Dermatologic manifestations in inflammatory bowel disease in Tunisia

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Manifestations cutanées des maladies inflammatoires chroniques de l'intestin en Tunisie

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R É S U M É

Prérequis : Les manifestations cutanées liées aux maladies inflammatoires chroniques de l'intestin (MICI) sont les plus fréquentes parmi les manifestations extra-digestives associées à MICI.
But : Evaluer le profil epidemio-clinique des manifestations cutanées liées aux MICI.
Méthodes : Une étude prospective descriptive a été conduite pendant un an. Nous avons systématiquement examiné la peau, les muqueuses, les cheveux et les ongles, de tous les patients ayant une MICI
Résultats : Cent quatre-vingt-quinze patients ont été inclus dans l'étude. La maladie de Crohn (MC) a été notée dans 154 cas (79.8%), la rectocolite ulcéro-hémorragique (RCH) dans 39 cas (21 %) et les colites inclassables dans 2 cas. Des manifestations cutanées ont été observées dans 91 % des cas de MC et dans 92 % de cas de RCH. Les lésions cutanées granulomateuses périanales étaient les manifestations cutanées les plus fréquemment notées au cours de la MC (53 %). Les aspects les plus communs étaient les fistules ano-périneales et les fissures oedémateuses et infiltrées ano-périnéales et génitales. Des dermatoses réactionnelles (érythème noueux, pyoderma gangrenosum, aphtes) ont été notées dans 14 cas. Les manifestations cutanées liées à une malabsorption étaient aussi fréquemment observées (101 cas) (51.7%)). D'autres dermatoses impliquant des mécanismes divers comme le psoriasis, la pelade, le vitiligo, la rosacée et le lichen plan ont également été signalés. Des manifestations cutanées secondaires au traitement (folliculite, acné, rash maculo-papuleux et DRESS syndrome) étaient présents dans 16 cas.
Conclusion : Notre série est caractérisée par une prévalence élevée des manifestations cutanées liées aux MICI. Une meilleure connaissance de ces manifestations cutanées pourrait améliorer la prise en charge de ces maladies chroniques.

M o t s - c l é s

Manifestations cutanées, Maladie, Inflammatoire, chronique, intestin, Crohn, rectocolite ulcéro-hémorragique

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S U M M A R Y

Background: Cutaneous manifestations are the most common extra intestinal manifestations associated with inflammatory bowel disease (IBD).
Aim: To assess the epidemio-clinical profile of skin manifestations in IBD.
Methods: A prospective and descriptive study was conducted. We have examined skin, mucosa, hair and nails, of all patients with an IBD during one year.
Results: One hundred-ninety-five patients were included. Crohn's disease (CD) was noted in 154 cases (79.8%), ulcerous rectocolitis (UC) in 39 cases (21.2%) and inclassable IBD in 2 cases. Cutaneous manifestations were found in 91% of Crohn's patients and in 92% of UC patients. Granulomatous perianal skin lesions were the main cutaneous manifestations of CD (53%). The most common affected sites were ano-perineal fistulae, perianal and perineal fissures and oedematous and infiltrated perianal and genital plaques. Reactive lesions (Erythema nodosum, Pyoderma gangrenosum, Aphthous stomatitis) were noted in 14 cases. Skin manifestations due to malabsorption were also frequently observed (101 cases: 51.7%). Other dermatoses implicating various mechanisms such as psoriasis, alopecia areata, vitiligo, rosacea, lichen planus, were also noted. Adverse skin manifestations due to treatment
(folliculitis, acne, macula-papular rash and DRESS syndrome) were present in 16 cases.
Conclusion: Our series is characterized by a high frequency of cutaneous manifestations associated to IBD. A better recognition of these skin manifestations by the physician may improve their management.

