GAVIN PUBLISHERS

Clinical & Experimental Dermatology and Therapies

Guglielmetti A. Clin Exp Dermatol Ther 2017: J116.

Case Report

DOI: 10.29011/2575-8268/100016

Remission of Metastatic Crohn's Disease Achieved with Dapsone: A Case Report and Review of the Literature

Antonio Guglielmetti[1], Matías Gompertz[2], Catalina Jahr[3], Sergio González[4], Tomás Silva[3]

[1]Chief of Dermatology Department, University of Valparaíso, Chile

[2]Dermatology resident, Pontifical Catholic University, Chile

[3]Medical student, University of Valparaíso, Chile

[4]Chief of Pathology Department, Pontifical Catholic University, Chile

[*]**Corresponding author:** Antonio Guglielmetti. Chief of Dermatology Department, University of Valparaíso, Chile Tel: +56-998260809; E-mail: antonioguglielmetti@yahoo.it

Citation: Guglielmetti A, Gompertz M, Jahr C, González S, Silva T (2017) Remission of Metastatic Crohn's Disease Achieved with Dapsone: A Case Report and Review of the Literature. Clin Exp Dermatol Ther 2017: J116. DOI: 10.29011/2575-8268/100016

Received Date: 1 February, 2017; **Accepted Date:** 24 February, 2017; **Published Date:** 2 March, 2017

Abstract

Metastatic Crohn's disease (MCD) is a rare manifestation of Crohn's disease (CD) defined by the presence of infiltrating granulomatous skin lesions in areas anatomically separate from the affected bowel sites. In adults, it is usually seen in patients already diagnosed with CD, while in children it can be the first manifestations of CD. There is no solid evidence to recommend treatment. We present a case of MCD successfully treated with oral dapsone achieving complete remission after failure of corticosteroids.

Introduction

Dapsone is an antibiotic of the sulfone family with bacteriostatic, anti-inflammatory and immunomodulatory effects. As an antibacterial, it inhibits bacterial synthesis of dihydrofolic acid via competition with para-amino-benzoate for the active site of dihydropteroate synthetase. The anti-inflammatory and immunomodulatory effects are still not fully understood and it's thought the to act through the blockade of myeloperoxidase. It's effective in inflammatory diseases that have in common an infiltration of large numbers of polymorphonuclear leukocytes, predominantly neutrophils [1,2].

There is no solid evidence to recommend treatment in MCD. MCD usually has a chronic course with exacerbations and remissions and treatment is often unsuccessful [3,4]. Corticosteroids and antibiotics (mainly metronidazole) are the most used therapies described in the literature [3-5]. Biologic therapies have become an important tool for managing a number of inflammatory dermatoses, and are often used to sustain remissions of CD. Their use for the treatment of MCD has also been recognized. Specifically, the TNF-alfa inhibitors adalimumab and infliximab have been used successfully in cases of MCD refractory to traditional therapies [6-8] never the less, its use in our country is limited by the high cost. The use of dapsone has been mentioned in few cases of cutaneous manifestations of CD, but not as treatment in MCD [1,2].

Case Report

An 82-year-old woman diagnosed with Crohn's disease 20 years ago with colostomy due to total proctocolectomy, presented with a 2-year story of painful lesions on her groin, genital region and gluteal cleft, with exacerbations and partial remissions. 10 years ago she had similar lesions in her infraabdominal fold with spontaneous resolution. (Figure 1,2,3)

