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CASE REPORT

Increased Colonic Fluorodeoxyglucose Uptake in Melanosis Coli—A Case Series of Three Patients

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We report 3 Japanese cases with increased colonic 18-fluorodeoxyglucose (FDG) uptake in association with melanosis coli. Case 1: A 56-year-old woman received 18-FDG positron emission tomography (PET) for comprehensive medical checkup. Case 2: A 79-year-old man received FDG-PET for follow-up evaluation for intestinal cancer. Case 3: A 51-year-old woman received FDG-PET for medical checkup. Each showed increased cecal and/or ascending colonic uptake without any colonic wall changes. Colonoscopy detected melanosis coli where FDG uptake was demonstrably increased. Neither malignancy nor inflammatory response was confirmed. Succeeding follow-ups showed neither malignant nor inflammatory lesions in any of the patients.

Keywords: Fluorodeoxyglucose F 18; Colonoscopy; Anthraquinones

Introduction

Melanosis coli (MC) is a rare disorder induced by regular anthraquinone use, characterized by brown or black pigmentation of the colonic mucosa.[1–3] Microscopic lipofuscin accumulation is thought to play a key role in this phenomenon.[4] MC has been reported to have a prevalence of 1.4%–4.6% and to be associated with several intestinal disorders such as adenomas, hyperplastic polyps, and ileal ulcers.[3,5,6] However, the degree of relationship between MC and these disorders is still unclear. Despite a meta-analysis indicating that MC was not associated with an elevated risk of colorectal cancer (CRC),[3] clinical concern remains because of one report suggesting that anthraquinone laxatives are associated with CRC risk.[7]

Fluorodeoxyglucose (18-FDG) positron emission tomography (PET) is useful to visualize malignant and inflammatory lesions in the whole body, including the gastrointestinal tract.[8] This examination is performed on initial diagnosis of cancer and for detection of metastasis; however, 18-FDG-PET can be applied during medical checkups and cancer screening.[9] Incidental increased uptake of 18-FDG at the colon is frequently observed in asymptomatic patients.[10] As neoplasms and inflammatory lesions are leading causes of the incidental colonic 18-FDG uptake, colonoscopy is recommended after visualization of colonic 18-FDG uptake.[11] However, some cases with increased colonic 18-FDG uptake show no malignant or inflammatory lesion. Here, we present 3 cases with incidentally increased colonic FDG uptake, diagnosed as MC by colonoscopy.

Case Reports

Case 1

A 56-year-old Japanese woman electively underwent a comprehensive medical checkup in our hospital at her own expense. She was generally well, with stable vital signs, without acute symptoms. She had chronic constipation and regularly took anthraquinone-containing herbal medicine. Blood tests were within normal limits. 18-FDG-PET revealed increased segmental cecal uptake up to the ascending colon without changes, including colonic wall thickening (Figure 1). Increased uptake was detected in both early and delayed phases (maximum standardized uptake value [SUV], 4.6/6.1 [early/delayed]). Subsequent colonoscopy detected cecal and ascending colonic MC (Figure 2) with intact mucosa in other colonic segments. Histopathology of the ascending colon with hematoxylin and eosin staining detected lipofuscin without inflammatory response (Figure 2). Neither malignant nor inflammatory lesions were found after a 5-year follow-up period.

Abbreviations used in this paper: **CRC, colorectal cancer; FDG, 18-fluorodeoxyglucose; MC, melanosis coli; PET, positron emission tomography; SUV, standardized uptake value.**

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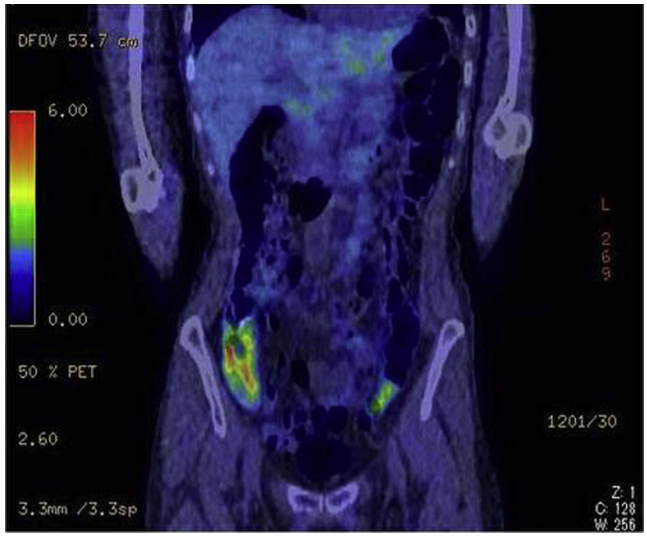

