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Case Report

Descending Colon Cancer Coincident with *Schistosoma japonicum* in an 89-year-old Male

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An 89-year-old male came to the hospital with a complaint of abdominal distension. Abdominal computed tomography showed wall thickening in the descending colon and marked dilatation of the proximal colon, and lower gastrointestinal endoscopy demonstrated a stenosis in the descending colon. Although a biopsy from the stenotic lesion showed calcified eggs of *Schistosoma japonicum* with no malignant findings, we suspected malignant involvement, so we performed a descending colectomy with regional lymph node dissection. Pathological examination revealed a moderately differentiated adenocarcinoma. The colon cancer was diagnosed as pT4bN0M0, Stage IIc. The patient's history as a resident of one of the formerly endemic areas of Japan suggests that he may have carried *S. japonicum* for a long time, and that it may have contributed to carcinogenesis.

Key words: *Schistosoma japonicum*, descending colon cancer, carcinogenesis

Schistosomiasis is a nematode infection that affects more than 200 million people worldwide [1]. In the mid-20th century, Japanese schistosomiasis was endemic in five areas of Japan. Its incidence peaked in 1958 and then declined sharply with the eradication of the intermediate host, the Miyairi (Katayama) mussel [2]. In the International Agency for Research on Cancer (IARC) list of possible carcinogenic targets, *Schistosoma japonicum* (*S. japonicum*) infections are classified as Group 2B because they are suspected to be carcinogenic to humans [3]. We report here a case of descending colon cancer coincident with *S. japonicum*.

Case Presentation

An 89-year-old male came to the hospital with a complaint of abdominal distension. Although the patient had a medical history of congestive heart failure and chronic obstructive pulmonary disease, he was independent and had a good performance status. Blood findings on admission showed mild anemia, renal dysfunction (hemoglobin 10.0 g/dl and creatinine 1.61 mg/dl), and normal liver function. Tumor markers were within normal limits, with a CEA of 4.3 ng/ml and CA19-9 of 32.5 U/ml. Echocardiographic findings demonstrated a left ventricular ejection fraction of 76% with moderate mitral regurgitation. Abdominal computed tomography showed marked wall thickening in the distal part of the descending colon, and proximal colon was dilated (Fig. 1). There were no findings suggestive of lymph node or distant metastasis including liver lesions. Lower gastrointestinal endoscopy showed a circumferential stenosis in the vicinity of the descending colon near the sigmoid-descending (SD) junction (Fig. 2), through which the endoscope could not pass.

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Biopsy of the stenosis revealed a large amount of calcified *S. japonicum* eggs in the mucosa and submucosa, with surrounding fibrosis. Although no malignancy was found on biopsy, we suspected neoplastic involvement in the descending colon stenosis and performed an open descending colectomy after decompression with a transanal ileus tube. Under the laparotomy, neoplastic lesions were found in the site of stenosis of the descending colon, and neoplastic invasion into the small intestine was suspected. Descending colectomy with partial resection of small intestine were performed, along with regional lymph node dissection. The operative time was 3 h and 3 min, and the intraoperative blood loss was 30 g. In the excised tissue, a 4×3 cm circumferential type 2 tumor was found, and the small intestinal mucosa, which was suspected to be tumor-infiltrated, was coarsely structured (Fig. 3). Histopathology revealed moderately differentiated adenocarcinoma with invasion to the mucosa of the small intestine, which had also been resected. There was no metastasis in the dissected lymph nodes, and the resected margins were negative. A large number of *S. japonicum* eggs were found in the walls of the small intestine and colon, mainly in the submucosal tissues (Fig. 4). The diagnosis of descending colon cancer D

