

Colonic Melanosis: Insights From A Moroccan Ambispective Study

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Abstract:

Background: Colonic melanosis (CM) is a benign pigmentation of the colonic mucosa, most commonly associated with chronic use of anthraquinone-containing laxatives. While traditionally considered clinically insignificant, its potential association with colonic neoplastic lesions remains debated.

Materials and Methods: This single-center ambispective study included all cases of CM diagnosed at Cheikh Khalifa International University Hospital (Morocco) between January 2021 and May 2023. Seventy patients with complete clinical, endoscopic, and histological data were analyzed. Participants were stratified into diffuse versus segmental CM, and comparative analyses were performed to identify factors associated with the extent of pigmentation.

Results: Among 2,082 colonoscopies, 70 patients (3.36%) were diagnosed with CM. The mean age was 61.1 ± 15.5 years, with a female predominance (sex ratio 0.79). Most patients (97%) reported chronic anthraquinone-based laxative use. Constipation was the most frequent symptom (74.2%), followed by diffuse abdominal pain (51.4%). Endoscopically, diffuse CM was observed in 75.7% of patients, while segmental involvement occurred in 24.3%, predominantly affecting the right colon. Colonic polyps were detected in 32.8% of patients, with no significant difference between groups. Logistic regression identified older age ($p = 0.02$) and the presence of colonic diverticula ($p = 0.04$) as independent factors associated with diffuse CM. Histological analysis confirmed lipofuscin deposits in 16% of biopsied cases. All patients were advised to discontinue anthraquinone-containing laxatives.

Key Word: colonic melanosis, lipofuscin, anthraquinone laxatives, colonoscopy, colonic polyps, histopathology

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I. Introduction

Colonic melanosis is characterized by a brown-to-black pigmentation of the colonic mucosa, often detected incidentally during endoscopic examinations. This benign histopathological entity is defined by the intracellular accumulation of lipofuscin within macrophages in the lamina propria. It is classically associated with prolonged use of anthraquinone-containing laxatives, although cases without laxative exposure have also been reported in the literature. Historically considered clinically insignificant, colonic melanosis has recently garnered renewed interest due to its potential association with an increased prevalence of colonic polyps, particularly low-grade adenomas. However, no definitive correlation with colorectal cancer risk has been established to date. In this study, we report a series of 70 cases of colonic melanosis, aiming to describe the clinical, endoscopic, and histological features of this condition and to discuss its clinical significance in light of recent literature.

II. Material And Methods

Study Design: Single-center, ambispective observational study aimed at evaluating the clinical, endoscopic, and histological characteristics of patients with colonic melanosis and associated risk factors.

Study Location: The study was conducted at Cheikh Khalifa International University Hospital, a tertiary hospital in Casablanca, Morocco.

Study Duration: 29-month period, from January 2021 to May 2023.

Sample size: A total of 70 patients diagnosed with colonic melanosis were included.

No formal sample size calculation was performed, as all consecutive patients meeting the inclusion criteria during the study period were included.

Subjects & selection method: The study population was drawn from consecutive patients who undergone colonoscopy in the endoscopy unit of the gastro-enterology department.

Inclusion criteria: Patients were included if they had a confirmed diagnosis of colonic melanosis based on endoscopic examination.

Exclusion criteria: Patients with incomplete medical records were excluded from the study.

Procedure methodology:

After informed consent was obtained, a well-designed questionnaire was used to collect the data of the recruited patients retrospectively and prospectively. Data were systematically extracted from medical records using a standardized form. Collected information included patient demographics, clinical history, endoscopic findings, and histological results. In order to evaluate potential differences in clinical, endoscopic, and histological characteristics, patients were divided into two groups for comparative analyses:

A: cases with diffuse melanosis.

B: cases with segmental melanosis.

Statistical analysis:

Data analysis was performed using Jamovi software (version 2.7.13.0).

Descriptive statistics were used to summarize patient characteristics.

Groups A and B were compared.

Comparative analyses between groups were conducted using appropriate statistical tests:

Chi-square and Fisher exact tests were performed to test for differences in proportions of categorical variables between the groups. The level $p < 0.05$ was considered as the cutoff value or significance with a confidence interval of 95%. In order to identify the associated factors, we then performed a binomial logistic regression.

III. Result

Out of a total of 2,082 colonoscopies, 70 patients (3.36%) were diagnosed with colonic melanosis.

The mean age of the cohort was 61.1 ± 15.5 years, with a female predominance (sex ratio 0.79).

Regarding medical history, 37.1% of patients ($n=26$) had hypertension, 10% ($n=7$) were chronic smokers, and 7.1% ($n=5$) had a history of colorectal cancer, including 4.3% ($n=3$) who had undergone colonic anastomosis. One patient had ulcerative colitis, and 2.9% ($n=2$) had irritable bowel syndrome.

A majority of patients (97%, $n=68$) had previously used anthraquinone-based laxatives. Additionally, 2.8% ($n=2$) had taken NSAIDs, and 1.4% ($n=1$) had ingested raw senna.

