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CASE REPORT

CROHN'S DISEASE (CD) AND HIDRADENITIS SUPPURITIVA (HS): A RELATION YET TO BE PROVEN. THREE CASE REPORTS WITH LITERATURE REVIEW

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ABSTRACT

Objective: CD is an inflammatory gastrointestinal tract disease that may involve extra intestinal systems. HS is a chronic inflammatory skin condition. Both disorders have poorly understood mechanism. A relation has been described in literature. Similarities in treatments and the way patients respond to them. We will discuss different aspects of disease presentation and available treatment modalities from available literature.

Design: A report of three cases.

Results: Two patients were diagnosed with CD first with complicated disease course. The third case was diagnosed with HS first. All had complicated HS course the required surgery. One patient failed one biological agent and responded to other. The second was treated with cytotoxic agents with acceptable results. No cytotoxic or biological agents were used on the third patient yet.

Conclusion: A possible relation between two conditions is likely based on several case reports and retrospective cohort, however, a prospective study is needed to establish the relation and to shed more light on treatment of both condition simultaneously. Both have an impact on patients' life styles; it is crucial to anticipate the correlation to provide the best treatment. Obstacles are likely to emerge due chronicity and delay in diagnosis.

INTRODUCTION

A relationship between CD and HS has been suggested in several case reports. CD is a disorder of uncertain etiology that is characterized by trans-mural inflammation of the gastrointestinal tract. CD may involve the entire gastrointestinal tract from the mouth to the perianal area. Approximately 80 percent of patients have small bowel involvement, usually in the distal ileum, with one-third of patients having ileitis exclusively. One-third of patients have perianal disease. Hidradenitis Suppuritiva is a chronic inflammatory skin condition. Primary sites of involvement for HS are the intertriginous skin areas of the axillary, groin, perianal, perineal, and infra-mammary regions. The clinical manifestations vary, ranging from recurrent inflamed nodules and abscesses to draining sinus tracts and bands of severe scar formation.

Both disorders are inflammatory in nature and have a poorly understood mechanism that is believed to be multifactorial. Smoking is identified as a risk factor for both diseases. Interestingly, anti-TNF treatment for CD has been shown to improve HS that is resistant to other treatment modalities. Known risk factors for HS are diabetes, female gender and obesity. (1),(2),(3),(4)

Here we present three cases with a literature review.

Case 1

A 23-year-old Caucasian female smoker who is known to have large and small bowel fistulizingCrohn's disease for the past 10 years with a complicated history and recurrent flares while being treated with mesalamine, MTX (methotrexate), 6MP (6-mercaptopurine)and adalimumab. Two years later, she developed severe HydradinitisSuppuritiva in the axillary and perianal regions that required treatment with antibiotics and surgeryin which partial relief was achieved 'biopsies histologically confirmed the diagnosis of HS with an absence of granuloma'. Recurrence of HS and a flare of CD occurred within seven months of the last surgical intervention for HS. After treatment with antibiotics the patient was started on Certulizumab given at week 0, 2 and 4 then every 30 days as maintenance. Three years have passed after starting

Certulizumab; symptoms of both CD and HS are fairly well controlled.

Case 2

37 year-old Caucasian female heavy smoker who was diagnosed with CD 8 years ago with perianal involvement that has been treated with mesalamine and MTX. Five years later she developed groin and perianal cutaneous lesions with purulent fluctuant painful nodules. The histological picture after biopsy confirmed HS with no granuloma. Several topical and systemic antibiotic treatments were tried with moderate response. Her lesions also required surgical intervention with skin grafting. After achieving a partial remission of HS; she had a flare of her CD that was managed with IV steroids and 6-MP. No Anti-TNF alpha treatment has been tried thus far.

Case 3

A 28-year-old African American non-smoker obese male patient has been suffering from severe HS over the course of the past 2 years. He was first treated with topical and systemic antibiotics. Relapse and progression of HS in the axillary, groin and back of his neck required surgical excision and skin grafting. During the course of his hospitalization it was noticed that he had ahemoglobin level of 9. Laboratory studies revealed iron deficiency anemia. On further history taking, he admitted having an episode of diarrhea, abdominal cramps and blood in his stools that was self-limited. After discharge, the patient was seen by his primary care physician. He was referred to Gastroenterology. A colonoscopy was done showing mucosal edema and inflammation with skip ulcerations suggestive of Crohn's disease. Pathology reports showed focal ulceration with evidence of chronic inflammation; a diagnosis of CD was made.Up until this point his CD and HS has been stable.