K e y - w o r d s

Dermatologic manifestations, Inflammatory Bowel Diseases, Crohn, Ulcerative rectocolitis

Extra intestinal manifestations (cutaneous, musculoskeletal, hepatobiliary, ocular, and metabolic conditions) may occur in one third of patients with inflammatory bowel disease (IBD) [1]. Of those patients, up to one third will develop skin manifestations [1]. Habitually, skin signs are related to the bowel disease activity but they may have an independent course. Five cutaneous manifestations may be identified:
1) specific granulomatous skin lesions including fissures and fistulas, mucosal nodularity (cobblestoning), pyostomatitis vegetans, and metastatic Crohn's disease,
2) Reactive lesions: erythema nodosum, pyoderma gangrenosum, aphthous stomatitis, and necrotising vasculitis,
3) Cutaneous manifestations secondary to nutritional malabsorption: acrodermatitis enteropathica (zinc), scurvy (vitamin C), purpura (vitamin C and K), pellagra (niacin), stomatitis-glossitis-angular cheilitis (vitamin B), non-specific eczema and dry skin (essential fatty acids) and abnormal hair and nails (protein) and 4) Miscellaneous: epidermolysis bullosa acquisita, vitiligo, psoriasis, alopecia areata, secondary amyloidosis, and bowel associated dermatosis-arthritis syndrome, probably explained by similar genetic and autoimmune mechanisms 5) skin drug effects [2].
The aim of our study was to assess the epidemio-clinical characteristics of cutaneous manifestations in IBD from a prospective recruitment of patients with IBD.

PATIENTS AND METHODS

Through a prospective descriptive study, we have systematically examined skin, mucosa, hair and nails, of all patients with an IBD followed in the Department of Gastroenterology of la Rabta Hospital from October 2007 to february 2009.

RESULTS

One hundred-ninety-five patients were included in the study. There were 103 male and 92 female with a sex-ratio (M/F) of 1.12. The mean age was 39.5 years ± 20.5.
Crohn's disease (CD) was noted in 154 cases (79.8%), ulcerous rectocolitis (UC) was observed in 39 cases (21.2%) and inclassable IBD was present in 2 cases.
The mean age of CD patients was 36 years +/- 20. Their sex ratio (M/F) was 1.44. The mean age of UC patients was 44.8 years +/- 22. Their sex ratio (M/F) was: 0.69.
Skin manifestations were observed in 182 cases (93%) [141 cases with CD (91%) and 36 cases in UC (92%)] (table1). Granulomatous perianal skin lesions were the most common skin manifestations in CD (81 cases: 53%) (table2). They occurred in 10% of cases at CD diagnosis and in 50% during the course of the disease. Digestive CD was located in the ileum in 35 cases (22.7%), in the colon in 40 cases (26%) and in the ileo-colonic areas in 79 cases (51%). Main aspects of granulomatous skin lesions were ano-perineal fistulae (30 cases = 37%), perianal genital and perineal fissures (20 cases = 24.7%), and oedematous infiltrated perianal and genital lesions (20 cases= 24.7%) (figures 1, 2). Severe lesions included profound infiltrated ulcerations that destroyed the anal sphincter in 5 cases (figure 3), abscesses of anoperianal areas in 2 cases, and communicating rectovaginal profound fistulae and scarring in 7 cases. Reactive lesions were present in 14 cases (table 1).

Figure 1 : Oedematous infiltrated perianal lesions with profound raghades and pseudocondylomatous skin lesions

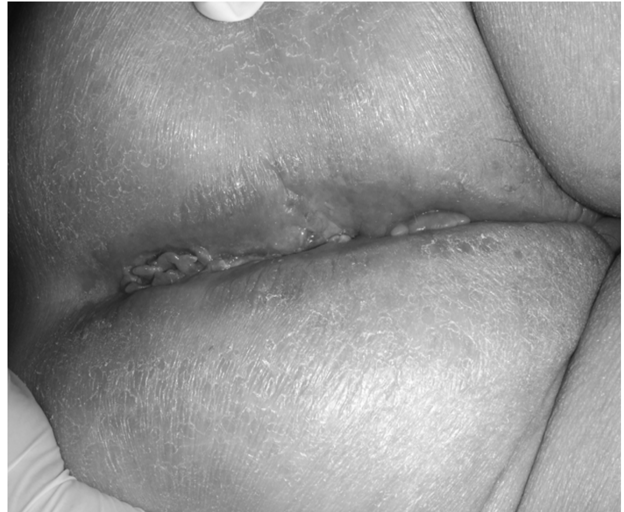
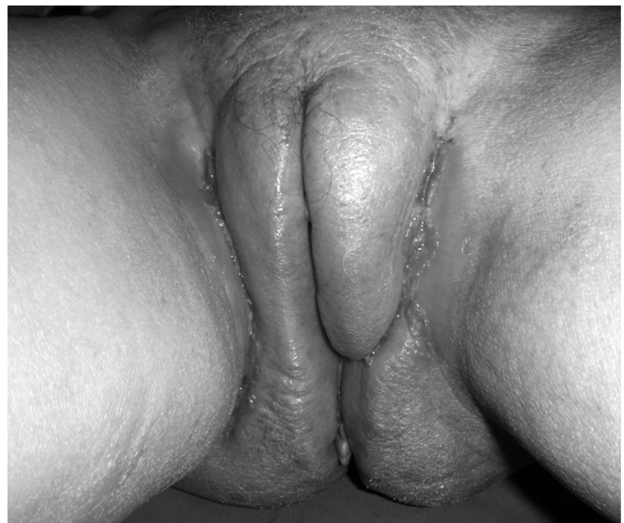