Figure 1. Increased fluorodeoxyglucose uptake in the cecum and the ascending colon in case 1.

Case 2

A 79-year-old Japanese man underwent FDG-PET for intestinal cancer workup. He had mild diabetes mellitus (HbA1c = 6.8%) and took anthraquinone laxatives for constipation. The blood test was within normal values on complete blood count and biochemistry. FDG-PET illustrated increased segmental uptake in the ascending colon on both early and delayed phases (maximum SUV, 4.7/5.9 [early/delayed]) without wall thickening (Figure 3). Colonoscopy revealed MC at the cecum and ascending colon (Figure 4). Histopathology of the ascending colon demonstrated lipofuscin without inflammation (Figure 4). Neither malignant nor inflammatory lesions were detected after a 2-year follow-up period.

Case 3

A 51-year-old Japanese woman with dyslipidemia and chronic constipation had FDG-PET on medical checkup. She was taking sennoside laxatives and statins. She was generally stable, and her blood tests were normal except for hypercholestorolemia. The FDG-PET demonstrated increased uptake at the cecum (maximum SUV, 6.5; Figure 5). MC at the cecum and ascending colon (Figure 5) and a 10-mm adenoma in the sigmoid colon were diagnosed by colonoscopy. No malignant or inflammatory lesions were found on the second year of follow-up. The characteristics of the 3 patients are summarized in Table 1.

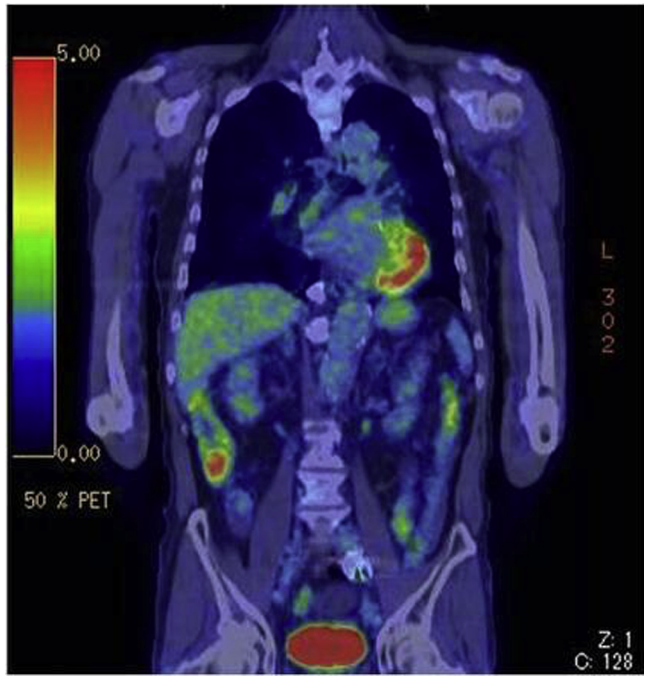

Figure 3. Increased fluorodeoxyglucose uptake in the ascending colon in case 2.