Antibiotics (topical and systemic) and surgical intervention. Histological exam of excised skin lesions was diagnostic of HS with no evidence of granuloma. First case received biologic treatment with impressive improvement of both HS and CD. Initial control of CD symptoms achieved with Adalimumab then diagnosis of severe resistant HS and relapse of CD. Certulizumab was used with stabilization of both conditions. HS occurred in different areas; axillary and perianal (Case 1), groin and perianal (Case 2) and axillary, groin and back of the neck (Case 3). This suggests a genetic component rather than assuming that peri-anal CD predisposed patients to HS.

Several case reports and two retrospective studies;

* Van der Zee *et al*. (5) interviewed 102 CD patients about recurrent painful boils in the axillae and/or groin, study showed that 17% of CD patients had a history compatible with HS, again suggesting an association between HS and CD.
* * Church *et al*. (6) performed a retrospective review of hospital records of 61 HS patients and found that 24 also had a diagnosis of CD. The diagnosis of CD predated that of HS by an average of 3.5 years.

The use of Biological treatment such as Infliximab, adalimumab and certulizumab has been shown to improve both conditions.

Based on the available literature after failing the usual HS treatment modalities such as topical and systemic antibiotics, methotrexate, azathioprine and surgery; the use of anti TNF alpha agents has shown good response. Sometimes there is an overlap between the use of treatments. Usually infliximab is the first agent used followed by adalimumab and certulizumab.

Author	Year	Design	No.	A: HS then CD B: CD then HS	Sex	Anti-TNF alpha R: Refractory; required second line
I Blazquez	2013	Case report	1	B	F	Infliximab
Marques dos Santos	2012	Case report	1	B	F	Infliximab(R) - Adalimumab
SKoilakou	2010	Case Report	1	B	M	Infliximab(R) - Adalimumab
S. Yazdanyar	2010	Case report	2	A,A	F,F	Infliximab
HH Van der Zee	2009	Retrospective	102	*	M,F	N/A
R S Goertz	2009	Case report	1	B	M	Infliximab(R)
Y.L. Rosi	2005	Case Report	1	B	F	Infliximab
M Roussomoustakaki	2003	Case report	1	A	F	Infliximab
K S *Katsanos*	2002	Case report	1	B	M	Infliximab
F Martinez	2001	Case report	1	B	F	Infliximab
M K Roy	1997	Case report	1	A	M	N/A
EV Tsianos	1995	Case Report	1	B	M	N/A
AA Kafity	1993	Case report	1	B	M	N/A
RL Attanoos	1993	Case report	3	B,A,B	F,M,M	N/A
J M Church	1993	Retrospective	61	**	M,F	N/A
C Gower -Rousseau	1992	Case report	3	B,B,B	M	N/A
NP Burrows	1992	Case report	2	A,A	M,F	N/A
LS Ostlere	1991	Case Report	3	B,B,B	F,F,M	N/A

DISCUSSION

Characteristics of the three cases: Two F and one M. The prevalence of both conditions is higher in females. All three had CD and severe HS. First two cases had a Diagnosis of CD first. Third case had a diagnosis of HS first that lead to investigation and diagnosis of CD. First two cases were smokers. Third patient is morbidly obese which is a risk factor is for HS. All three did not have a family history of either HS or CD. Complicated management of HS that required

As mentioned above two of the reported cases (Marques dos Santos and SKoilakou)were refractory to Infliximab in relieving symptoms of HS and preventing CD relapses which required the use of another Anti TNF alpha agent; adalimumab with better results. However, R S Goertz suggested that the longer the duration lapses before the use of infliximab the more likely it will fail. Hence the use infliximab sooner is better. Also, L Machet *et al* (8) reported that failure of

infliximab treatment for HS when it coexists with other inflammatory conditions such as CD is high.

CONCLUSION

A possible relation between two conditions is likely based on several case reports and retrospective cohort. A retrospective study can be useful to establish an association; however, more solid data needs to be gathered from a prospective study. That can also provide more data on best available treatment options. Limitations for a prospective study are likely to emerge due to the nature of both diseases in terms of chronicity and delay in diagnosis hence long term follow up is needed. A high dropout rate will be expected so a large sample size will be necessary which will be difficult to attain even if the study is done in a tertiary Gastroenterology referral center.

The coexistence of both diseases in one patient has a robust impairment on life style; which is why it is crucial to anticipate the correlation to provide the best treatment. This co-morbidity has great influence on the management of the two diseases and all health care providers should be aware of the association to prevent inappropriate or sub-optimal treatment.

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