

Colonoscopic Resolution of Melanosis Coli After Cessation of Senna Laxative Use

Toshimi Chiba^{1,*}, Ting Wang^{1,*}, Satoshi Kikuchi^{2,*}

¹Division of Internal Medicine, Department of Oral Medicine, Iwate Medical University, Morioka, Iwate, Japan; ²Department of Gastroenterology, Sanai Hospital, Morioka, Iwate, Japan

*These authors contributed equally to this work

Correspondence: Toshimi Chiba, Division of Internal Medicine, Department of Oral Medicine, Iwate Medical University, 19-1 Uchimarui, Morioka, Iwate, 020-8505, Japan, Tel +81 19 651 5111, Fax +81 19 654 3281, Email toschiba@iwate-med.ac.jp

Abstract: Melanosis coli occurs with the administration of stimulant laxatives for the relief of constipation. However, the duration of macroscopic improvement of melanosis coli after discontinuation of anthracene laxatives is not well understood. We describe the case of an 81-year-old female diagnosed with melanosis coli via colonoscopy who had been taking senna laxatives for 5 years. Seven months after cessation of senna laxatives, colonoscopy showed no melanosis coli in the colon. This impressive report describes the observation of melanosis coli with colonoscopy; 7 months after the withdrawal of senna stimulant laxatives, melanosis coli resolved.

Keywords: melanosis coli, colonoscopy, discontinued, senna laxative, anthraquinone

Introduction

Melanosis coli demonstrates abnormal brown or black pigmentation of the colonic mucosa and frequently found in patients with stimulant laxatives use.¹ It is often caused by the chronic use of anthracene derivatives, such as sennosoids and aloe.^{2,3} Stimulant laxatives can cause cellular damage to colonic epithelial cells, leading to apoptosis. Apoptotic cells are phagocytosed by macrophages and converted to brown lipofuscin pigment in the lamina propria, the coloration of melanosis coli may be due to accumulation of lipofuscin.⁴ Although melanosis coli did not represent a higher incidence of colorectal cancer compared with controls, clinical concern remains because melanosis coli is associated with a higher detection rate of colorectal adenoma.⁵⁻⁷ Melanosis coli can occur within only a few months of chronic laxative administration, and treatment of melanosis coli is stop laxative use.^{8,9} Once laxative use is halted, the dark pigmentations may resolve, it would take up to a year.¹⁰ The mean duration from the last diagnosis without melanosis coli to the time of initial diagnosis of melanosis coli was 24 months, whereas at least 2 years is period for melanosis coli to disappear.⁵ However, we do not know well the duration of macroscopic improvement of melanosis coli after discontinued anthracene laxatives. Here, we report a case of melanosis coli we could observe colonoscopy findings for 7 months after causative senna laxative cessation.

Case Report

An 81-year-old female had been an outpatient for treatment of hypertension for 10 years and was taking oral carvedilol 5 mg daily. She has been taking senna laxatives for 5 years because of constipation. She had been undergoing hemodialysis for about 2 years due to renal failure caused by membranous nephropathy. She underwent colonoscopy for further examination of constipation, a colonoscopy showed a sessile polyp in the sigmoid colon and revealed a brown and grey pigmented appearance throughout the colon, which was diagnosed as melanosis coli (Figure 1). We also graded the severity of melanosis coli (Grades I–III) based on the extent of pigmentation.⁷ Grade II melanosis coli was present in the rectum and descending colon, transverse colon, ascending colon and cecum, and Grade I melanosis coli was present in the sigmoid colon (Table 1). She was admitted to the hospital for a colon polypectomy. One year later, when the



Figure 1 Colonoscopy findings in the ascending colon after administration of senna laxatives for 5 years. Colonoscopy findings revealed a brown and grey pigmented appearance throughout the colon, which was diagnosed as melanosis coli Grade II in the ascending colon.

patient underwent colonoscopy for surveillance after colon polypectomy, colonoscopy findings showed that Grade II melanosis coli remained in the rectum, sigmoid colon, descending colon, ascending colon and cecum (Figure 2), and Grade III melanosis coli was present in the transverse colon. Then, the senna laxative was discontinued, and polyethylene glycol was administered. Seven months after cessation of senna laxatives, colonoscopy revealed that melanosis coli had disappeared in the rectum, sigmoid colon, descending colon, transverse colon, ascending colon and cecum (Figure 3).