Figure 2 : Oedematous infiltrated genital lesions with profound raghades on inguinal folds



Erythema nodosum was observed in 5 cases (4 with Crohn's disease and one with UC). Pyoderma gangrenosum (PG) mainly the pustular (n=2) and ulcerative (n=3) forms were noted in 5 cases (4 cases in CD, 1 case in UC) (figure 4). Recurrences of PG lesions were linked to CD digestive disease in 3 cases. Aphthous stomatitis was present in 2 cases of CD (table 2).
Skin signs in relationship with malabsorption were frequently observed (101 cases: 51.7%) (table 1).

Table 1 : Main skin manifestations in IBD cases

	Total Cases (195)	Type of lesions	Detailed cases	%
Specific lesions	84 cases (43.1%)	fistulas, infiltrated deep rhagades and ulcers site: anoperineal and genital folds	84	43.1
Reactive lesions	12cases (6.1 %)	Pyoderma gangrenosum	5	2.5
		Erythema nodosum	5	2.5
		Stomatitis aphtosis	2	1
Cutaneous manifestations due to malabsorption	101 cases (51,7 %)	Ichtyosiform skin	53	27
		Hair loss	31	15.8
		Eczematous dermatitis	15	7.6
		Glossitis	2	1
Other dermatoses	28 cases (14.3 %)	Psoriasis	10	5.1
		Rosacea	8	4.1
		Lichen planus	4	6.1
		Vitiligo	3	1.5
		Alopecia areata	2	1
		Neurofibromatosis	1	0.5
Fungal infections	46 cases (23 %)	Tinea pedis, intertrigo	46	23
Adverse skin manifestations due to treatment	16 cases (8.2%)	Acneiform dermatitis	4	2
		Folliculitis	6	3
		Maculopapular rash	5	2.5
		DRESS syndrome	1	0.5