Chronic constipation was the most prevalent symptom, affecting 74.2% of patients ($n=52$), followed by diffuse abdominal pain (51.4%, $n=36$) and abdominal bloating (20%, $n=14$).

Laboratory tests revealed anemia in 18.5% of patients ($n=13$) and hypocalcemia in 4.2% ($n=3$).

Endoscopic findings showed diffuse melanosis in 75.7% of cases ($n=53$), while 24.3% ($n=17$) exhibited segmental melanosis, predominantly affecting the right colon (52.9%, $n=9$). (Figure n°1, n°2)

Figure n°1: Severe diffuse melanosis with a leopard-skin appearance.

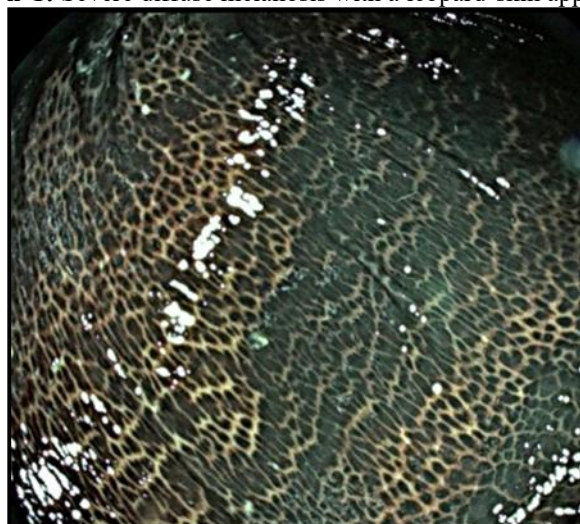
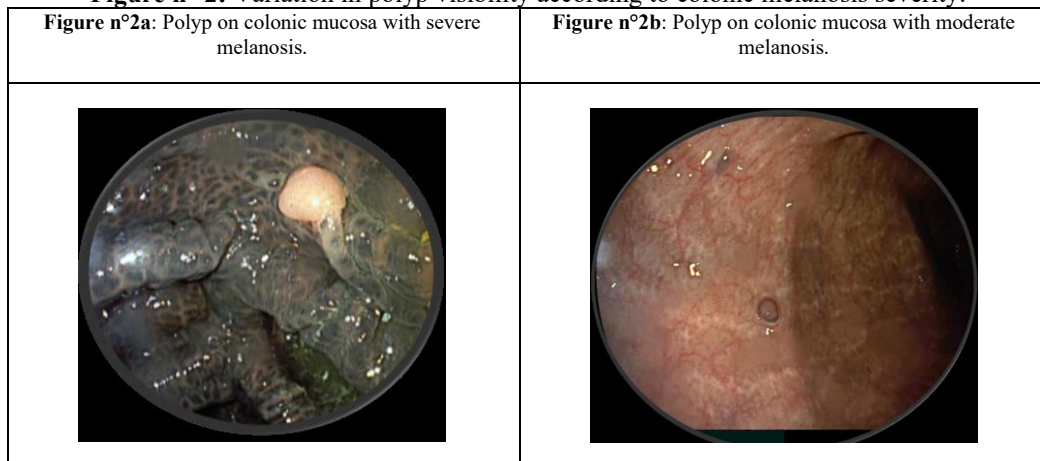


Figure n° 2: Variation in polyp visibility according to colonic melanosis severity.

Associated lesions included colonic polyps in 32.8% patients (n=23), uncomplicated colonic diverticula in 24.2% of patients (n=17), and ulcerative ileitis in 2.8% (n=2).

The overall polyp detection rate was 32.9%, with no significant difference between the two groups (p=1.00). Colonic biopsies were performed in 62.9% of patients (n=44), of which 16% (n=5) demonstrated lipofuscin deposits.

Table n°1 presents our patients characteristics according to the groups A (diffuse melanosis coli) and B (segmental melanosis coli).

Following colonoscopy, all patients were advised to discontinue anthraquinone-based laxatives and adopt hygienic-dietary measures for the management of constipation.

Table n°1: Patient characteristics according to the two groups.

N = 70	Group A (n=53)	Group B (n=17)	p value
Demographic features			
Gender (female)	27 (38.6%)	12 (17.1%)	0.17
Blood Hypertension	19 (27.1%)	7 (10%)	0.69
Smoking	7 (10%)	0 (0%)	0.18
History of colorectal cancer	5 (7.1%)	0 (0%)	0.32
Clinical features			
Chronic constipation	39 (55.7%)	13 (18.5%)	1.00
Abdominal pain	26 (37.1%)	10 (14.3%)	0.48
Abdominal bloating	10 (14.3%)	4 (5.7%)	0.73
Associated endoscopic lesions			
Colonic polyps	18 (25.7%)	5 (7.1%)	1.00
Uncomplicated diverticula	12 (17.1%)	5 (7.1%)	0.75
Ulcerative Ileitis	1 (1.4%)	1 (1.4%)	0.43
Histological findings			
Lipofuscin deposits	3 (4.3%)	2 (2.8%)	0.09

Comparative analysis using binomial logistic regression identified two factors associated with the extent of melanosis: age (p=0.02) and the presence of colonic diverticula (p=0.04). (Table n°2)

Table n° 2: Factors associated with diffuse colonic melanosis.