Discussion

Colonoscopy reveals melanosis coli in patients receiving chronic administration of stimulant laxatives containing anthraquinone.¹ These laxatives pass through the colon, with a direct toxic effect on colonic epithelial cells, and may cause cell damage in the colon, leading to apoptosis. The apoptotic cells, which are thought to be a precursor of pigmentation formation, are ingested by macrophages and converted into brownish lipofuscin pigment in the lamina propria.⁴

Severe abdominal symptoms would not occur in patients with melanosis coli; colonic motility might be suppressed because of impairment to the myenteric plexus.¹¹ The age of onset is more than 60 years,^{10,12} and the incidence is higher in females than in males.¹²

Melanosis coli may develop 4 to 12 months after initiation of chronic laxative use.¹³ Melanosis coli is most commonly found in the proximal colon,³ probably due to the difference in the distribution of macrophages in the colon.¹⁰ The appearance of melanosis coli may vary throughout the colon on the basis of the amount of pigmentation or

Table 1 Grades of Melanosis Coli Severity by Location in the Colon

	First Colonoscopy	One Year After First Colonoscopy	Seven Months After Withdrawal of Senna Stimulant Laxatives
Cecum	Grade II	II	None
Ascending colon	Grade II	II	None
Transverse colon	Grade II	III	None
Descending colon	Grade II	II	None
Sigmoid colon	Grade I	II	None
Rectum	Grade II	II	None

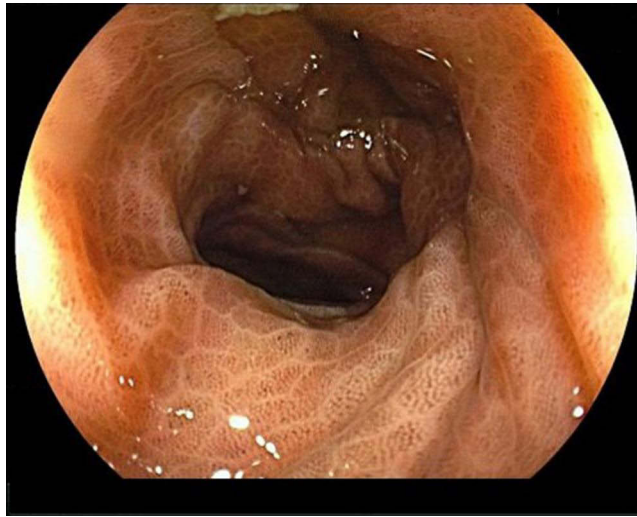


Figure 2 Colonoscopy findings in the ascending colon with continued administration of senna laxatives one year after the first colonoscopy. Melanosis coli Grade II was observed in the ascending colon.

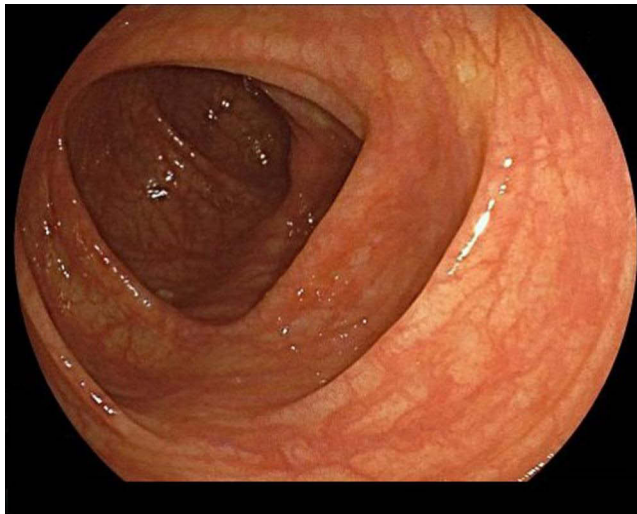


Figure 3 Colonoscopy findings in the ascending colon 7 months after discontinuation of senna laxatives. Seven months after discontinuation of senna laxatives, colonoscopy revealed disappearance of melanosis coli.

the amount of laxative absorbed.³ Stimulant laxatives inhibit epithelial tissue function, absorption, secretion and motility, and cause apoptosis, reflecting the qualitative and quantitative differences in colonic microbial flora.³ With the improvement of constipation symptoms and the withdrawal of laxatives, a large amount of lipofuscin is digested and decomposed by lysosomes, and pigmentation of melanosis coli can be alleviated and even disappear.¹⁴ In this case, 7 months after the discontinuation of senna laxatives, colonoscopy showed the disappearance of Grade II to III melanosis coli.

