have explored the use of HBOT as an adjuvant treatment of perianal disease, acute wounds, as well as pyoderma gangrenosum.\textsuperscript{36,37} Although there are scarce controlled data, HBOT is an appealing option for a non-healing wound related to Crohn’s disease or for pyoderma with pathergy in the perianal region.

**EDITOR’S COMMENT**

Perianal complications of Crohn’s disease are fairly common.\textsuperscript{38} Manifestations such as fissures and fistulae are burdensome to clinicians and patients, and are associated with significant morbidity. Lesions in the perineal area can be extremely challenging to heal due to the mechanics of sitting, standing, and daily activities. Clothing can cause friction and also trap moisture, leading to secondary infection. Discerning whether a large non-healing lesion is related to
pathergy or pyoderma, or is a consequence of an untreated infection, often necessitates consultation with colleagues from Dermatology or Infectious Disease.

When a perianal wound arises in a patient with Crohn’s disease, ruling out infection is a logical first step. Nevertheless, the risk of worsening the extent of a lesion should be taken into account prior to biopsy. Systemic therapy with an anti-TNF agent may prove to be adequate treatment for smaller lesions. For larger lesions that are resistant to single agents, a combination of systemic and topical therapies is often employed. Novel antioxidant therapies, such as Medihoney®, are proving to be helpful topical remedies for various types of skin injuries. While its use is still in the early stages, HBOT may play a valuable role in achieving durable healing of problem wounds.
Figure 1: This photograph shows a deep, linear fissure surrounded by a thin, rolled margin with extension from the anus to the gluteal cleft at the level of the coccyx. The fissure was noted to be 18 cm long, 2 cm wide, and 1 cm deep.
Figure 2: On closer view, there was evidence of erythema and serous exudate from the gluteal lesion.

Figure 3

Figure 3: After close to one year of treatment with adalimumab and hyperbaric oxygen therapy in conjunction with Medihoney® and topical corticosteroid cream, the patient's gluteal lesion is almost completely healed.

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<td>Fistulas</td>
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