	OR	CI 95%	p value
Age	1.10	[1.01 – 1.20]	0.02
Gender	0.77	[0.12 – 3.89]	0.75
Blood Hypertension	0.22	[0.04 – 1.29]	0.94
Colonic polyps	0.60	[0.11 – 3.23]	0.56
Colonic diverticula	0.10	[0.01 – 0.86]	0.04

IV. Discussion

Colonic melanosis (CM) is a brown-to-black pigmentation of the colonic mucosa, most frequently detected incidentally during colonoscopy. It is generally regarded as a benign and asymptomatic condition, although its clinical significance remains debated, particularly regarding its potential association with colonic neoplastic lesions. In our study, the prevalence of 3.36% and the absence of a significant association with polyp detection support its benign nature, in line with most published data.

Histologically, CM is characterized by the intracellular accumulation of lipofuscin within macrophages of the lamina propria, without associated inflammatory response [1]. Contrary to what its name might suggest, the pigment is neither melanin nor hemosiderin. It does not stain with Fontana-Masson for melanin but is typically positive on periodic acid-Schiff (PAS) staining, confirming its lipofuscin nature [1]. In our cohort, lipofuscin deposits were confirmed in 16% of biopsies, which supports the lipofuscin nature of CM but also highlights variability in detection depending on the severity and distribution of pigmentation.

Pathophysiologically, colonic melanosis is strongly linked to chronic use of anthraquinone-containing laxatives, such as sennosides, cascara sagrada, or rhubarb [1,4]. These substances induce apoptosis of colonic epithelial cells, which are subsequently phagocytosed by macrophages, leading to lipofuscin accumulation. However, several studies have reported cases of CM in the absence of laxative exposure, suggesting that other mechanisms may contribute, including chronic constipation, low-grade inflammation, or alterations in the gut microbiota [4,7]. In our study, 97% of patients reported anthraquinone laxative use, which strongly reinforces this association, although a few isolated cases without exposure also support the possibility of alternative mechanisms.

Endoscopically, CM is easily recognized by its dark brown or black pigmentation, most commonly affecting the right or transverse colon, though it can involve the entire colon [4]. The rectal mucosa is typically spared in classic cases, although rectal involvement has been reported. CM should be distinguished from other forms of colonic pigmentation, such as intestinal pseudo melanosis, drug-induced deposits (iron, activated charcoal), or sequelae of colonic ischemia [6]. Our endoscopic findings, with diffuse involvement in 75.7% of cases and segmental melanosis predominantly affecting the right colon (52.9%), are consistent with these descriptions and confirm the right-sided predominance of CM.

The predictive or correlative value of CM regarding colonic polyps or adenomas remains controversial. Several studies have reported a higher prevalence of adenomatous polyps in patients with colonic melanosis [5,7], although this association is not considered independent after adjustment for age and other risk factors. In a prospective study by Nusko et al., including 304 patients, adenoma prevalence was significantly higher in patients with CM (31% vs. 18%) [5]. Conversely, other studies, such as that by Chien et al., found no statistically significant correlation between CM and polyps or colorectal cancer, suggesting that the observed association may be related primarily to aging and laxative use [7]. In our cohort, the overall polyp detection rate was 32.8%, with no significant difference between diffuse and segmental melanosis ($p=1.00$), aligning with studies reporting no independent association between CM and colorectal neoplasia.

Another important consideration is the reversibility of melanosis following laxative discontinuation. Studies have shown that pigmentation can resolve within a few months, typically between 6 and 12 months after cessation of anthraquinone-containing laxatives [2,3]. This supports the benign and reversible nature of CM, although persistence beyond one year has also been reported. In our study, all patients were advised to discontinue anthraquinone laxatives, but the absence of systematic follow-up prevents us from assessing reversibility, unlike many published prospective studies.

Our study has several methodological limitations, including its retrospective design, relatively small sample size, and lack of systematic long-term follow-up. Moreover, data on laxative use were primarily self-reported, which may introduce bias. Nevertheless, the study also has notable strengths, particularly the rigorous histological analysis and the diversity of clinical profiles included.

V. Conclusion

Colonic melanosis remains a benign and reversible condition, most commonly linked to chronic anthraquinone laxative use, as confirmed in our cohort. In this study of 70 patients, diffuse forms of melanosis were significantly associated with older age and a higher prevalence of colonic diverticula, while no difference was observed between diffuse and segmental melanosis regarding the detection of polyps or adenomas. These findings support the notion that CM is not an independent risk factor for colorectal neoplasia. Clinicians should nonetheless identify and address laxative overuse and consider CM as a marker of chronic bowel dysfunction. Further prospective studies are needed to better understand factors influencing the severity and distribution of melanosis.

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