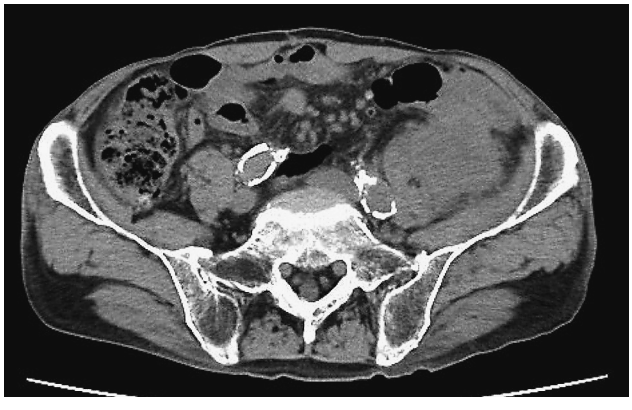

Fig. 1 Abdominal computed tomography finding. There was marked wall thickening in the distal part of the descending colon.

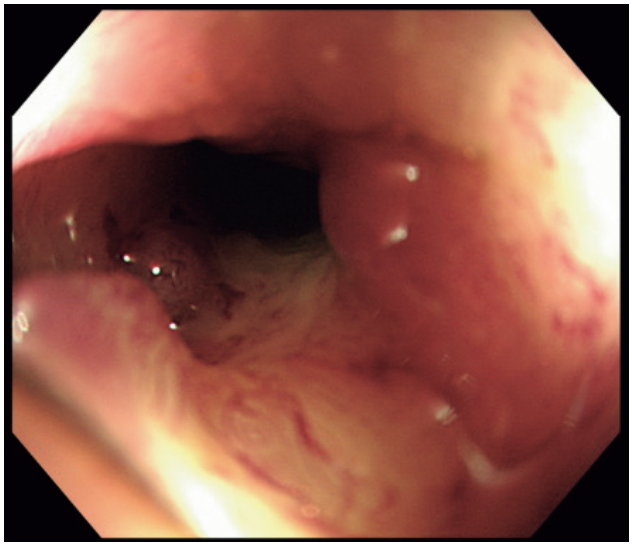

Fig. 2 Lower gastrointestinal endoscopy finding. A circumferential stenosis was found in the vicinity of the descending colon.

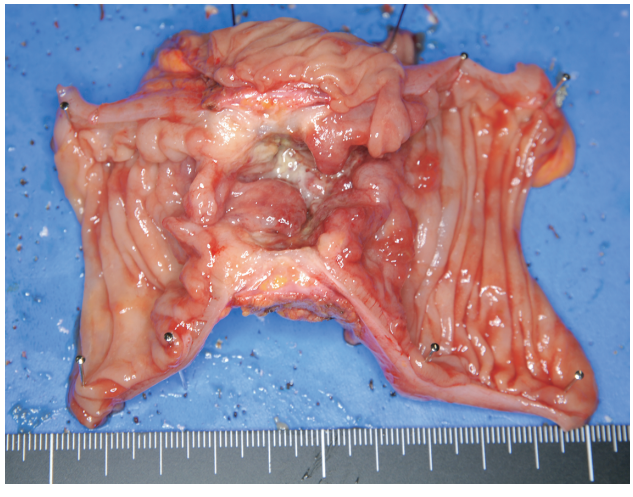

Fig. 3 Specimen extraction. A 4×3 cm circumferential type 2 lesion was found in the descending colon.

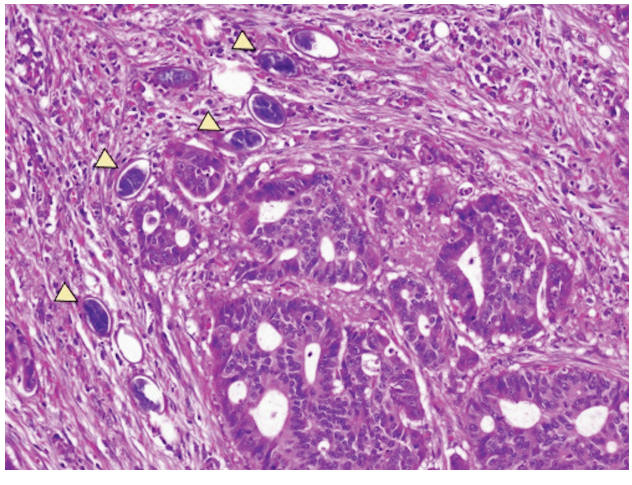

Fig. 4 Histopathological finding. Histological examination revealed moderately differentiated adenocarcinoma with *Schistosoma japonicum* eggs in the submucosal tissue (arrowhead).