Figure 3 : Profound infiltrated ulcerations that destroyed the anal sphincter

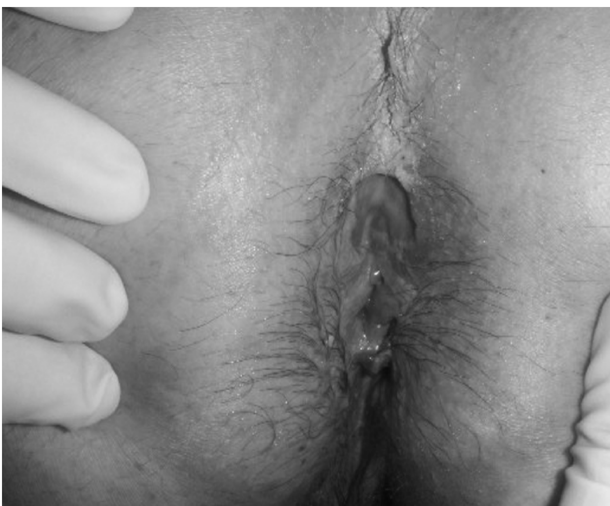


Figure 4 : Pyoderma gangrenosum lesions in a patient with Crohn's disease

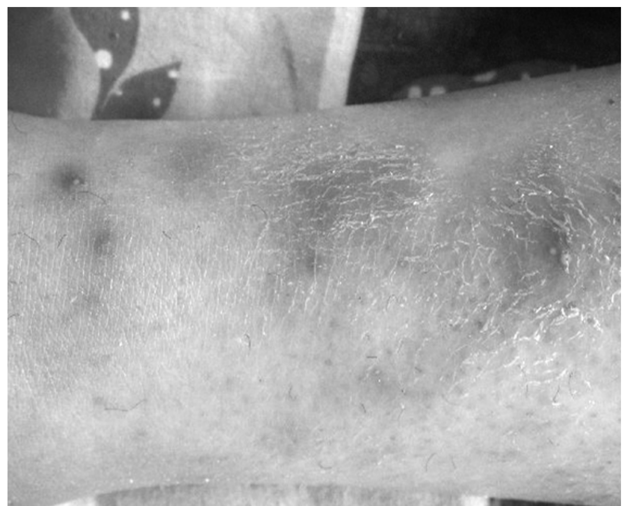


Table 2 : Prevalence of cutaneous signs in CD

Crohn's disease	Total 154 cases	Type of lesions	Detailed cases	%
Specific lesions related to CD	81 cases (52.8 %)	fistulas, infiltrated deep rhagades and ulcers Lesions site: anoperineal and genital folds	81 / 154 CD cases	52.6
Reactive lesions	10 cases (6.4 %)	Pyoderma gangrenosum	4	2.6
		Erythema nodosum	4	2.5
		Stomatitis aphtosis	2	1.2
Cutaneous manifestations due to malabsorption	64 cases (41.5 %)	Ichtyosiform skin	37	25.3
		Eczematous dermatitis	12	7.7
		Alopecia - hair loss	24	15.5
		Glossitis	1	0.6
Association to other dermatoses	22 cases (14.2 %)	Psoriasis	7	4.5
		Rosacea	7	4.5
		Lichen planus	3	1.9
		Vitiligo	2	1.3
		Alopecia areata	2	1.3
		Neurofibromatosis	1	0.6
Fungal infections	39 cases (25.3 %)	Tinea pedis, intertrigo	39	25.3
Adverse skin manifestations due to treatment	9 cases (5.8%)	Acneiform dermatitis	3	1.9
		Folliculitis	2	1.2
		Maculopapular rash	4	2.6

An acquired icthyosiform aspect of lower limbs was the most common manifestation (53 cases: 27%), mainly observed in CD patients (70%) (table 2). Hair loss, in relationship with iron deficiency anaemia was also frequently noted (31 cases: 15.8%), especially in CD patients (77%). Besides, eczematous dermatoses were noted in 15 cases (7.6%), mainly in CD patients (80%). On the other hand various dermatoses including psoriasis, alopecia areata, neurofibromatosis, vitiligo, rosacea and lichen planus were associated to IBD in 28 cases (14.3%), mainly with CD cases (78.5%) (table 1). Fungal infections of feet were commonly reported in our series (46= 23%) especially in CD patients (84.6%).

Finally, drug skin effects were noted in 16 cases. Acneiform dermatitis and folliculitis were the most common skin side effects (10 cases), observed equally in 5 cases in CD and UC cases. A maculo-papular rash was noted in 4 cases of CD and 1 case of UC and a DRESS syndrome were reported in UC (table 3). A skin biopsy was performed in 30 cases. It revealed specific granulomatous lesions in relationship with CD in 22 cases, an aspect of pyoderma gangrenosum in 5 cases, an aspect of lichen planus in 2 cases, and epidermal necrosis with dermal lymphocytic infiltrate predominating around vessels in relationship with drug rash eruption in one patient.

DISCUSSION

Inflammatory bowel diseases (IBD) are chronic systemic disorders that are often associated with extra intestinal manifestations, complications, and other autoimmune disorders [1, 3]. Cutaneous alterations are the most frequent extra intestinal manifestations associated with IBD [4]. Their prevalence varies from 2% to 36% [3, 5]. Cutaneous manifestations are more common in CD than in UC [3]. Christodoulou reported a skin sign incidence of 13% in UC patients and of 24.3% in CD patients [3]. In our series, 141 patients with CD (91%) and 36 with UC (92%) had cutaneous manifestations.