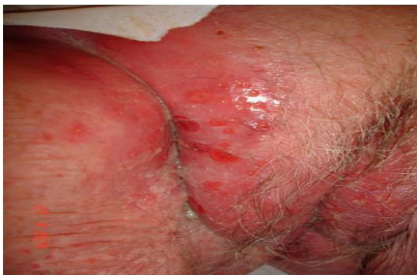

Figure 1: Lesions in the groin and genital area

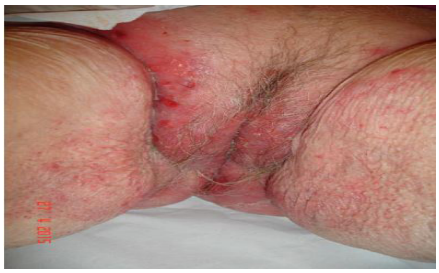

Figure 2: Lesions in the genital area

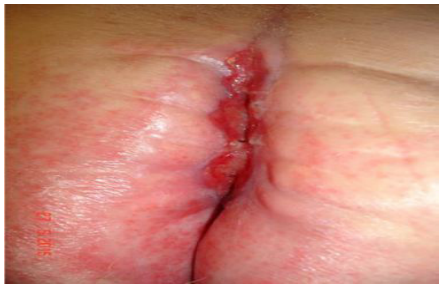

Figure 3: Lesions in the gluteal cleft

On examination, erythematous plaques with shiny surface, erosions and multiple ulcers with little purulent exudate were seen in the mentioned areas. Routine laboratory test were normal. Skin biopsy showed perivascular and periadnexal noncaseating granulomas, with numerous giant cells and dermis with perivascular lymphocytic infiltration. The diagnosis of metastatic Crohn's disease was made.

We first started topical therapy with corticosteroids and antibiotics along with oral prednisone (0.5 milligram per kilogram per day). There was no significant improvement, so a change to dapsone was made, raising the dose up to 150 milligram per day with fast and significant response, achieving almost full remission in three months. (Figure 5,6)

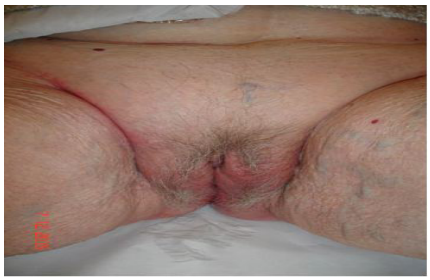

Figure 4: Lesions in the genital region after treatment with dapsone

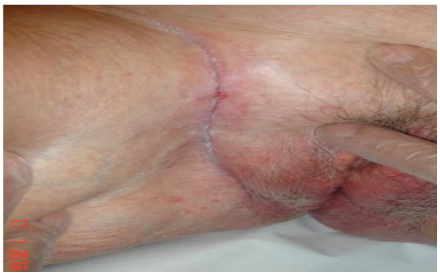

Figure 5: Lesions in the groin after treatment with dapsone

Discussion

MCD is considered a rare disease, therefore it doesn't exist enough evidence to support any specific treatment, although multiple case-report therapies have been informed as successful [3-5]. Even though spontaneous resolution of MCD has been described, it is infrequent and unpredictable, usually behaving as a chronic disease with multiple relapses. Medical treatment is frequently unsuccessful [3,4]. It is essential not just to treat MCD, but to manage with expertise CD, as this varies severity of the presentation. A retrospective review of 700 cases of CD suggested that skin lesions occur more frequently in patients with colon involvement compared with those having ileal involvement alone [9] this finding was supported by a subsequent large review. [10]

It is important to highlight that surgical resection of the affected bowel does not guarantee resolution of CD nor the skin lesions [3,4,11]. Severity of EC is not correlated with skin manifestations [3,12,13]. Most investigators have failed to detect a connection between the activity of skin and GI lesions. [14,15] MCD is considered an autoimmune chronic inflammatory disease, and the first choices of treatment are immunosupressors. Corticosteroids are considered the first line of treatment, either topical of high potency, or oral as prednisone 30 mg/day, with progressive

reduction. There are reports in literature that validate the use of oral metronidazole in high doses 800-1500 mg/day for at least 4 months. Other drugs such as metotrexate, azatioprine, ciclosporine and tacrolimus have also been used. In refractory MCD, biological treatment has been used (infliximab yadalimumab) [3,4,5,16].

There are no randomized clinical studies nor case reports of dapsone efficacy in MCD. The only information available is of its use in managing CD and skin lessions secondary to CD and refractory to conventional treatment. Cutaneous manifestations of CD not MCD respond well to treatment with dapsone, achieving full recovery in most cases [17-20]. Given the similar pathophysiologic and histology between EC and MCD, we thought dapsone to be a valid therapeutic option in view of the results previously described.

Dapsone toxicity may be categorized as either dose-dependent or idiosyncratic reaction. Most of the side effects are dose related and uncommon at doses lower than 100 mg/day. It's relevant to mention that the most dangerous adverse effects of dapsone are DRESS syndrome and hematologic alterations such as methemoglobinemia, aplastic anemia, leukopenia, agranulocytosis, eosinophilia, macrocytic anemia and Heinz bodie, which are dose-dependent and more common and severe in patients with gluclose-6-phosphate dehydrogenase deficiency. Patients generally tolerate 100 mg/day with very little hemolysis, at doses of 200-300 mg/day all patients develop hemolysis [1,2].