Melanosis coli has a higher detection rate of colorectal adenomas, while melanosis coli does not have a higher incidence of colorectal cancer compared to controls,⁵⁻⁷ the pathophysiology of these associations is not well understood. However, polypoid lesions appear pale and devoid of pigmentation in the colon.¹⁵ Because macrophages in the lamina propria are diminished in adenomas associated with melanosis coli,¹⁶ the presence of melanosis coli facilitates the detection of small adenomas in the colon.^{6,12} In one analysis, patients with melanosis coli were more likely to have an adenoma <5 mm.⁷ Some studies have suggested a possible relationship between melanosis coli and colorectal cancer risk;¹⁷ however, melanosis coli is not associated with a greater risk for colorectal cancer,¹⁰ and the association between

melanosis coli and colorectal cancer is controversial. The rate of apoptosis in patients with colonic melanosis was significantly higher than that of controls.^{16,18} The expression of p53, bcl-2, and Ki-67 was increased in severe melanosis coli compared with mild melanosis coli and controls.¹⁸ G-protein subunit γ 5 (GNG5) and lysophosphatidic acid receptor 3 (LPAR3) might be candidate biomarkers associated with apoptosis in melanosis coli.¹⁹

The prognosis of melanosis coli is favorable.⁶ It typically resolves with causative laxative cessation; however, rebound constipation can result. Recently, instead of stimulant laxatives, polyethylene glycol, secretagogues such as lubiprostone, and ileal bile acid transporter inhibitors such as elobixibat were recommended for constipation.^{20,21} In this case, the patient was on hemodialysis, but there are no reports on the relationship between melanosis coli and hemodialysis.

Histopathological follow up of the colonoscopy was not identified in this case, further investigation is required to confirm both colonoscopy findings and pathology examinations. The function of melanosis coli is still unclear, and its pathophysiology must be clarified.

In conclusion, this report describes the observation of melanosis coli with colonoscopy; 7 months after the withdrawal of senna stimulant laxatives, melanosis coli resolved. Histopathological follow up of colonoscopy should be considered in the future.

Ethics Statement

Based on the regulations of Iwate Medical University, institutional review board approval is not required for case reports.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case reported and any accompanying images.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

There were no funding sources.

Disclosure

The authors declare no conflicts of interest in this work.

References

1. Bockus HL, Willard JH, Bank J. Melanosis coli. The etiologic significance of the anthracene laxatives: a report of forty-one cases. *JAMA*. 1933;101(1):1–6. doi:10.1001/jama.1933.02740260003001
2. Modi RM, Hussan H. Melanosis coli after long-term ingestion of cape aloe. *ACG Case Rep J*. 2016;3(1):e157. doi:10.14309/crj.2016.130
3. Freeman H. "Melanosis" in the small and large intestine. *WJG*. 2008;14(27):4296–4299. doi:10.3748/wjg.14.4296
4. Benavides SH, Morgante PE, Monserrat AJ, Zárate J, Porta EA. The pigment of melanosis coli: a lectin histochemical study. *Gastrointest Endosc*. 1997;46(2):131–138. doi:10.1016/S0016-5107(97)70060-9
5. Katsumata R, Manabe N, Fujita M, et al. Colorectal neoplasms in melanosis coli: a survey in Japan and a worldwide meta-analysis. *Int J Colorectal Dis*. 2021;36(10):2177–2188. doi:10.1007/s00384-021-03970-2
6. Liu ZH, Foo DCC, Law WL, Chan FSY, Fan JKM, Peng JS. Melanosis coli: harmless pigmentation? A case-control retrospective study of 657 cases. *PLoS One*. 2017;12(10):e0186668. doi:10.1371/journal.pone.0186668
7. Blackett JW, Rosenberg R, Mahadev S, Green PHR, Lebwohl B. Adenoma detection is increased in the setting of melanosis coli. *J Clin Gastroenterol*. 2016;52(4):313–318. doi:10.1097/MCG.0000000000000756
8. Lecomte T, Chautard R, Orain I. A melanosis coli associated with a large flat adenoma of the cecum. *Clin Res Hepatol Gastroenterol*. 2019;43(3):228–229. doi:10.1016/j.clinre.2018.10.006
9. Cohen GS. Melanosis coli. *Clin Gastroenterol Hepatol*. 2020;18(7):e71. doi:10.1016/j.cgh.2019.03.032