Discussion

To our knowledge, this is the first case series indicating increased 18-FDG uptake at the colon, where MC was macroscopically and histopathologically diagnosed. Previous studies suggested that patients with an SUV max of more than 4.35 on PET have higher likelihood of having advanced colorectal neoplasms[12]; despite this, our cases

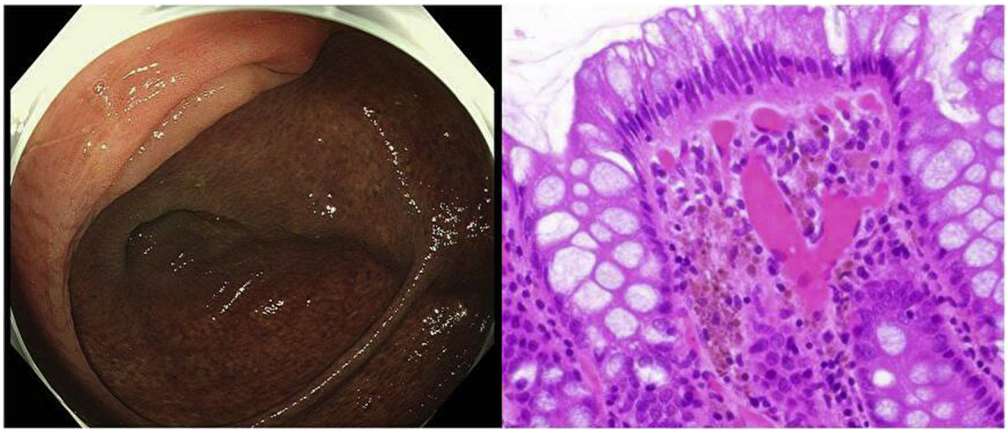

Figure 2. Colonoscopic findings of melanosis coli detected in the cecum and the ascending colon and accumulated lipofuscin pigment in the biopsy sample from the ascending colon in case 1.

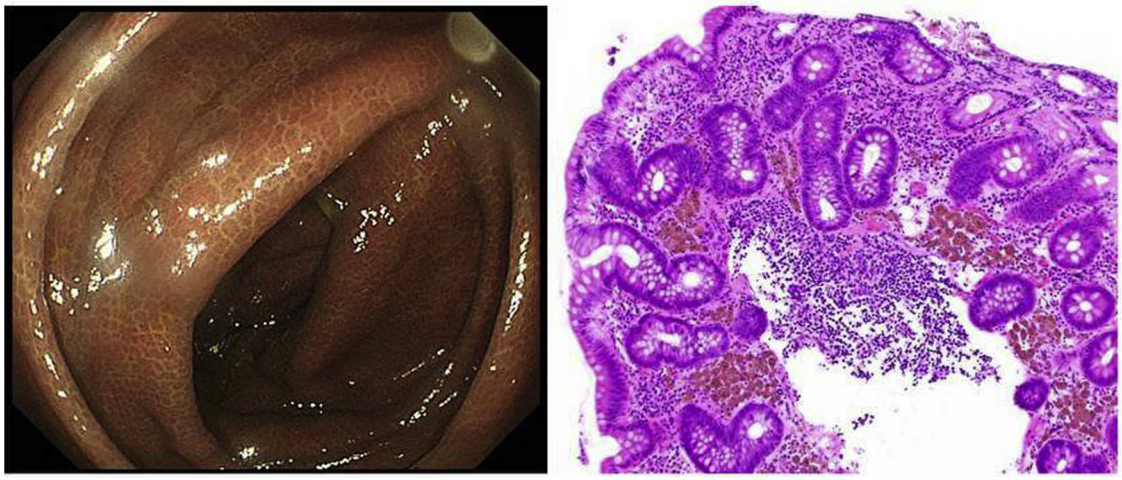

Figure 4. Colonoscopic finding of melanosis coli detected in the cecum and the ascending colon and accumulated lipofuscin pigment in the biopsy sample from the ascending colon in case 2.

with SUV max over 4.35 showed no malignant lesions. Other possible causes of incidental colonic FDG uptake without other findings include colonic contents[13] and constipation.[14] Among our cases, we confirmed that uptake was not altered in either phase in 2 cases. Furthermore, colonic FDG uptake due to constipation is typically concentrated at descending colon,[14] which is not consistent with our cases.

Differential diagnoses of increased 18-FDG uptake include neoplasms and inflammatory lesions.[15] Segmental patterns of uptake, like in this case, were reported to have a higher probability of inflammation.[13] Of note, MC usually does not accompany inflammation, although activated macrophage scavenging colonic epithelial cells have been considered to precipitate evolution of MC.[16] Macrophages do not induce evident inflammatory reactions such as cytokine emission and lymphocyte induction.