In summary, in MCD refractory to first line treatment with corticosteroids and metronidazole, dapsone should be considered as an alternative, taking into account the full recovery observed in our patient and the evidence available in the literature. Unfortunately, there is no solid evidence for it to be recommended, bearing in mind the low frequency of this disease, which complicate investigation.

References

1. Grunwald MH, Amichai B (1996) Dapsone - the treatment of infectious and inflammatory diseases in dermatology. Int J Antimicrob Agents 7: 187-192.
2. Wozel G, Blasum C (2014) Dapsone in dermatology and beyond. Arch Dermatol Res 306: 103-124.
3. Kurtzman D, Jones T, Lian F, Peng LS (2014) Metastatic Crohn's disease: A review and approach to therapy. J Am Acad Dermatol 1: 804-813.
4. Palamaras I, El-Jabbour J, Pietropaolo N, Thomson P, Mann S,et al. (2008) Metastatic Crohn's disease: a review. J Eur Acad Dermatol Venereol 22: 1033-1043.
5. Siroy A, Wasman J (2012) Metastatic Crohn Disease: a rare Cutaneous Entity. Arch Pathol Lab Med 136: 329-332.
6. Escher JC, Stoof TJ, van Deventer SJ, van Furth AM (2002) Successful treatment of metastatic Crohn disease with infliximab. J Pediatr Gastroenterol Nutr 34: 420-423.
7. Miller AM, Elliott PR, Fink R, Connell W (2001) Rapid response of severe refractory metastatic Crohn's disease to infliximab. J Gastroenterol Hepatol 16: 940-942,
8. Lestre S, Ramos J, Joao A, Serrao V (2010) Cutaneous Crohn's disease presenting as genital warts: successful treatment with adalimumab. Eur J Dermatol 20: 504-505
9. Greenstein AJ, Janowitz HD, Sachar DB (1976) The extraintestinal complications of Crohn's disease and ulcerative colitis: a study of 700 patients. Medicine (Baltimore) 55: 401-411.
10. Rankin GB, Watts HD, Melnyk CS, Kelley ML Jr (1979) National Cooperative Crohn's Disease Study: extraintestinal manifestations and perianal complications. Gastroenterology 77: 914-920.
11. Thukral C, Travassos WJ, Peppercorn MA (2005) The Role of Antibiotics in Inflammatory Bowel Disease. Curr Tret Options Gastroenterol 8: 223-228.
12. S, Pasmatzi E, Monastirli A, Tsambaos D (2006) Cutaneous manifestations of inflammatory bowel disease. Hosp Chron 1: 158-168.
13. Marotta PJ, Reynolds RP (1996) Metastasic Crohn's disease. Am J Gastroenterol 91:373-375.
14. Macaya A, Marcova IJ, Bordas X, Moreno A, Vazquez S, et al. (2003) Crohn's disease presenting as prepuce and scrotal edema. J Am Acad Dermatol 49: S182-183.
15. Parret CM, Bahmer FA (1987) Extensive necrobiosis in metastatic Crohn's disease. Dermatologica 175: 208-212.
16. Romero M, Alcántara M, Muñoz C, Zaida A, Guardiola A, et al. (2010) Enfermedad de Crohn metastásica. Gastroenterol Hepatol 33: 440-444.
17. Ward M, Mcmanus J (1975) Dapsone in crohn's disease. Lancet 305: 1236-1237.
18. Prantera C, Argentieri R, Mangiarotti R, Levenstein S. (1988) Dapsone and remission of Crohn's disease. Lancet 1: 536.
19. Spencer B, Nanavati A, Greene J, Butler DF. (2008) Dapsone-responsive histiocytoid Sweet's syndrome associated with Crohn's disease. J Am Acad Dermatol 59: 58-60.
20. Kemmler N, Pfannschmidt N, Strohal R (2012) Orofacial granulomatosis as first manifestation of Crohn's disease: successful treatment of both conditions with a combination of infliximab and dapsone. Acta Derm Venereol 92: 406-407.