

## CLINICAL CASE

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# Melanosis coli in two patients with colorectal neoplasia

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### Summary

*Melanosis coli is characterized by pigment deposition in the lamina propria and caused by increased epithelial apoptosis. Chronic laxative use induces melanosis coli and possibly increases colorectal cancer risk. We*

*report on two cases of melanosis coli, one with colorectal carcinoma and the other with adenoma.*

**Key words:** colorectal adenoma, colorectal carcinoma, melanosis coli

### Introduction

Melanosis coli refers to an abnormal brown or black pigmentation of the colonic mucosa caused by the presence of lipofuscin in macrophages within the lamina propria. Previous studies have linked the presence of lipofuscin to phagocytosis of epithelial cells which have undergone apoptosis.

We report on two cases of documented melanosis coli and colorectal neoplasia in adult men with laxative use which induce apoptosis of epithelial cells of the large intestine.

### Case presentations

#### Case 1

A 45-year-old man presented complaining of diarrhoea and blood in stools. He had hypertension and

was using laxatives for the last 3 years. Beginning in the rectum and extending to the hepatic flexure, the length of the colon was examined by colonoscopy and a 6 cm long dark pigmentation of the mucosa with a polypoid tumor in the distal colon were found.

Colonoscopic biopsy specimens were taken from the large intestine, were fixed in formalin and embedded in paraffin. The sections were stained with haematoxylin and eosin (H&E). Histochemistry and autoimmunohistochemistry were also performed.

In the biopsy specimens, numerous pigment granules of varying size were found exclusively in enlarged macrophages predominantly located in the superficial areas of the lamina propria (Figure 1). In sections stained with H-E these pigment granules displayed a yellowish-brown color. With Masson-Fontana stain the pigment showed an intense charcoal dark color. The pigment granules were negative to Melan-A, and HMB-45 stains. The PAS reaction was positive and the pigment did not have iron (negative Pearl's reaction). Biopsies of the tumor showed colorectal adenocarcinoma.

#### Case 2

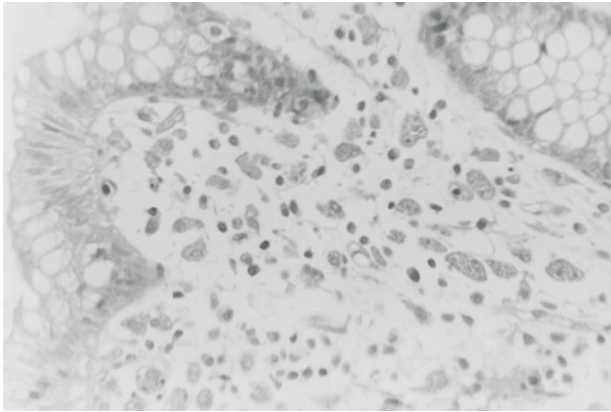
The patient was a 52-year-old man. He usually passed normal stools once a day but had a recent history of constipation, and laxatives had been used for the last 10 months.

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**Figure 1.** Aggregation of macrophages containing pigment in the lamina propria of the colon (H&E X400).

At sigmoidoscopy, pigmentation of the colonic mucosa was found for a length of about 10 cm. A solitary polyp which was observed also in this patient appeared grossly unpigmented.

Biopsies from the large intestine confirmed an accumulation of pigment (Masson-Fontana and PAS positive; iron stain, Melan-A and HMB-45 negative) in macrophages of the lamina propria. Microscopically, the excised polyp was adenoma which, although macroscopically unpigmented, showed accumulation of brown pigment in macrophages within the lamina propria, characteristic of melanosis coli, but with lesser intensity.

## Discussion

Melanosis coli refers to abnormal brown or black pigmentation of the colonic mucosa. It was first described by Billiard in 1825. The term melanosis coli was first used by Virchow in 1857.

Although the pigment does have some properties in common with melanin, it is more closely related to, though not identical, lipofuscin. Because the pigment is not melanin some have used the term pseudomelanosis coli. Melanosis coli remains the best term for this condition because, as Ghadially and Walley have noted, the term melanosis simply describes the dark coloration of the colonic mucosa and does not imply the pigment is melanin [1].

An association between melanosis coli and laxative use was first noted by Bartle et al. in 1928 [2]. Melanosis coli is usually related to chronic laxative use but has also been closely associated with chronic inflammatory bowel disease [3] or colonic neoplasms [4]. High grade microscopic melanosis was signifi-

cantly associated with anthranoid laxative use but not with colorectal adenomas or carcinomas. Low grade microscopic melanosis was found to be significantly associated with colorectal carcinoma but not adenomas. In a study by Nusco et al. [5] a significant association of colorectal adenomas, but not of colorectal carcinoma, with macroscopic melanosis coli was found. There is good reason not considering melanosis coli as a reliable marker of chronic laxative use as only 73.4% of patients with melanosis coli admitted laxative use [5].

The mechanism by which melanosis is established has been fairly well elucidated. In response to various stimuli, damage to the colonic surface epithelial cells occurs because of induction of apoptosis. As a result, there is an increase in the number and size of macrophages in the superficial lamina propria, with phagocytosis of the apoptotic cells and cells fragments. Within these macrophages there is an increase in the density of lysosomes that fuse with and oxidize the sequestered cellular fragments. The residual material forms the lipofuscin-like granules which give to macrophages their pigmented appearance [2].

It is known that the lipofuscin pigment can be present 18 to 24h after laxatives use and gradually disappears over a period of 6-11 months after stopping laxatives [6].

This condition can affect the entire length of the large bowel including the appendix, but has rarely been described elsewhere in the gastrointestinal tract. The cecum and rectum are the most common sites of involvement [7]. The melanosis coli incidence showed an increasing trend with age and was considerably higher in women (9%) than in men (4.5%) [8].

Previous histochemical studies suggested that this pigment has certain similarities with lipofuscin and ceroid and that it may contain, therefore, polymerized glycolipids and glycoproteins. The pigment showed autofluorescence, sudanophilia, acid fastness and positiveness to PAS and Schmorl's reaction, all of which are common to lipofuscin and ceroid, plus an intense argentaffin reaction abolished by bleaching, indicative of a melanin-like substance [9].

Melanosis coli may be a non-specific marker of increased epithelial apoptosis, of which laxatives are only one cause. This is in keeping with an incidence of 59.9% when detected microscopically and with an increased frequency in older people [4]. The incidence of melanosis coli was 3.13% in patients without pathological changes. In those with colorectal adenomas the incidence increased to 8.64% and in those with colorectal carcinomas it was 3.29%. This lower rate was probably caused by incomplete documentation

of melanosis coli with carcinoma. According to Siegers et al. the incidence of melanosis coli was 6.9% for patients with no abnormality seen on endoscopy, 9.8% for the patients with adenomas and 18.6% for patients with colorectal carcinomas [8].

In view of the results of other authors and of our study, there seems to be rather strong association between melanosis coli and colorectal tumors. At the moment, experimental data on carcinogenicity in rodents allow us to assume a carcinogenic risk for melanosis coli.

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