10. Abu Baker F, Mari A, Feldman D, Suki M, Gal O, Kopelman Y. Melanosis coli: a helpful contrast effect or a harmful pigmentation? *Clin Med Insights Gastroenterol.* 2018;11:1179552218817321. doi:10.1177/1179552218817321
11. Smith B. Pathologic changes in the colon produced by anthraquinone purgatives. *Dis Colon Rectum.* 1973;16(6):455–458. doi:10.1007/BF02588868
12. Wang S, Wang Z, Peng L, et al. Gender, age, and concomitant diseases of melanosis coli in China: a multicenter study of 6090 cases. *Peer J.* 2018;6:e4483. doi:10.7717/peerj.4483
13. Ahasan H, Khan M, Mahbub M, et al. Melanosis coli-an atypical presentation. *J Med.* 2010;11:183–185. doi:10.3329/jom.v11i2.5469
14. Chen L. Effect of evidence-based nursing in patients with melanosis coli and the influence on improving constipation. *Clin Med Eng.* 2017;13:2180–2184.
15. Hung CY, Shyung LR, Chen MJ. Pigmentation sparing on melanosis coli. *Gastroenterology.* 2012;142(3):e10–e11. doi:10.1053/j.gastro.2011.07.032
16. Regitnig P, Denk H. Lack of Pseudomelanosis coli in colonic adenomas suggests different pathways of apoptotic bodies in normal and neoplastic colonic mucosa. *Virchows Arch.* 2000;436(6):588–594. doi:10.1007/s004289900178
17. van Gorkom BA, de Vries EG, Karrenbeld A, Kleibeuker JH. Review article: anthranoid laxatives and their potential carcinogenic effects. *Alim Pharmacol Ther.* 1999;13(4):443–452. doi:10.1046/j.1365-2036.1999.00468.x
18. van Gorkom BA, Karrenbeld A, van der Sluis T, Zwart N, de Vries EG, Kleibeuker JH. Apoptosis induction by sennoside laxatives in man; escape from a protective mechanism during chronic sennoside use? *J Pathol.* 2001;194(4):493–499. doi:10.1002/path.914
19. Hua X, Chen J, Wu L. Identification of candidate biomarkers associated with apoptosis in melanosis coli: GNG5, LPAR3, MAPK8, and PSMC6. *Biosci Rep.* 2019;39 pii(1):BSR20181369. doi:10.1042/BSR20181369
20. Lindberg G, Hamid SS, Malferteiner P, et al. World Gastroenterology Organisation. World Gastroenterology Organisation global guideline: constipation-a global perspective. *J Clin Gastroenterol.* 2011;45(6):483–487. doi:10.1097/MCG.0b013e31820fb914
21. Nakajima A, Taniguchi S, Kurosu S, Gillberg PG, Mattsson JP, Camilleri M. Efficacy, long-term safety, and impact on quality of life of elobixibat in more severe constipation: post hoc analyses of two phase 3 trials in Japan. *Neurogastroenterol Motil.* 2019;31(5):e13571. doi:10.1111/nmo.13571.

International Medical Case Reports Journal

Dovepress

Publish your work in this journal

The International Medical Case Reports Journal is an international, peer-reviewed open-access journal publishing original case reports from all medical specialties. Previously unpublished medical posters are also accepted relating to any area of clinical or preclinical science. Submissions should not normally exceed 2,000 words or 4 published pages including figures, diagrams and references. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/international-medical-case-reports-journal-journal>