pType2 tub2 Ly1b, V1b, Pn1b, PM0, DM0 T4b (SI, small intestine) N0M0 pStage IIc was made based on the Japanese Classification of Colorectal, Appendiceal, and Anal Carcinoma (3rd. edition) [4]. The patient was discharged at 3 months post-operatively with no other complications, although the start of oral intake had been delayed due to impaired intestinal peristalsis, and rehabilitation took time. Six months after surgery, a CT scan showed a local recurrence in the retroperitoneum near the left iliopsoas muscle, and the patient died of primary adenocarcinoma 12 months after surgery.

Discussion

Schistosomiasis is a nematode infection that affects more than 200 million people worldwide. Among five schistosome species, *S. japonicum* is the most pathologically aggressive, mainly because of its high egg production [1]. In the 20th century, Japanese schistosomiasis was endemic in five areas in Japan: the Kofu Basin in Yamanashi Prefecture, the Katayama area in Hiroshima Prefecture, the Chikugo River basin, the Numazu and Mishima areas in Shizuoka Prefecture, and the Tone River basin. Our patient had spent his childhood in the Katayama area in Hiroshima Prefecture. The incidence of Japanese schistosomiasis peaked in 1958 and then declined sharply with the eradication of the intermediate host, the Miyairi (Katayama) mussel [2]. On the other hand, *S. japonicum* is still an important infectious disease worldwide, and reports of colorectal cancer complicated by *S. japonicum* continue to arise from China, Sudan, and Tanzania, where *S. japonicum* is endemic [5-7]. Indeed, chronic infection has been reported to be associated with a risk of colorectal malignancy [8], and the international agency for research on cancer (IARC) has classified *S. japonicum* infection as a Group 2B carcinogen, or possibly carcinogenic to humans [3].

Although the correlation between *S. japonicum* and colorectal carcinogenesis is still unclear, it was reported that p53 positivity is significantly higher (80% vs. 40%) in colorectal cancers associated with *Schistosoma mansoni*, which invades the Nile River basin in Africa, than in uncomplicated cases [9]. It was also shown that a higher proportion of p53 gene mutations was observed in *S. japonicum*-associated rectal carcinomas [10]. Moreover, in basic experiments using mouse peritoneal macrophages, it was demonstrated that stimulation with *S. japonicum* egg antigen causes secretion of TGF-β [11]. Based on these molecular findings, p53 gene abnormalities are important for the progression from late adenoma to carcinoma, and TGF-β signaling is important for the development of metastasis. A recent study showed that *c-MYC* amplification could predict poor prognosis in schistosomiasis-associated colorectal cancer [12]. It has been also suggested that the chronic inflammatory response induced by schistosomiasis may produce genotoxic mediators such as reactive oxygen and nitrogen species and inflammatory cytokines, leading to genomic instability and dysregulation of oncogenes and oncosuppressor genes, and that the accumulation of these molecular disturbances may promote progression to dysplasia and cancer [5]. The mechanism of carcinogenesis caused by *S. japonicum* infection should be further elucidated. In any case, a history of intestinal schistosomiasis is likely to be an independent risk factor for colorectal carcinogenesis. Therefore, patients with a history of intestinal schistosomiasis should undergo regular endoscopic examinations and thorough colorectal cancer screening [13, 14].

A recent report showed that the site of deposition of schistosome eggs was significantly correlated with overall survival but was not an independent prognostic factor. Interestingly, the presence of schistosome eggs at the resection margin did not affect the risk of anastomotic leakage. The authors suggest that in the case of colorectal cancer complicated by *S. japonicum* infection, standard surgical resection is sufficient; there is no evidence that extended surgery is necessary [15].

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