Concerning specific granulomatous skin lesions in CD disease, perineal and peri anal lesions are commonly reported (50% cases). They include infiltrated ulcerations, fissures, oedema, abscesses and complex fistulae [6]. Patients who have CD in the colon alone or in the colon and bowel are more likely to have perianal involvement than those who have small bowel disease alone [7]. Typical genital finding are swelling, fissure ulcerations, oedema, and skin tags involving the vulvar and perivulvar regions [8]. Metastatic cutaneous CD is a rare

Table 3 : Prevalence of cutaneous signs in UC

UC	Total 39 Cases	Type of lesions	Detailed cases	%
Ano-genital lesions	3 cases (7.6 %)	Fissure	3	57.6
Reactive lesions	2 cases (5 %)	Pyoderma gangrenosum	1	2.5
		Erythema nodosum	1	2.5
		Ichtyosiform skin	16	41
Cutaneous manifestations due to malabsorption	36 cases (92.3 %)	Eczematous dermatitis	12	30.7
		Hair loss	7	17.9
		Glossitis	1	2.5
Other dermatoses	6 cases (15.3 %)	Psoriasis	3	7.6
		Rosacea	1	2.5
		Lichen planus	1	2.5
		Vitiligo	1	2.5
		Alopecia areata	0	0
		Neurofibromatosis	0	0
Fungal infections	7 cases (17.9 %)	Tinea pedis, intertrigo	7	17.9
Adverse skin manifestations due to treatment	7 cases (17.9%)	Acneiform dermatitis	1	2.5
		Folliculitis	4	10.2
		Maculopapular rash	1	2.5
		DRESS syndrome	1	2.5

complication defined as the occurrence of specific granulomatous skin lesions remote from the intestinal disease [9]. Typical histopathological findings in specific skin lesions show habitually lymphocyte and macrophage infiltration of the lamina propria mucosae, non-caseating granulomas, oedema, fibrosis and crypt abscesses [8].
In our series, 52% CD's cases had granulomatous perianal and genital lesions. No metastatic skin lesions were observed.
Concerning reactive lesions, erythema nodosum, neutrophilic dermatoses and aphtous lesions are commonly reported. In his IBD series, Danese has noted 10% of aphtous stomatitis, 5% of erythema nodosum and 2% of pyoderma gangrenosum [6].
Besides, in another study, Christodoulou reported oral aphtous ulcers in 8.1% of CD cases versus 6% in UC cases, erythema nodosum in 10.8% of CD cases versus 2.7% in UC cases and pyoderma gangrenosum in 5.4% of CD cases versus 0% in UC cases [3].
In our series, reactive lesions were present in 6.4% of CD and in 5% of UC. They mainly included pyoderma gangrenosum and erythema nodosum.
Malabsorption skin signs in IBL diseases are often due to ileal disorders (7,10). The main factors involving malabsorption in MICI diseases include low energy intake, poor digestion and absorption, bacterial overgrowth surgical resection, colonic losses and some pharmacologic agents [10]. The most frequent skin signs related to malabsorption are pigmentary disorders, skin xerosis, ichtyosiform and eczematiform dermatoses, follicular hyperkeratosis and mucous involvement (glossitis, cheilitis). Acrodermatitis enteropathica, caused by zinc deficiency, is rarely reported in IBD [6]. Latent forms of this dermatosis may occur more frequently in quiescent digestive IBL, taking aspects of localized genital intertrigo, oedematous vulvitis, scrotal painful erythema, cracked eczema [6].
In our series, ichtyosiform and eczematous dermatites and hair loss were the most frequent manifestations in relationship with malabsorption. Some inflammatory skin disorders associated with IBL are frequently reported. Psoriasis was the most common reported dermatosis (7-11% of cases). Autoimmune skin disorders such as vitiligo, polimyositis, lupus erythematosus, scleroderma and bullous pemphigoid are also associated, similarly in CD and in UC [7, 11, 12].
In our series, psoriasis and vitiligo, were found respectively in 5.1% and 1.5%.
Concerning cutaneous side effects of systemic therapies, only few cases of severe skin reactions are described [7]. Most of cases are related to systemic steroids such as cushingoid

changes, telangiectasia or skin infections and acneiform. Other commonly IBL prescribed drug such as sulfasalazine and azathioprine may cause maculo-papular rashes, erythroderma, DRESS (drug reaction eosinophilia syndrome) syndrome or exanthematic pustulosis [7, 10]. In our series, IBL Treatments were responsible of 8.2% of skin manifestations (5 cases of maculo papular rash and one case of DRESS syndrome in relationship with sulfasalazine and 10 cases of acneiform dermatitis and folliculitis in relationship with corticosteroids.

CONCLUSION

Our series is characterized by a high frequency of various cutaneous manifestations associated to IBD. A better recognition of the main cutaneomucosal manifestations of IBL disease may improve their management and early treatment.

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