It was initially proven that MC was associated with a higher adenoma and hyperplastic polyp detection rate; on the other hand, a worldwide meta-analysis subsequently demonstrated that MC showed similar CRC incidence in subjects without MC.[3] The subjects had no neoplasms in the colon; however, potential for neoplasms at the molecular level might explain increased FDG uptake. Further cases and pathological studies, including on p53, a known marker of cell proliferation,[17] are required to confirm this hypothesis.

In addition, Soyka et al reported that enhanced bowel activity causes increased 18-FDG uptake.[18] Therefore, they recommended against laxatives before FDG-PET. Our patients had been taking anthraquinone laxatives, thus enhancing colonic motility, which may lead to increased FDG uptake.

Lipofuscin, a pigment causing chromatic alteration of the colonic mucosa, could influence 18-FDG uptake. Prior reports suggested that black adrenal adenomas showed increased 18-FDG uptake, even though the lesions were benign.[19] Ishikawa et al indicated that black adrenal adenoma cases with increased FDG uptake showed enhanced glycolytic pathways[20] and that the altered metabolic condition can result in FDG uptake. Metabolic status in MC has not been elucidated, and further research in this field is needed.

In conclusion, 3 cases with MC showed increased colonic 18-FDG uptake and demonstrated spatial correlation between location of MC and increased 18-FDG uptake. Further similar cases and subsequent molecular analysis might

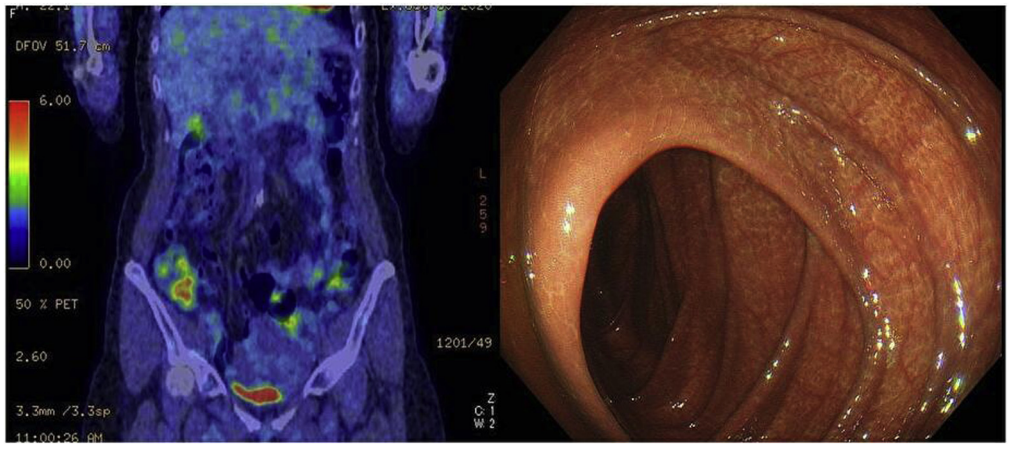

Figure 5. Increased fluorodeoxyglucose uptake at the cecum and colonoscopic findings of melanosis coli detected in the cecum and the ascending colon in case 3.

Table 1. Summary of Characteristics of Three Patients

Case	Case 1	Case 2	Case 3
Age	56 y	79 y	51 y
Sex	Female	Male	Female
Medication	Anthraquinone-containing herbal medicine	Anthraquinone laxative	Sennoside and statin
Indication of FDG-PET	Medical checkup	Follow-up of intestinal cancer	Medical checkup
Location of increased uptake of FDG	Cecum and ascending colon	Ascending colon	Cecum
Location of melanosis coli	Cecum and ascending colon	Cecum and ascending colon	Cecum and ascending colon

elucidate the cause of 18-FDG uptake in the setting of MC. MC may be considered on visualization of colonic 18-FDG uptake in the colon.

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The corresponding author, on behalf of all authors, jointly and severally, certifies that their institution has approved the protocol for any investigation involving humans or animals and that all experimentation was conducted in conformity with ethical and humane principles of research.

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The corresponding author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported.